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Megadyne Medical Products Inc.

Clinical Evaluation Report

Megadyne Electrosurgical Generators
SCN073157 Revision A

Ethicon Megadyne Electrosurgical Generator

Megadyne Mega Power Electrosurgical Generator

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Executive summary

The clinical evaluation is based on a comprehensive analysis of available clinical data relevant to the intended purpose of the devices in question: the Ethicon Megadyne® Electrosurgical Generator (new line extension*) and the Megadyne Mega Power® Electrosurgical Generator (existing). Both subject devices are intended as general-purpose electrosurgical generators, designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue, through an accessory electrode during open and laparoscopic surgical procedures. These generators are utilized as part of a system to produce radio frequency (RF) current for cutting and coagulation RF energy, with that system comprised of handpieces / end-effectors, patient return electrodes and other devices and accessories such as foot pedals and power cords. Additionally, this CER demonstrates that Megadyne RF energy generators and systems are a technology that has a long-established record of acceptable safety and performance and remain state of the art. This is demonstrated by the clinical evaluation contained herein and also demonstrated via the fact that the system that comprises the Megadyne generators and electrodes are extensively used in surgeries across the EU and the world.

*The line extension adding a "new" version of the Megadyne Generator will be mainly referred to herein as the "new" generator.

The subject devices conform to the European Council Directive 93/42/EEC (Medical Device Directive (MDD) as amended by 2007/47/EC with respect to the State of the Art for clinical evaluations as informed by the guidance document, MEDDEV 2.7/1 rev 4. per the regulations and are defined as Class IIb medical devices by Annex IX rule 9. The existing Megadyne Mega Power Electrosurgical Generator has been available for 15 years with the initial CE mark on 12 May 2005 and US FDA 510(k) clearance on 24 March 2005. The new subject device, Ethicon Megadyne Electrosurgical Generator and new bipolar footswitch accessory received US FDA 510(k) clearance on 24 March 2020. The new subject device and accessory are pending initial CE Mark. The Mega Power Generator has two released footswitches (1400JJ and 1450J which are compatible with both generators. The new bipolar footswitch accessory (1459J) is only compatible with the new subject device at this time.

The body of evidence includes clinical data on the existing Megadyne Mega Power Electrosurgical Generator and will also serve as the equivalent subject device for the new Ethicon Megadyne Electrosurgical Generator, following the literature route of conformity. The equivalence rationale between the existing Megadyne Mega Power Electrosurgical Generator and the new Ethicon Megadyne Electrosurgical Generator is duly justified in regard to clinical, technical, and biological characteristics - technologically the subject devices are 83% identical and 17% sufficiently the same to be rationalized as equivalent with no impact on the clinical safety and performance outcomes.

The Megadyne Mega Power Electrosurgical Generator was selected as the equivalent subject device, drawing on the existing, robust safety and performance data on the established Mega Power generator which also provides clinical evidence for the newly developed Ethicon Megadyne Electrosurgical Generator. The clinical data sources from the existing Mega Power generator include published clinical literature and post-market surveillance (PMS) data. Non-Clinical data sources, including an ex vivo study comparing the new generator performance and function to the existing generator, will capture

the verification and validation data specific to the new Ethicon Megadyne Electrosurgical Generator's function and performance and, thereby also supporting the equivalence analysis provided in Section 5. Also, Post-Market Clinical Follow-up studies (PMCF) will capture additional proactive clinical data for both subject devices.

The systematic scientific literature review covers published clinical data on the equivalent subject device, between 01 January 1986 to 03 September 2019. The literature review includes 3 articles that met the predefined selection criteria on 69 patients/devices when used for on-label clinical uses of the Megadyne Mega Power Electrosurgical Generator. The PMS analysis covers data on the Megadyne Mega Power Electrosurgical Generator for the period from November 2014 through October 2018. Five years' worth of data was stratified into multiple time periods (the current time period being Nov 2018-Oct 2019) to allow for comparison of complaint rates and identification of trends.

Collectively, the systematic literature review and PMS analysis, totaling 15 years of use on the equivalent subject device, provides clinical data that does support the safety and performance of the existing Megadyne Mega Power Electrosurgical Generator and also, through demonstrated equivalence of the subject device, supports the safety and performance of the new Ethicon Megadyne Electrosurgical Generator in accordance with the intended purpose, as stated in the both the Mega Power IFU/Operator's Manual (3000158-01, **Windchill**) and Megadyne Electrosurgical Generator IFU/Owner's Manual (3000315-01, **Windchill**).The volume of clinical literature included for this evaluation is limited but commensurate with the device type and risk level (a generator that is utilized as part of an RF energy system, with RF energy being a clinically mature technology) sufficient to show acceptable safety and performance for the Megadyne generators, in line with the intended purpose of generators, which is to provide controllable, uninterrupted power, via surgeon command, to the respective handpieces/end-effectors and patient return electrodes that can be used with the generator. To supplement the existing clinical evidence analyzed within this clinical evaluation and to provide assurance of additional proactive monitoring of the existing generator and the new line-extension generator, post-market clinical follow-up (PMCF) studies will be initiated to collect additional proactive clinical data on both subject devices. The PMCF data will contribute further toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device.

Further to the safety and performance of the generators, and as noted, generators are part of a system that include electrodes. Often the focus of clinical publications is on the actual handpiece/end-effector and/or the overall surgical outcomes for the subject procedure(s). Since generators are part of a system, proper safety and performance are also measured in the devices that are utilized as part of that system, i.e. handpieces / end-effectors and patient return electrodes. Therefore, the data contained in the CERs that cover the devices utilized with the Megadyne Generators also contributes direct evidence of the safety and performance profile of the generators (Reference Megadyne ACE Blade CER RA-RPT-007, Megadyne Electrodes Electrosurgical Pencils and Suction Coagulators

SCN070741, Megadyne Lietz Loop Electrodes CER RA-RPT-009, Megadyne Patient Return Electrodes Disposable SCN070739, and Megadyne MegaSoft Reusable Patient Return Electrodes and Accessories).

Based on the data appraisal and analysis in this report, all residual risks are deemed acceptable, when weighed against the benefits to the patient based on current knowledge / the State of the Art. Therefore, the clinical evaluation conforms with the relevant ERs (Annex I) of the European Council Directive 93/42/EEC. Due to the risk evaluation of the subject devices, the frequency of updates for the clinical evaluation is determined to be at least every 2 years.

Refer to Appendix 9.1 for supporting documents referenced in the CER.

1. SCOPE

1.1. Objective

The objective of the clinical evaluation process is to establish conformity with the relevant Essential Requirements (ERs) of the European Medical Device Directive (MDD) 93/42/EEC. The planning and execution of the clinical evaluation is conducted in accordance with internal process "Clinical Evaluation Report Procedure" PR-0000277 Rev 20 Franchise Procedure for Evaluation of Clinical Data for CE Marking, **ADAPTIV**.

The clinical evaluation report (CER) is an output of the process to document the collection, appraisal, and analysis of the available clinical data relevant to the subject devices and to determine whether there is sufficient clinical evidence on the safety and performance in accordance to the intended purpose.

In addition, the report documents the benefit-risk profile including side-effects in the intended target patient populations and medical indications by assessing the clinical evidence against the hazards and patient harms as informed by the Risk Management and PMS documentation. The report also demonstrates the acceptability of that profile with basis from the current knowledge/state of the art for energy-based surgical cutting, dissection, and sealing.

1.1.1. Subject Device Overview and Regulatory History

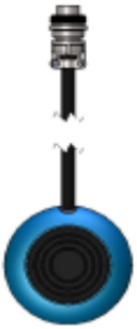
1.1.1.1. Subject Device Overview

According to the Device Master Records (ENG-DMR-015, ENG-DMR-008, **Windchill**) the (new) Ethicon Megadyne Electrosurgical Generator and (existing) Megadyne Mega Power Electrosurgical Generator subject devices have application in open and laparoscopic procedures and are intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode. The Generators have the ability to perform both monopolar cutting and coagulation and bipolar coagulation of tissue in a wide range of surgical applications.

The footswitch accessory (1459J) is new on the market (purchased separately) and is intended to provide a foot control option (in addition to hand control) for bipolar outputs only. Currently, this footswitch is only compatible with the new Ethicon Megadyne Electrosurgical Generator. The existing two footswitches that are compatible with either of the Megadyne Generators are 1400JJ and 1450J and used for monopolar and bipolar functions.

This clinical evaluation of two Megadyne Electrosurgical Generator subject devices and a bipolar footswitch is a post-market CER that includes 3 product codes described in Table 1-1 below.

Table 1-1: Megadyne Electrosurgical Generators Variants Covered within the CER

Variant #	Description	Representative Image*
MEGEN1	**Ethicon Megadyne Electrosurgical Generator (new)**	
1459J	**Round Bipolar Footswitch (new)**	
1000	**Megadyne Mega Power Electrosurgical Generator (existing)**	

The Electrosurgical Generator subject devices for this CER, are a single component of an integrated electrosurgical system that includes a generator, an active electrode and a dispersive/return electrode (monopolar only). The electrosurgical generators are non-sterile, non-patient contacting, multiuse devices that are microprocessor controlled, isolated output, high frequency generators designed for

use in cutting and coagulating of tissue that only operate when the required electrosurgical accessories (forceps, scissors, pencil electrodes etc.) are attached.

The accessory footswitch (foot control option in addition to hand control operation) can be purchased and is intended for use with Bipolar outputs only – not for use with monopolar outputs. The bipolar footswitch activates the bipolar functions of the instrument. This footswitch (1459J) is new in design only. The functionally of this footswitch is the same as the existing Bipolar pedal currently used with the Mega Power Electrosurgical Generator. The only difference between the two footswitches is ergonomic – the new footswitch is round, and the existing footswitch is square shaped. Currently, the new bipolar footswitch is only compatible with the new Ethicon Megadyne Electrosurgical Generator. The monopolar and bipolar footswitches for the existing Megadyne Mega Power Electrosurgical Generator are compatible with both Megadyne Generators.

1.1.1.2. Subject Device Regulatory History

The existing Megadyne Mega Power Electrosurgical Generator received initial US FDA 510(k) Clearance on 24 March 2005 (#K050579) followed by a self-certified CE Mark on 12 May 2005 (#640176).

The newly developed Ethicon Megadyne Electrosurgical Generator and footswitch accessory received FDA 510(k) clearance (#K193145) on 24 March 2020 and is currently pending CE Mark certification (#640176).

Both subject devices are manufactured by:
Megadyne Medical Products, Inc.
11506 South State Street
Draper, Utah 84020
USA

The Authorized Representative Name (ARN) for the Megadyne Electrosurgical Generators is:
Johnson & Johnson Medical GmbH
Robert - Koch - Strasse 1
22851 Norderstedt
Germany

The Notified Body associated with the Megadyne Electrosurgical Generators is:
British Standards Institute (BSI)
FM 639651

1.2. State of the Art Methods and Results

The purpose of the systematic literature review is to evaluate the State of the Art (SOA) surrounding the Target Therapy of energy-based surgical cutting, dissection, and sealing (coagulation), which includes both the existing subject device, the Mega Power Electrosurgical Generator and new subject device, the Ethicon Megadyne Electrosurgical Generator for this clinical evaluation. The review will provide a comprehensive search of the available published literature to evaluate the clinical safety and

effectiveness outcomes of the Target Therapy (monopolar and bipolar electrosurgical devices), in comparison to Alternative Therapies (advanced bipolar electrosurgical devices [also known as electrosurgical vessel sealing systems], ultrasonic surgical devices, laser surgical devices or argon beam devices) for the Target Medical Condition/Surgical Job of Tissue Cutting, Dissection, and Sealing.

The literature search for the SOA was designed to focus on higher-level evidence study designs (e.g. systematic reviews, meta-analyses) when possible where the target therapy is compared to the alternative therapies. These more well-designed studies, OCEBM (Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence) Level 1 and 2, provide the proper evidence to support the benefit-risk acceptability of the target therapy in comparison to the alternatives and thus are deemed for inclusion into the SOA section. When such study designs are not available, the search focuses on lower level comparative study design types as available. The detailed search strategy including key search terms, dates, and databases searched is provided in appendix of this CER.

In brief, a total number of 527 references resulting from the search were screened for inclusion/exclusion. References were included if they contained data regarding the target condition etiology or epidemiology, clinical performance or safety information relevant to the target and alternative therapies, information pertaining to relevant clinical practice guidelines, or information pertaining to the maturity of the target therapy. References were excluded if they did not contain such data or if the data were superseded by a more recent source of high level of evidence. Ultimately, 40 references overall from the search were included for synthesis of the SOA resulting in 487 references excluded for reasons provided in the screening log. An additional 37 references book chapters/clinical guidelines/high level articles were identified ad hoc for inclusion from either the bibliographies of included references or from the Medical Director's knowledge and guidance; resulting in a total of 77 references and unique data sources for State of the Art information. The bibliography of included references is listed in appendix 9.2.2 of this CER.

1.3. Current Clinical Evaluation Route of Conformity

The clinical evaluation route of conformity (ROC) was initially determined during the planning stage (Stage 0) through the Clinical Evaluation Plan (CEP) and continuously evaluated through the execution stage (Stage 1-3).

The ROC is based on relevant scientific literature relating to the safety, performance, design characteristics and intended purpose of the existing (equivalent) subject device, the Mega Power Electrosurgical Generator and a critical evaluation of the results of post-market clinical follow-up (PMCF) studies for both subject devices.

The equivalent subject device, Megadyne Mega Power Electrosurgical Generator, has been in clinical use for 15 years. The newly developed Ethicon Megadyne Electrosurgical Generator was deemed equivalent to the existing subject as detailed in Section 4: EQUIVALENCE.

No premarket clinical trials were conducted for either subject devices of this CER. The Megadyne Mega Power Electrosurgical Generator and the Ethicon Megadyne Electrosurgical Generator are intended to be used as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures. Not conducting pre-market clinical trials was duly justified for the existing equivalent subject device by Megadyne Inc., noting that the rationales presented at the time of launch 15 years ago, were deemed compliant with the evolving interpretations of the MDD via Notified Body audits and reviews.

1.4. Key Safety and Performance Parameters

The clinical evaluation report will analyze the following key safety and performance parameters deriving outcome information based on the following but not limited to; intended use, Instructions for Use (IFU), design requirements and information related to the state-of-the-art and post market surveillance reporting.

The specific measures of safety and performance for the Megadyne Electrosurgical Generators, when used as a system in conjunction with electrosurgical devices (electrodes), include the following:

Safety:

No unanticipated adverse events and no discernable trends in the clinical safety data compared to State of the Art for tissue cutting/dissection and control of bleeding.

- Decreased blood loss
- Better wound healing
- No adverse events

Performance:

Successful tissue cutting (monopolar and bipolar) and coagulation, hemostasis (bipolar).

- Decreased operative time
- Decreased complications

Refer to Section 0 for additional safety and performance details.

2. STATE OF THE ART

2.1. Clinical Problem

2.1.1. Target Surgical Job (Tissue Cutting, Dissection and Coagulation)

Surgery is a technology that involves manual and instrumental interventions for investigating or treating a pathological condition such as a disease, injury, deformity, or defect. Surgical interventions result in physical changes to body tissues and organs, including exposure of anatomical structures beneath the skin, as well as bleeding or release of other bodily fluids from tissues or growths that have been penetrated using surgical instruments (Francis, 2006).

The tasks of cutting, dissection, and control of bleeding are performed in both traditional open operations and laparoscopic, or minimally invasive surgery (MIS) surgical procedures. Prior to the advent of robotic surgery, the term “minimally invasive surgery” was interchangeable with endoscopic surgery. In the current medical climate, however, endoscopic surgery refers to non-robotic minimally invasive surgery, including laparoscopic surgery, and thoracoscopic surgery. The defining feature of minimally invasive surgery is the use of an endoscope to access internal organs through very small and sometimes fewer incisions. Endoscopy involves insertion of a microchip video camera with a fiber optic telescope containing a light source and specially designed long-handled surgical instruments into the target cavity via the gastrointestinal, respiratory or urinary tract. The surgeon performs the procedure by manipulating the endoscope while viewing the anatomical area of interest a video screen or peering downward into the eyepiece of the instrument (Francis, 2006). While surgery encompasses a variety of techniques, the core interventions needed for any operation in which tissues are altered include cutting, dissection, and control of bleeding.

2.1.1.1. Tissue Cutting, Dissection, and Sealing

2.1.1.1.1. Surgical Cutting (Incision)

Cutting is a fundamental technique in both open and laparoscopic surgical procedures that is indispensable to accessing the tissues of interest below the skin. A surgical operation is initiated with an incision, defined as a deliberate cut in the skin that is usually made by a scalpel or similar instrument with a sharp edge. Sharps, also known as cutting, incising, or dissecting instruments, refer to scalpels, knife handles, and blades of various lengths, and include scissors, as well as needles and glass. Surgical incisions allow adequate exposure of the anatomical region or structure of interest, so that the operation can be performed safely and quickly (Francis, 2006).

The number, length, and type of incision(s) used may vary, depending on the specific surgical procedure performed and on whether it is open or laparoscopic. For example, in removal of a gallbladder, a minimum 20 cm incision is required in traditional cholecystectomy, whereas four

incisions of 0.5–1.0 cm, and more recently a single incision of 1.5–2.0 cm is adequate for a laparoscopic procedure.

Critical outcomes used to evaluate the safety and effectiveness of surgical skin incisions include wound infection rates, scar cosmesis, incision time, incisional blood loss, and postoperative wound pain (Aird and Brown, 2012). The published literature reports differences in some of these outcomes between non-energized and energized forms of surgical cutting instruments (Aird and Brown, 2012) (see Comparative Studies section 2.3).

2.1.1.1.2. Surgical Dissection

Surgical dissection refers to the process of cutting apart or separating tissue to isolate the structure(s) of interest from surrounding connective tissue and other structures with a minimal amount of trauma and bleeding. Ideally, this technique should be performed along tissue planes that are relatively avascular (Francis, 2006). The surgical separation of tissues can be achieved with blunt dissection (using fingers, gauze pledget, hand or other blunt instruments), sharp dissection (using a scalpel or scissors), or diathermy (using high-frequency electric current to stimulate heat generation within body tissues) (Francis, 2006).

2.1.1.1.3. Hemostasis and Coagulation

Surgical hemostasis is defined as the termination of bleeding that occurs when blood vessels are transected during surgical cutting and dissection. It is a broad concept that encompasses related processes such as coagulation, physical hemostatic techniques, and chemical hemostatic agents. Hemostasis is critical for preventing blood loss during surgery and hematoma formation postoperatively, and its importance has increased exponentially with the growth of laparoscopic surgeries over the last two decades. Hemostasis must be achieved at the end of a surgical procedure as well as intraoperatively to maintain visibility of the surgical field, particularly during laparoscopic procedures.

A variety of primary and adjunctive hemostatic interventions are available for surgical use (see Table 2-1). Traditional methods of surgical hemostasis include application of a hemostatic clamp to a blood vessel and then ligation with a surgical ligature; suture ligation of a vessel (i.e., under-running a bleeding vessel with a figure-of-8 suture which is tied firmly); diathermy coagulation; and localized pressure for several minutes to allow coagulation to occur naturally (Francis, 2006). However, since the conventional means of tying, suture ligating, and pressure used to control bleeding in open operations are less practical and effective in minimally invasive procedures, surgeons must rely on various other techniques of tissue and vessel coagulation (Lantis et al., 1998). Nearly 20 years ago, it was demonstrated that while energy surgical devices in general can achieve some degree of hemostasis during surgery, certain types of instruments are relatively more effective than others (Lantis et al., 1998). Clinical comparisons have focused on bipolar electrosurgical instruments as well as ultrasonic surgical tools and surgical lasers.

Table 2-1: Pertinent Characteristics of Various Hemostatic Devices and Agents

(Klingler et al., 2006)

Device	Hemostatic Background	Ease of Use	Collecting System Sealing	Major Disadvantage
Sutures, loops	Mechanical	-	Yes	Difficult to learn
Titanium clips	Mechanical	+++	No	May slip off
Polymer clips	Mechanical	++	No	Hook-like tip
Vascular endostapler	Mechanical	+	No	Bulky to use, costs
Electrocautery monopolar	Thermal coagulation & cutting	+++	No	Current leakage,
Electrocautery bipolar	Thermal coagulation	++	No	No cutting
Argon beam	Thermal coagulation	+	No	No dissection, capillary bleeding only
Harmonic scalpel	Tissue vaporization & ultrasonic coagulation	++	No	Vessel < 4mm
Bipolar vessels sealer	Thermal coagulation & sealing	++	No	Very slow, vessels ≤ 6mm
Lasers	Tissue vaporization & thermal coagulation	++	No	Expensive, cell spillage
Fibrin glues	Clotting cascade	++	Yes	Dry surface needed
Oxidized methylcellulose	Clotting cascade & hemostyptic bolster	-	Yes	Suturing skills required
Fibrin coated collagen fleece	Clotting cascade & surface covering	+	Yes	Tricky to apply
Gelatin matrix	Clotting cascade	++	Unknown (no)	Bloody surface needed
Polyethylene glycol	Artificial sealants	++	Yes	Experimental

Ease of use: [+++] = very simple/easy to use, [-] = very difficult/elaborate

Coagulation, or blood clotting (i.e., the transformation of blood to a gel in the solid or semi-solid state) potentially produces hemostasis, or the termination of blood loss from a damaged vessel, followed by vessel repair. Surgical coagulation is defined as “disruption of tissue by physical means to form an amorphous residuum.” Two forms of electrosurgical coagulation can be achieved in blood vessels: (1) obliterative coagulation, which involves direct contact with or electrical arcing to tissue; and (2) coaptive coagulation, which is produced by mechanical apposition of the edges of the vessel with the hemostat or forceps. Obliterative coagulation, which shrinks the vessel wall and occludes the lumen, is appropriate for vessels < 1mm in diameter. In coaptive coagulation, the adventitia of vessel is destroyed, the muscular layer shrinks, and the intima fuses. This technique is preferred for vessels larger than 1mm and up to 2mm diameter.

Key concepts related to hemostasis include cautery, or the coagulating of blood and destruction of tissue with hot iron, by freezing, or with caustic agent; and electrocautery, or cauterization (cutting or hemostasis) achieved by bringing electrically heated metal instrument into contact with target tissue.

Diathermy refers to the generation of heat in tissue by means of electrical current, a process that is distinct from the electron flow which occurs in electrosurgery. Desiccation, or coagulation that produces dehydrated cells, is synonymous with fulguration; and is one of the main types of effects that can be produced with electrosurgery.

2.2. Treatment Options and Interventions

2.2.1. Therapeutic Alternatives/Treatment Options

Certain gastrointestinal, gynecologic, thoracic, urologic, spinal, and other conditions may require a nonsurgical rather than a surgical approach, in which case surgical devices are not utilized. The absence of any intervention in a “watch and see approach” constitutes a conservative treatment. However, this approach is not an alternative to electrosurgery or to other energy-based surgical systems. There are no non-surgical or pharmaceutical options for dissection and coagulation of tissue, since these tasks by definition require physical manipulation of tissues with sharp instruments and/or heat. Therefore, all of the alternative therapies included in this State of the Art assessment involved use of either traditional surgical dissection (i.e., cold /blunt dissection) or an energy-based system such as monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, or ultrasonic surgery.

2.2.1.1. Surgical

2.2.1.1.1. Surgical - Non-energy based options

Dissection, one of the core tasks required for surgery, refers to the separation of various parts of the body in order to expose or study its anatomical structures. Surgical dissection encompasses both blunt dissection, or the meticulous separation of tissues by the fingers or blunt instruments, and sharp dissection, or the separation of tissue with the sharp edge of a knife, scissors, or scalpel. Non-energy based surgical devices for dissection have been used for millennia, but these instruments are usually too bulky and inappropriately designed to be leveraged in modern laparoscopic procedures. However, they may be used in some minimally invasive procedures, depending on the surgeon’s preference and on the availability of manual versus energy-based cutting and hemostatic devices. Additional manual tools such as cautery, forceps, and scissors may be utilized in conjunction with scalpels during surgical dissection.

The “clamp-and-tie” technique for hemostasis was initially standardized in the 19th century, but with several modifications it is still used in current surgical techniques where ligatures, titanium vessel clips or staples are applied. While new tools based on the transmission of electricity and ultrasonic energy have been introduced as hemostatic aids in a variety of surgeries, the traditional “clamp-and-tie” technique remains a state of the art approach for controlling intraoperative and postoperative bleeding (Binsaleh, 2011; Garas et al., 2013). In addition, cautery can be used manually to remove a part of the body or to seal a blood vessel using heat. Topical hemostatic agents provide another medicinal technique for promoting coagulation during surgery. Topicals encompass physical agents that facilitate

hemostasis through a passive process as well as biologically active agents that increase coagulation at the bleeding site (Galanakis et al., 2011). The alternative therapies included in this report did not include topical hemostatic agents.

2.2.1.1.2. Surgical - Energy based options

In contemporary clinical settings energy-based surgical systems are used to facilitate the application of energy in the surgical or endoscopic field where they produce clinical effects such as cutting, coagulation, or desiccation of tissue, or fulguration for the destruction or manipulation of the tissue (Sankaranarayanan et al., 2013; Schwaitzberg, 2012). These systems encompass devices that utilize technologically sophisticated energy sources such as high frequency (radiofrequency) electrical energy and ultrasonic energy for a wide range of procedures, including minimally invasive surgery (MIS). Energy-based modalities used in laparoscopic procedures and other forms of MIS include monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, ultrasonic energy, laser devices, argon beam devices and hybrid devices that combine electrosurgical and ultrasonic energies. These devices sometimes incorporate additional functions such as tissue sealing, temperature feedback regulation, and simultaneous tissue cutting and hemostasis (Grochola and Vonlanthen, 2016). Some general benefits and risks of these energy based modalities are detailed in Table 2-2.

Energy systems such as electrosurgery are used in clinical practice in compliance with Clinical Practice Guidelines such as the Dutch Health Care's multidisciplinary evidence-based guideline for minimally invasive surgery and electrosurgical techniques (la Chapelle et al., 2012), AORN's Recommended Practices for Electrosurgery (AORN, 2012; Spruce and Braswell, 2012), AST Standards of Practice for Use of Electrosurgery (AST, 2012), and Guideline Implementation: Surgical Smoke Safety (Fencl, 2017).

Table 2-2: Benefits/Advantages and Disadvantages/Risks of Energy-based Systems

(Law et al., 2014; Sankaranarayanan et al., 2013; Vilos and Rajakumar, 2013)

Energy System	Benefits/Advantages	Disadvantages	Risks
Monopolar Electrosurgery	Varied tissue effects – e.g., desiccation, vaporization, fulguration, coaptation Parameters are under surgeon's control Minimal smoke production or carbonization Superior dissecting capabilities according to some surgeons Relatively low cost	Higher voltage requirement to achieve desired tissue effect Risk for thermal injury Smoke plume Technique requires extensive knowledge, understanding, and vigilance to avoid inducing unintentional thermal injury	More pronounced lateral thermal spread than vaporization or fulguration Potential stray current injuries due to capacitive coupling, insulation coupling, and direct coupling Laparoscopic electrosurgical injuries: reported rate of 1 to 5 per 1000 operations
Bipolar	Decreased risk of stray current injury than with	Decreased ability to modify operational parameters	Lateral thermal spread

Energy System	Benefits/Advantages	Disadvantages	Risks
Electrosurgery	monopolar electrosurgery Ability to seal larger vessels Lower voltage requirement than monopolar electrosurgery to achieve desired tissue effect More even distribution of thermal effect that might reduce risk of lateral thermal spread Reduced risk of stray current injury from capacitive coupling Shorter dissection time High success rates Better sealing quality Less blood loss Fewer conversion rates More cost effective than monopolar electrosurgery	compared with monopolar electrosurgery Lack of versatility of tissue effects (e.g., no vaporization or fulguration) Requires mechanical cutting blade because bipolar electrodes cannot cut tissue Smoke plume Risk for thermal injury	Electrode adherence to tissues Disengagement of instrument tips may cause tissue trauma or tearing of blood vessels
Advanced Bipolar Electrosurgery	Thermal effects may be minimized with advanced bipolar Seal vessels up to 7 mm in diameter Lowest possible power setting can be used utilized to achieve desired tissue effect Advanced Bipolar electrosurgery systems alert the operator via an audio signal when desired tissue effect has been achieved, minimizing risk for thermal injury Optimal thermal and mechanical properties to seal	Instruments need to be changed to transect the desiccated tissue Smoke plume Risk for thermal injury Requires mechanical cutting blade because bipolar electrodes cannot cut tissue	Lateral thermal spread risk still exists (potentially associated with prolonged device activation) Electrode adherence to tissues Disengagement of instrument tips may cause tissue trauma or tearing of blood vessels

Energy System	Benefits/Advantages	Disadvantages	Risks
	the tissues		
Ultrasonic Surgery	No need for electric current to pass through the tissues Provides hemostasis and cuts tissues Vessel-sealing tissue effects are comparable to those of advanced bipolar electrosurgery Can perform desiccation and coagulation with resultant coaptation at temperatures lower than 100°C Harmonic ACE+7 seals vessels up to 7-mm diameter (beyond 5-mm limit associated with all the other ultrasonic devices) Overall dissection time may be shorter after initial learning curve Less instrument traffic due to the combined vessel-sealing and tissue cutting functionality, less tissue and charring, reduced lateral thermal spread Less smoke plume (Harmonic Scalpel)	More expensive than conventional electrosurgical devices Instrument tip temperatures higher than with advanced bipolar devices Risk for thermal injury Dissection capability of some ultrasonic devices is more limited compared to monopolar scissors or conventional bipolar forceps Slower coagulation compared to electrosurgery; can coagulate only while cutting Changing frequency or impedance of surgical system may be due to blade fatigue, temperature elevation, excessive applied pressure, or improper use Some ultrasonic devices are less efficient than other advanced energy devices in sealing medium to large sized blood vessels Higher average temperatures that are not reliable in sealing vessels larger than 3mm Sealing efficiency is more technique dependent than advanced bipolar instrumentation	Lateral thermal spread risk still exists Plume aerosol produced consisting of tissue, blood, and blood products can adversely affect patients and OR personnel. Heat generated from use can cause tissue burning.
Argon Beam Coagulation	Enhances vessel sealing capabilities of monopolar electrosurgery Argon jet blows away blood and debris from the surgical	Cannot be used for tissue dissection Inappropriate for control of significant bleeding or larger vessels	Insolubility of argon gas results in risk for serious complications (e.g., potentially fatal argon gas embolism, pneumothorax) Risks for complications of

Energy System	Benefits/Advantages	Disadvantages	Risks
	field. Suitable for minor capillary bleeding after dissection Beneficial for procedures involving major blood loss Oncological indications (e.g., advanced tumor resection) Non-oncological indications (endoscopic bleeding control in the gastrointestinal tract and general surgery)	Risk for thermal injury	pseudoaneurysm formation and hemobilia in laparoscopic cholecystectomy May interference with surgical equipment Higher risk for death from complications than other energized surgical methods (except for laser surgery coagulation)
Laser Energy Surgery	Used largely in surgical procedures to treat benign prostatic hyperplasia (BPH) and gynecological, eye, and dermatological condition Reduces the risk of infection, promoting healing	Expensive Requires specialized training and skill Poor sealing capability Higher risk for causing damage away from the operative site Risk for thermal injury	Risks for pregnancy Contra-indications for the use of photosensitizing drug Higher risk for death from complications than other energized surgical methods (except for argon beam coagulation) Laparoscopic cholecystectomy pseudoaneurysm formation and hemobilia in laparoscopic cholecystectomy Risk for hemorrhage

2.2.1.2. Electrosurgery

Overview

Electrosurgery is an umbrella term encompassing multiple surgical modalities that use a high-frequency (radiofrequency) electric current of alternating polarity. More than 80% of surgical procedures performed in the current clinical environment utilize advanced devices such as electrosurgical instruments (Meeuwsen et al., 2017).

Electrosurgical instruments are precisely crafted to allow skilled surgeons to perform a variety of techniques during surgical procedures that involve tissue grasping, tissue cutting (incision, dissection, resection) and coagulation to achieve hemostasis (sealing of blood vessels). Electrosurgical devices

play a pivotal role in MIS such as laparoscopic procedures, including appendectomy, cholecystectomy, colorectal procedures, and various other gastrointestinal operations, as well as hepatic, gynecologic, thoracic, urologic, and spinal procedures. MIS is performed with the use of various instruments, often custom designed, that have been scaled down in size or in some cases miniaturized for ease of insertion into the surgical field. Electrosurgical instruments are also increasingly used in traditional or open, operations as an alternative to the conventional dissection and hemostatic techniques. The core equipment in electrosurgery, as performed in clinical practice, is an electrosurgical unit (ESU) consisting of a generator and hand piece with one or multiple electrodes. The operator controls the unit with the use of a hand- or foot-controlled pencil or switch (Cordero, 2015). High-frequency electrical current, generated from the flow of electrons, is applied to living tissue in order to perform surgical cutting or to control bleeding (Law et al., 2014).

Of note, electrocautery is technically not a form of electrosurgery, but instead refers to direct current in which electrons flow in one direction without passing through the patient's body (Cordero, 2015). By contrast, electrosurgery uses alternating current that enters the patient's body (see Table 2-3). An overview of key terms used in discussion of electrosurgery are noted in Table 2-4.

Table 2-3 : Comparison of Electrosurgery vs Electrocautery

From: (Taheri et al., 2014)

Electrosurgery	Electrocautery
High frequency alternating current through living tissue	Direct current through a high resistance metallic (alloy) conductor
Manipulation of electrons to generate heat within cells that destroys the tissue	Heated alloy is then applied to the tissue

Table 2-4: Definitions of Key Terminology in Electrosurgery

From: (AORN, 2012)

Terminology	Definition
Active electrode	The electrosurgical unit (ESU) accessory that directs current flow to the surgical site (e.g., pencils, various pencil tips).
Alternate site injury	Patient injury caused by an electrosurgical device that occurs away from the dispersive electrode site.
Bipolar electrosurgery	Electrosurgery in which current flows between two tips of a bipolar forceps that are positioned around tissue to create a surgical effect. Current passes from the active electrode of one tip of the forceps through the patient's desired tissue to the other dispersive electrode tip of the forceps—thus completing the circuit without entering another part of the patient's body.
Capacitance	Ability of an electrical circuit to transfer an electrical charge from one conductor to

Terminology	Definition
	another, even when separated by an insulator.
Capacitive coupling	Transfer of electrical current from the active electrode through intact insulation to adjacent conductive items (e.g., tissue, trocars).
Direct coupling	The contact of an energized active electrode tip with another metal instrument or object within the surgical field.
Dispersive electrode	The accessory that directs electrical current flow from the patient back to the electrosurgical generator—often called the patient plate, return electrode, inactive electrode, or grounding pad.
Electrosurgical accessories	The active electrode with tip(s), dispersive electrode, adapters, and connectors to attach these devices to the electrosurgery generator.
Electrosurgery	The cutting and coagulation of body tissue with a high-frequency (i.e., radio frequency) current.
Generator	The machine that produces radio frequency waves (e.g., ESU, power unit).
Insulation failure	Damage to the insulation of the active electrode that provides an alternate pathway for the current to leave that electrode as it completes the circuit to the dispersive electrode.
Monopolar electrosurgery	Electrosurgery in which only the active electrode is in the surgical wound, and the electrical current is directed through the patient's body, received by the dispersive pad, and transferred back to the generator, completing the monopolar circuit.
Ultrasonic scalpel	A cutting/coagulation device that converts electrical energy into mechanical energy, providing a rapid ultrasonic motion.
Vessel sealing device	Bipolar technology that fuses collagen and elastin in the vessel walls and permanently obliterates the lumen of the vessel.

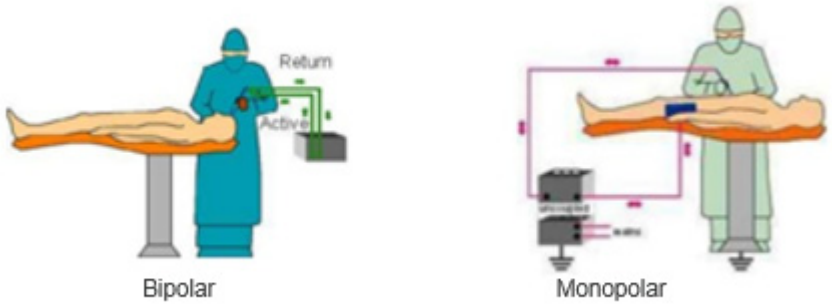
Radiofrequency electrosurgery requires the creation of an electrical circuit that includes two electrodes, the patient, the ESU, and the connecting wire (Munro, 2012). There are two configurations of electrosurgery: monopolar and bipolar. Both modes of electrosurgery revolve around the production of electrical energy followed by the transfer of the electrical currents and voltages from an active (i.e., operative) electrode to a return (i.e., dispersive) electrode (Law et al., 2014; Sarkisian et al., 2015). The electrical energy traveling between two electrodes completes a circuit while heating the tissues. Regardless of their exact placement in relation to the patient, two electrodes are essential for both types of electrosurgery. All forms of radiofrequency electrosurgery are therefore technically bipolar because both electrosurgical modes require two poles, or essentially two electrodes, to complete the electrical circuit through which the electrical current passes (Law et al., 2014).

The two modes of electrosurgery are distinguished by the location and function of the second electrode (Munro, 2012) (See Figure 2-1). Monopolar electrosurgery involves a focused electric current entering the patient at the point of contact of the active electrode. With monopolar devices, only one

electrode, called the “active electrode,” is mounted on the device. The patient’s full body is then placed between this “active electrode” and the large dispersive electrode, which is also connected to the ESU, though situated relatively distant from the target tissue, such as on the thigh or back. The narrow active electrode focuses the current (and therefore the power) at the targeted site, which increases the intracellular temperature. The dispersive electrode serves as the other pole by “processing” the same amount of current (and power) but dispersing it over the totality of the large surface area. The wide dispersion prevents the temperature in the underlying skin from rising, thereby preventing tissue injury (Munro, 2012). In monopolar electrosurgery, therefore, the circuit is completed via the dispersive or return electrode which is located distally from the surgical site (Law et al., 2014).

Earlier monopolar electrosurgical systems were ground referenced, meaning that that the “ground” became an intrinsic part of the circuit, However, contemporary electrosurgical systems use isolated circuits, such that the “ground” is excluded. The term “ground pad” which sometimes appears in the older literature is no longer applicable (Munro, 2012). Bipolar electrosurgery utilizes the electrical current flowing between an active electrode and a return electrode in close proximity within the device (e.g., bipolar forceps), with the circuit completed as the current passes from one electrode to the other (Law et al., 2014). Bipolar instruments have both electrodes mounted on the device, usually located on or near the distal end so that only the tissue located between the two electrodes is included in the circuit (Munro, 2012).

Figure 2-1: Electrode Positions in Monopolar and Bipolar Electrosurgical Circuits



Whereas the entire patient is affected in systems that use monopolar devices, with bipolar instruments only the tissue interposed between the two electrodes is involved in the circuit. These differences underlie the safety and performance features that distinguish the two systems (Munro, 2012). Despite these differences, however, the fundamental principles of electrosurgery apply to the circuit systems used with both the monopolar and bipolar modes. Depending upon its strength and resistance, the electrical current yields variable effects of vaporization, charring, coagulation, desiccation (drying), and fulguration of the target tissue. (Fulguration is a superficial form of coagulation involving destruction and removal of quickly desiccated and coagulated tissue.) The intended effect on the tissue is determined by a number of electrical properties and by factors such as tissue exposure time as well as

the size and shape of the surface of the electrode near to or in contact with the target tissue (Munro, 2012). These key factors are discussed in the next section.

Impact of Alternating Current on Intracellular Activity and Tissues

Cells contain electrically charged particles/ions in the form of atoms and molecules. Cations are positively charged particles whereas anions are negatively charged particles. When direct current (DC) is applied to the cell, the ions move towards oppositely charged electrode, a phenomenon known as the galvanic effect. When an alternating current (AC) is applied to the cell, the ions migrate to the opposite poles, but instead of maintaining a single orientation within the cell they oscillate in conjunction with the different polarity of the output. When the frequency of the AC is low (20-30KHz), the radiofrequency (RF) current depolarizes the muscles and nerves due to an action potential, resulting in muscle fasciculation and pain. This action is called the faradic effect (Munro, 2012).

The depolarization process is initiated via the voltage gated sodium and potassium channels in the neural and muscular cell membranes. However, neural and muscular stimulations do not occur if the current switches rapidly (100KHz-3MHz). When high frequency current is applied across a cell membrane, the pulse duration is so short that the sodium and potassium ionic channel gates do not open, preventing depolarization from occurring. In this case, the electromagnetic energy is converted to mechanical energy since the cations and anions rapidly oscillate within the cellular structure. The frictional forces subsequently convert mechanical energy into thermal, or heat, energy, which then facilitates the rise in temperature of cellular/ tissue structures, producing the desired tissue effects. When either AC or DC flows through a resistor, the resulting effect is the production of heat because the resistance/impedance to the flow of current generates thermal (heat) energy. This effect is explained by Joule's law (Q= (I^2×R×t)) (Munro, 2012).

The three interacting properties of electricity that affect the temperature rise in tissue are current (I), voltage (V), and impedance or resistance (R), measured in amperes.(see **Table 2-5**) .Voltage refers the electrical differential created between two points in a circuit that determines the pressure with which electrons are "pushed" within the circuit, including the parts of the circuit comprising tissue. Voltage is measured in volts. Resistance is measured in ohms and is an indicator of the difficulty a particular substance (e.g., tissue or the composition of the electrical wires) presents to the passage of electrons. The term resistance is typically used for DC whereas the term impedance is generally employed for AC (Munro, 2012).

Table 2-5: Variables in Electrosurgery Associated with Cellular and Tissue Effects

From: (Munro, 2012)

Variable	Definition	Units
Current (I)	Flow of electrons past a point in the circuit/unit time	Amperes (coulombs/second)
Voltage (V)	Difference in electrical potential between two points in the circuit; force required to push a charge along the circuit	Volts (joules/coulomb)
Impedance (resistance) (R)	Degree to which the circuit or a portion of the circuit impedes the flow of electrons	Ohms

Variable	Definition	Units
Power (P)	Work; amount of energy per unit time; Product of V and I	Watts (Joules/second)
Energy	Capacity of a force to do work; cannot be created or destroyed	Joules (watts/second)

The ability of the radiofrequency current to increase cellular and tissue temperature is responsible for the varied tissue effects of electrosurgery. As noted previously, these effects are due to two basic mechanisms: (1) the conversion of electromagnetic energy to mechanical (kinetic) energy, which is subsequently is converted to thermal energy by frictional forces; and (2) resistive heating, which though less significant, signals the flow of current across a resistor to elevate the temperature of that resistor. RF electrosurgical devices achieve hemostasis by the first mechanism.(Munro, 2012; Park and Porteenier, 2012). In addition, an indirect mechanism of tissue heating is conductive heat transfer in which the tissue adjacent to the area being touched is affected by the RF current

The temperature of the human body is normally 37°C, occasionally reaching as high as 40°C during infection, but a cellular temperature of 50°C results in cell death in about 6 minutes. At a local temperature of 60°C cellular death is instantaneous. Heightened temperatures produce two distinct cellular effects -- coagulation and desiccation -- that bear directly on the efficacy and performance of electrosurgical procedures. Between approximately 60°C and 95°C protein denaturation occurs, causing bonds between protein molecules to break and then quickly reform as the local temperature cools. The reformed molecules produce homogenous coagulum through a process called “coagulation” (Munro, 2012). This elevated temperature range is also associated with cellular loss of water that exits through the thermally injured cellular wall, resulting in dehydration or desiccation. The process is akin to boiling the white of an egg until it is dehydrated enough to form a homogenous, coagulum or gelatinous structure, known as “white coagulation This tissue effect is well-suited for occluding blood vessels in order to achieve hemostasis. If the intracellular temperature rises to 100°C or higher, intracellular water boils and becomes steam. The intracellular contents then expand, causing the cell to vaporize with a cloud of steam, ions, and organic matter. At still higher local temperatures of 200°C or more, the organic molecules are degraded through carbonization, a process that gives the tissue a black and/or brown appearance.

From: (Sinha, 2014)

Table 2-6: Tissue Effect and Electrosurgical Generator Output

	Electrosurgical Cutting	Electrosurgical Coagulation	Electrosurgical Fulguration
Tissue temperature	100 C	60 – 95 C	>200 C
Tissue effect	Vaporization	White coagulation	Black coagulation
Best achieved with	Cut output	Cut output	Coag output
Electrode position	Near contact	Contact	None or near contact
Electrode shape	Needle	Wider	Needle

2.2.1.2.1. Categories of Electrosurgical Devices

Electrosurgical instruments utilized in both MIS and traditional open operations fall into three main categories: monopolar, traditional bipolar, and advanced bipolar. In addition, a small number of hybrid devices are currently commercially available that combine two or more distinct types of RF energy, integrate RF energy with ultrasonic energy, offer multifunctional clinical applications, or provide both multiple energy platforms and multifunctional features within the same instrument (Law et al., 2014; Obonna and Mishra, 2014).

RF electrosurgery is now widely used as an effective method of cutting and, to some extent, of achieving hemostasis, at least in smaller blood vessels, during a broad array of surgical procedures (Munro, 2012). In contrast to other modes of electrosurgery, monopolar electrosurgical devices are typically used in clinical settings for achieving hemostasis in vessels smaller than 2mm in diameter (Ferreira, 2015). Bipolar electrosurgical instruments offer some safety advantages when used for the processes of coagulation and desiccation, but in general these devices provide limited benefit for cutting or vaporization (Munro, 2012).

ESUs utilize three different waveforms known as Cut, Coag, and Blend output settings to achieve different tissue effects (Alkatout et al., 2012). The “cut” setting delivers an unmodulated, continuous current, whereas the “Coag” setting delivers a modulated, interrupted current. Per Ohm’s law, at the same power settings, an interrupted waveform has a higher voltage but a lower current than a continuous waveform. Continuous waveform current uses lower-energy electrons than those used in interrupted waveform current, thereby making continuous waveform a safer waveform option for most laparoscopic applications. Various “blend” settings can be adjusted on most ESUs to alter the proportion of time in which the current flow is interrupted (Law et al., 2014). All modern ESUs are designed to provide power in either monopolar or bipolar configurations (Vilos and Rajakumar, 2013).

2.2.1.2.1.1 Monopolar Electrosurgery

Background

Monopolar electrosurgery represents the oldest of the modern energy-based systems and is used for cutting and coagulation (i.e., sealing vessels < 2mm) in a wide range of laparoscopic and open surgical procedures. The monopolar configuration utilizes both an active (i.e., high power density pole) electrode, or probe, and a second dispersive (i.e., low-power density pole) electrode (return pad), which is placed on the patient at a location remote from the surgical site. The relatively large surface area of the dispersive electrode is designed to defocus or disperse the current in order to prevent tissue injury (Munro, 2012).

Active electrodes have multiple designs, depending on their intended uses. Those with a point, hook, narrow tip, or bladed edge are typically utilized to concentrate current and power in order to facilitate tissue vaporization and cutting. When the active electrode has a slightly larger surface area, such as the side of a blade or when it is shaped like a ball or takes the form of a grasper, the same output used for

cutting will produce only local coagulation and desiccation, thereby making it suitable for hemostasis (Munro, 2012).

Dispersive electrodes are usually designed with an adhesive that allows continued contact with the patient while also helping to prevent a clinically significant local thermal effect. However, if there is partial detachment, the current or power density will increase, causing the dispersive electrode to become “active”, potentially triggering a thermal injury, or “burn”. Most ESUs sold in the past 20 years can measure the impedance at the level of the dispersive electrode. This “upgraded ability” also necessitates a specialized dispersive electrode design, which generally takes the form of a “split pad” with two dispersive electrodes in one. Any difference between the measured impedance in the two dispersive electrodes usually signals a partial attachment or detachment, thereby preventing the machine from starting, or, if it already “on”, forces the ESU to shut off automatically (Munro, 2012).

Monopolar electrosurgery can perform diverse functions such as desiccation, vaporization, fulguration (for ablation), and coaptive coagulation. These different tissue effects are achieved by selecting specific parameters such as current power settings, contact versus noncontact mode, current waveform, duration of current activation, electrode size/configuration, and tissue conductivity (Law et al., 2014). Vaporization is employed for cutting, while fulguration and desiccation are utilized for hemostasis of small vessels (<1mm), and coaptive coagulation or sealing is used for small-medium vessels (<2mm) (Law et al., 2014).

In monopolar electrosurgery tissue cutting is achieved through activation of the continuous waveform without tissue contact, which results in a flow of low-energy electrons that causes vaporization of the cells (Law et al., 2014). This technique is associated with minimal smoke production or carbonization. By contrast, activation of the interrupted waveform without tissue contact results in a spray of high-energy electrons to the tissue and fulguration, an effect suitable for hemostasis of small blood vessels (Law et al., 2014). However, in cases involving adipose tissue transection, interrupted waveform is more appropriate due to the high fat content of the tissues (Law et al., 2014). The medium through which the current passes influences the tissue effect. Activation of either continuous or interrupted waveform with tissue contact yields tissue desiccation and protein coagulation, whereas contact with small-medium vessels results in vessel sealing or coaptation (Law et al., 2014).

Advantages and Benefits of Monopolar Electrosurgery

The advantages of monopolar electrosurgery configuration include its wide availability, relatively low cost, and ease in leveraging both the active electrode and return electrode at the surgical site (Cordero, 2015). Monopolar electrosurgery is valued by some surgeons for the continuous and ‘‘mix/blend’’ current used to perform dissection with ease while simultaneously enabling sufficient fulguration in the interrupted mode to achieve hemostasis, as well as a wide range of tissue effects (Jaiswal and Huang, 2017). Furthermore, monopolar grasping forceps can be used for coaptive coagulation (i.e., compression and cauterization) of grasped tissue in desiccated areas with denatured proteins to achieve hemostatic sealing (i.e., a ‘‘collagen weld’’) (Munro, 2012; Vilos and Rajakumar, 2013).

Disadvantages and Risks of Monopolar Electrosurgical Devices

The use of monopolar electrosurgery carries well-documented risks, particularly electrothermal injury due to accidental direct application of the device (Vilos and Rajakumar, 2013). Although tissue desiccation is associated with lower tissue temperatures, it is also linked with a larger amount of lateral thermal spread compared to both vaporization or fulguration. On the other hand, contact monopolar electrosurgery overall results in a tissue effect comparable to that produced using bipolar electrosurgery (Law et al., 2014).

In the monopolar configuration, the electrical current completes a full circuit via an active cable. As noted previously, the current passes from the probe electrode to the target tissue and through the patient's body to the dispersive electrode placed at a different location on the patient's body. Resistance to the electrical current in the target tissue results in a localized rise in temperature to produce either coagulation or cutting, depending upon the parameters of the device set by the operator. The dispersive electrode has a relatively large surface area designed to reduce the current intensity of the high frequency current as it flows back to the patient, thus preventing burns. However, if the current is not safely dissipated by the dispersive electrode, the patient will likely suffer a return electrode burn (Cordero, 2015).

In monopolar electrosurgery, particularly when used as laparoscopically, the risk of stray current injuries is specifically linked with insulation failure, direct coupling, and capacitive coupling (Law et al., 2014).The use of older grounded electrosurgical generators reportedly could trigger "alternate site" burns if the current flow through the patient failed to return to ground via the operating table, but instead was directed through other sites such as the adhesive pads of electrocardiogram leads. This problem has been eliminated with the widespread use of isolated electrosurgical generators, which allow the circuit to be is completed via the patient return electrode pad back to the generator (Law et al., 2014). However, the patient return electrode introduced a new risk of burns at the return electrode if the current flow to the pad were directed through a small area of the patient's skin due to poor pad attachment. This problem was largely resolved by utilizing a return electrode monitoring system via an interrogation circuit that traveled back to the electrosurgical generator, using a split electrode return pad (Law et al., 2014).

In laparoscopic procedures, the overall reported incidence of electrosurgical injuries is 1 to 5 per 1000 operations (0.010%-0.05%). Some of these injuries are linked with a lack of surgical proficiency, but others arise from inadvertent current leakage from the active electrode device via capacitive coupling, insulation failure, and direct coupling (Law et al., 2014). Many of the electrosurgical injuries associated with MIS are not immediately evident since only about 10% of laparoscopic instruments are within the laparoscope field of vision (Law et al., 2014). Additionally, patients may present with nonspecific symptoms rather than an unequivocal cause of the injury, thereby postponing an accurate diagnosis by 4 to 11 days (Law et al., 2014). For instance, a region of thermal coagulation necrosis may be difficult to diagnose histologically when accompanied by prolonged inflammation and secondary infection. In such a case, a thermal injury may be erroneously categorized as a mechanical laceration or trocar-related

injury (Law et al., 2014). Accordingly, some authors have suggested that the incidence of electrosurgical injuries may be higher than currently reported (Law et al., 2014).

In addition to potential harms that may result from leakage of electrical current, electrosurgery generates smoke that is hazardous to both patients and OR personnel. Surgical plume is also formed during procedures that utilize lasers and ultrasonic equipment such as the Harmonic Scalpel, but until recently, little attention was paid to the "'diathermy emissions," or smoke, linked with specifically electrosurgery. Surgical smoke is produced when mechanical tools or heat-producing devices commonly used in dissection and hemostasis interact with tissue, disrupting and vaporizing tissue protein and fat (ULMER 2008). The resulting diathermy plumes are filled with visible and odorous gaseous by-products. Surgical smoke is composed of 95% water or steam and 5% cellular debris in the form of particulate material containing chemicals, blood and tissue particles, viruses, and bacteria (ULMER 2008).

While the limited amount of high quality published data on the potential health hazards of surgical smoke reflect gaps in this area, there is no expert consensus on the precise risks of ill health caused by exposure to surgical smoke (Beswick 2012). Nonetheless, empirical data reveal that electrosurgical smoke contains volatile toxic, carcinogenic and mutagenic compound, which, if inhaled, pose a potential chemical risk that can affect the health of personnel in surgical spaces (ULMER 2008). (Tramontini). Accordingly, clinical practice guidelines for management of electrosurgical smoke call for compliance with safety measures, including proper air exchange, surgical masks, wall suction, and portable smoke evacuation systems in theaters where electrosurgical equipment is used. ULMER 2008. In addition, some of the newly developed electrosurgical instruments on the market have innovative design features that facilitate smoke evacuation during procedures, thereby reducing possible health risks linked with the use of both monopolar and bipolar electrosurgical devices (see Maturity of Technology).

To mitigate the risk of any potential adverse events and hazards, the surgeon must gain adequate knowledge, understanding, skill, and vigilance to avoid unintentional thermal injury by accidental contact of active or heated electrodes with the patient's viscera. Moreover, surgeons who perform monopolar electrosurgical procedures need to be aware of potential direct or capacitive coupling, insulation defects in the instruments or connecting wires, problems with the functionality or positioning of the return electrode, and potential combustion of volatile substances (Law et al., 2014; Vilos and Rajakumar, 2013).

2.2.1.2.1.2 Traditional Bipolar Electrosurgery

Background

Despite the ability of monopolar electrosurgical instruments to desiccate, coagulate, vaporize, cut, and fulgurate tissues, these devices have limitations. In addition to the risk for collateral injury associated with the remote placement of the dispersive electrode, many monopolar RF electrosurgical devices lack precision and control. This limitation hampers the surgical effectiveness of using monopolar RF

electrosurgical devices in electricity-sensitive tissues, complex surgical procedures, and "wet" surgical fields contaminated by blood and other fluids (Park and Porteenier, 2012). Bipolar RF electrosurgical instruments were first developed in the early twentieth century specifically to overcome these shortcomings of the monopolar mode (Park and Porteenier, 2012). As the bipolar modality evolved, the focus turned to designing devices that could reduce the risk of stray current injury associated with monopolar electrosurgery while simultaneously occluding and sealing larger vessels (Law et al., 2014).

In contemporary medicine, traditional bipolar electrosurgery refers to an energy-based surgical technology indicated especially for hemostasis and coagulation, including larger vessel sealing, that is designed to decrease complications from stray current risk of stray current in in various operations. In contrast to the monopolar mode with one wire connecting the ESU and the dispersive electrode and another linking the ESU to the "active" electrode, in the bipolar configuration both electrodes are contained in one cable that joins the generator to the bipolar instrument. In the bipolar mode, the only part of the patient involved in the circuit is the tissue interposed between the two electrodes. The bipolar configuration prevents complications associated with current diversion and provides more accurate measurements of local tissue parameters such as temperature and impedance (Munro, 2012).

Advantages and Benefits of Traditional Bipolar Electrosurgical Devices

Bipolar devices are designed primarily in configurations of forceps and clamps. In both cases, the circuit allows electrons to travel from the ESU to the active electrode, through the grasped tissues to the return electrode, and then back to the ESU (Vilos and Rajakumar, 2013). A grasper provides an appropriate design for bipolar electrosurgical devices since one electrode can be positioned in each jaw. Electrical current travels from one jaw of a grasper (the equivalent of the active electrode) to the other jaw (the equivalent of the return pad electrode. This design is well-suited for facilitating the flow of electrical current through only the targeted (i.e. ,"grasped) tissue area, thereby eliminating the potential of unintended stray current circuits through the patient if a return pad electrode were attached to the patient (Law et al., 2014) (Park and Porteenier, 2012). Consequently, only the target tissues and tissues in the immediate surrounding area are affected by the heat produced from the flow of electrons (Vilos and Rajakumar, 2013) (Law et al., 2014). The risks of burns are reduced because the leakage currents are smaller and produce a more evenly distributed area of thermal spread (Law et al., 2014). An additional advantage of this design is that the desired tissue effect can be achieved with a decreased amount of voltage (Law et al., 2014) (Park and Porteenier, 2012). The two electrodes embedded in the grasper have high density power and are positioned across from one another (Law et al., 2014; Vilos and Rajakumar, 2013). Current traveling through tissue between the instrument jaws will therefore be desiccated in a manner similar to that occurring in "closed circuit" (i.e., with the active electrode in direct contact with the tissues) (Law et al., 2014).

Bipolar electrosurgical devices facilitate tissue sealing and hemostasis by two main mechanisms: (1) compression of tissue and (2) local delivery of RF energy to produce cellular and tissue heating. The direct compression of a bleeding vessel obstructs the continued flow of blood, resulting in the development of a proximal thrombus and eliminating "heat sink" (e.g. where the ongoing flow of blood

cools the tissues and interferes with coagulation) (Park and Porteenier, 2012). If compression of the tissue is excessive or inadequate, electrical bypass may occur, leading to ineffective sealing of the target tissue. Once compression has been achieved, the delivery of RF energy to a target vessel generates heat and rearranges the protein matrix of the vascular wall. These changes result in the formation of a hemostatic seal. The presence of water and ions within the tissue creates ionic oscillation which in turn triggers the conversion of RF energy into intracellular heat. Depending upon the degree to which the temperature of the tissue is increased, different surgical effects such as coagulation, desiccation, and vaporization may be achieved (Park and Porteenier, 2012).

However, bipolar electrosurgical devices can affect only a relatively small amount of tissue at a time, limiting its performance and effectiveness in rapid cutting and dissection of tissue. Bipolar instruments were designed specifically to disperse energy over a larger electrode surface area than can be achieved using monopolar instruments. These devices were initially intended to produce coagulation and provide vessel sealing in intricate surgical fields. As such, they were not intended to produce substantial tissue vaporization, which is needed for effective tissue cutting (Park and Porteenier, 2012). Electrosurgical cutting requires sufficient energy delivery to increase the intracellular temperature to 100°C or more to rapidly allow thermal energy to impact the cell wall, resulting in cellular vaporization. Vaporization is achieved with focused delivery of RF energy using electrodes such as a blade or needle tip that have a very small surface area (Park and Porteenier, 2012).

Total destruction of tissue is undesirable when attempting to achieve electrosurgical coagulation or vessel sealing while simultaneously providing at least basic cutting abilities. Most currently available, proprietary bipolar ESUs are designed to deliver only enough energy to elevate the target tissue temperature above the threshold for protein bond to degradation (around 60°C). The electrosurgical energy is delivered in an interrupted fashion (with the ESU rapidly cycling on and off) to promote tissue cooling and to decrease lateral thermal spread (Park and Porteenier, 2012).

Compared with the monopolar mode, bipolar technology uses a lower voltage and less current to achieve the desired effect (Law et al., 2014). Since the electrodes on bipolar devices are placed in close proximity to each other, tissue impedance is relatively low. This essentially eliminates the possibility of alternate site burns as well as the likelihood of direct and capacitive coupling (Vilos and Rajakumar, 2013). There is no risk of stray current injury from capacitive coupling in bipolar electrosurgery because the bidirectional flow of current in the instrument does not induce capacitive current (Law et al., 2014). Furthermore, since no dispersive electrode is used, the electrical interference from pacemakers or other devices (e.g., ECG, EEG) connected to the patient is less than occurs when using monopolar electrosurgical instruments (Law et al., 2014). Since electrosurgery utilizes alternating current, the active and return electrodes rapidly alternate, yielding a more even distribution of a thermal effect (Law et al., 2014). Also, there no threat of hyponatremia during resectoscopic surgery because bipolar technology is used with a conductive irrigant solution such as saline (Vilos and Rajakumar, 2013).

Disadvantages and Risks of Standard Bipolar Electrosurgical Devices

Despite the overall advances of bipolar electrosurgery, this mode is associated with several disadvantages. Chief among them is the surgeon's decreased ability to change operational parameters, which he can do when using monopolar electrosurgery (Law et al., 2014). Although bipolar electrosurgical devices allow the electrical current to be delivered only in a "closed circuit," the tissue effects are limited due to the continuous electrical waveform, which is combined with relatively large electrodes that permit optimal contact with the tissues (Law et al., 2014). As a result, standard bipolar electrosurgery is unable to achieve tissue vaporization and fulguration (Law et al., 2014).

Bipolar electrosurgical devices do not totally eliminate the risk of stray current injury from insulation failure (with or without direct coupling to other instruments) (Law et al., 2014). The use of reusable bipolar instruments is associated with a risk of adverse events due to stray current injury from insulation failure (Alkatout et al., 2012). In addition, prolonged activation of the electrode can generate substantial heat, which is absorbed by the metal electrode head, potentially causing injury to other tissues upon contact (Vilos and Rajakumar, 2013).

In monopolar electrosurgery the heat energy in the pure cut mode, which is commonly used, is so intense that it causes cells to vaporize. But in conventional bipolar electrosurgery, the blended cut rather than "pure cut" function is applied, which allows simultaneous cutting and coagulation. The term "blended" refers to a blend of surgical effects on the target tissue rather than to a mixing of electrical currents. However, traditional bipolar devices are inefficient for cutting tissue because only a small quantity of tissue can be cut at a time.

The blended cut waveform is characterized by the slow dehydration of cellular fluid and protein, with cooling periods slowing down the action to a dehydrating crawl. This action stops the bleeding precisely when the cuts are being made. The surgeon must adjust the blend to produce different degrees of hemostasis. This waveform is acceptable for sealing off small bleeding vessels when cutting through soft tissue. It is also suitable for resecting tissue masses and decreasing and recontouring redundant tissue using continuous cutting. Additionally, it allows the surgeon to minimize bleeding and work in a clear operating field.

Unlike monopolar electrosurgery, traditional bipolar electrosurgery performs poorly in achieving tissue coaptation. The instrument tips of bipolar electrosurgical devices may disengage, resulting in tissue trauma or tearing of blood vessels that can lead to charring and subsequent poor performance in achieving tissue coaptation (Law et al., 2014). Disconnection of the instrument tips can be prevented by a pulsatile activation of energy and by releasing the tissue right before current flow is terminated (Law et al., 2014). (These thermal effects are minimized with the use of advanced bipolar electrosurgical devices.)

As noted previously, the main disadvantage of bipolar electrosurgery compared to monopolar electrosurgery is that bipolar electrodes cannot efficiently cut tissue (Vilos and Rajakumar, 2013). The main goal of bipolar electrosurgery is not to achieve cutting or dissection, even though this modality can be utilized for this purpose. Bipolar electrosurgical devices are capable of using a continuous waveform associated with the "cut" feature but cutting is relatively inefficient because only a small

amount of tissue can be targeted at a time. Older models of bipolar devices may require changing instruments to cut the desiccated tissue, which in turn extends the time of the procedure. Furthermore, vaporization produced by bipolar electrosurgical devices is cumbersome and unproductive. Nonetheless, bipolar electrosurgical devices signal an important advancement because of their main benefit: vessel sealing ability. Advanced bipolar devices, discussed in the next section, were designed to overcome the obstacle of limited cutting capacity in an efficient vessel sealing device (Vilos and Rajakumar, 2013).

2.2.1.2.1.3 Advanced Energy Surgical Devices

Overview

"Advanced Energy Surgical Devices" comprise a relatively new class of energized surgical instruments that utilize different forms of energy, such as advanced bipolar (e.g. LigaSure™ Small Jaw, Medtronic, Covidien; Enseal, Ethicon) and ultrasound (e.g. Harmonic Focus; Ethicon, Johnson and Johnson), as well as hybrid devices that integrate these two technologies (e.g. Thunderbeat by Olympus, Japan) (Materazzi et al., 2017).

Background

Traditional ESUs were not designed to deliver pulsed outputs to decrease lateral thermal spread during electrosurgery and therefore did not require feedback control systems for impedance or temperature. This limitation prevented operators from controlling the delivery of RF energy to target tissues (Park and Porteenier, 2012). Instead, RF energy delivery was ineffective, forcing the surgeon to use manual operations based on visual cues (such as tissue color changes, smoke production, etc.). Inadequacies in the design of the bipolar hand piece with both jaws active worsened problems with this type of device. In some cases, energy was transmitted from both jaws to a target vessel from the outside in, which desiccated the superficial tissues and visibly changed their color before the core tissues were sufficiently denaturated to produce hemostasis. Furthermore, the intense application of energy to a target vessel increased the impedance (electrical resistance) due to desiccation, allowing the electrical current to preferentially follow the path of least resistance. The movement of current through less resistive, surrounding tissues produces the "mushroom effect" where the risk of collateral damage extends beyond the lateral thermal spread. To compensate for this potential problem, operators were forced to rely on estimation rather than quantitative assessments of the correct timing for terminating energy delivery (Park and Porteenier, 2012).

Advantages and Benefits of Advanced Bipolar Electrosurgical Devices

The last few years have seen the development of a new generation of bipolar devices, known in the industry as "advanced bipolar electrosurgical devices" that are designed primarily to improve homeostasis by providing enhanced coagulation for vessel sealing. Accordingly, modern ESUs and proprietary advanced bipolar electrosurgical devices are sometimes referred to as vessel sealing

systems (VSS) or electrothermal bipolar vessel sealers (EBVS) in the published literature. Some of these devices have received FDA approval to seal blood vessels up to 7 mm in diameter (Law et al., 2014).

Advanced electrosurgical systems feature innovative electrosurgical generators paired with various ligating-cutting instruments. These devices have overcome limitations surrounding the proper amount of energy delivery by incorporating sophisticated microprocessors and feedback systems to monitor and provide continuous feedback about tissue impedance (resistance) and/or temperature at the treatment site. The computer-controlled tissue feedback response system installed in proprietary electrosurgery generator units allows delivery of either pulsed or continuous electrical output with constant voltage by moderating the output current. Because of the nearly instantaneous response to incremental changes in tissue resistance, the total energy delivery using these newer devices is substantially less than with traditional bipolar systems (Brill, 2011; Law et al., 2014; Obonna and Mishra, 2014).

The feedback mechanisms of these “smart generators” automatically adjust the delivery of RF electrical energy in real time, thereby ensuring adequate tissue sealing while minimizing collateral tissue damage (Park and Porteenier, 2012). The electrosurgical energy is delivered in an interrupted fashion (with the ESU rapidly cycling “on and off) to promote tissue cooling and decrease lateral thermal spread (Park and Porteenier, 2012).Audible signals are relayed to the operator to indicate when adequate coagulation has been achieved, thereby facilitating consistent vessel sealing (Law et al., 2014). Additionally, the potential for collateral tissue injury is reduced, and relatively less smoke and carbonization develop during the procedure. These features combined help to ensure that most currently available proprietary bipolar ESUs deliver only enough energy to elevate the target tissue temperature above the threshold for protein bond degradation (around 60°C).

With the growing demand for multi-functional surgical devices in MIS, newer versions of bipolar devices on the market typically incorporate proprietary modifications to deliver sufficient energy to safely seal bleeding vessels and also cut target tissues without compromising patient safety and effective hemostasis (Park and Porteenier, 2012). *S*ome advanced bipolar devices are equipped with innovative components such as a mechanical cutting blade (built into the center of the jaw). Other instruments have specialized jaw designs to maximize ESU energy delivery for bipolar vessel sealing and electrosurgical cutting simultaneously and/or sequentially (Park and Porteenier, 2012; Vilos and Rajakumar, 2013).The addition of a blade into certain contemporary bipolar devices at the electrode site allows nearly virtually bloodless dissection after excellent tissue desiccation without changing instruments. This feature saves time by decreasing “instrument traffic” (Law et al., 2014; Vilos and Rajakumar, 2013). Other novel designs and additions that minimize instrument exchanges to reduce surgery time include a dual action jaw that supports mechanical tissue dissection, bipolar instruments with built-in monopolar electrosurgical dissection tips, and laparoscopic bipolar devices capable of grasping and manipulating intra-abdominal organs with more stability and less tissue trauma (Park and Porteenier, 2012).

Advanced bipolar instruments can achieve consistent vessel sealing within seconds at seal bursting pressures significantly above physiologic blood pressure levels (Park and Porteenier, 2012). By alerting the surgeon when the desired tissue effect has been achieved, the audio signaling system helps to mitigate against potential device-related injuries. The alert systems have been credited with minimizing charring (and grasper sticking during release) and lateral thermal spread that may be associated with prolonged device activation (Law et al., 2014). One of the defining features of state-of-the-art advanced bipolar electrosurgical devices is impedance monitoring with grasper designs that optimize mechanical pressure delivery to the vascular pedicle. This configuration optimizes the vessel-sealing capabilities of advanced bipolar electrosurgical devices.

In summary, the major advantages of advanced bipolar electrosurgical devices, or EBVS, include diminished thermal injuries, decreased thermal spread, reduced tissue necrosis, visual control of sealing (translucent seal of the vessel walls), and sealing of vessels up to 7 mm in diameter (FDA cleared), diminished charring, and an absence of foreign material left behind post-procedure (Entezari et al., 2007). Though controversial, some evidence suggests that the burst strength of EBVS is comparable to that of the clip (Entezari et al., 2007).

There are three innovative bipolar platforms currently on the market that utilize low constant voltage and impedance feedback in conjunction with paired ligating– cutting devices: LigaSure Vessel Sealing Device (Covidien, Boulder, CO, USA); EnSeal Laparoscopic Vessel Fusion System (Ethicon Endo-Surgery, Inc, Cincinnati, OH, USA); and Plasmakinetics Cutting Forceps (Gyrus ACMI, a division of Olympus Corporation, Southborough, MA, USA) (Brill, 2011). While LigaSure remains the premier advanced bipolar electrosurgical device used in clinical practice, all of these devices integrate optimal thermal and mechanical capabilities that improve tissue sealing for hemostasis relative to conventional monopolar and bipolar electrosurgical instruments.

Disadvantages and Risks of Advanced Bipolar Electrosurgical Devices

The major disadvantages of EBVS include the high cost as well as the firing time 3 to 6 seconds per cycle which is reportedly less effective than clips and which results in more thermal spreading than clips (Entezari et al., 2007). In addition, EBVS is associated with poor grasping, in contrast to Harmonic forceps, and requires more time to achieve vessel occlusion (Entezari et al., 2007).

2.2.1.2.1.4 Ultrasonic Energy Devices

Background

Ultrasonic shears or scissors utilize sound waves characterized by vibrations with a high frequency greater than 20,000 Hz, falling beyond the audible spectrum of the human ear. These devices are often referred to by the generic name (i.e., proprietary eponym) of Harmonic Scalpel, the leading trademarked product among ultrasonic energy shears and scissors. The Harmonic Scalpel delivers a form of energy that simultaneously divides and coagulates tissue using a titanium blade vibrating at 55,000 Hz while preventing bleeding. The resulting temperature (ranging from 50 to 100°C) creates

denatured protein coagulum (Binsaleh, 2011). This device differs from electrosurgical tools by not requiring conduction through tissues, but it does demand contact with tissues (Baggish, 2012). In MIS, ultrasonic energy is used in the operation of surgical devices designed mainly to provide vessel sealing. Ultrasonic devices are based only on mechanical action without passage of any current affecting the patient, thereby decreasing the risk of nerve damage.

Advantages and Benefits of Ultrasonic Shears

Modern ultrasonic technology reportedly allows for more uniform hemostasis as well as increased functionality and improved efficiency when compared to other energized surgical instruments during procedures (see Table 2-7). Ultrasonic surgical devices generate physiologic burst pressure for sealing blood vessels that is comparable to the burst pressure used in earlier versions of surgical clips or ligatures. Ultrasonic energy systems are associated with minimal lateral thermal damage and minimal smoke (mist or vapor) (Broughton et al., 2013). The Ethicon Harmonic Scalpel and related devices in this product family are multifunctional ultrasonic devices used to perform coagulation and transection of tissue, vessel sealing, and fluid evacuation.

Clinical evidence shows that the Harmonic Scalpel seals vessels ≤ 5mm with decreased operating time and intraoperative blood loss than observed with other energy surgical devices. The Harmonic ACE+7, another product in this line, has received FDA clearance for sealing of vessels up to 7mm. The benefits of Harmonic Scalpel instruments include minimal heat production, less charring and plume, and less thermal injury to surrounding tissues compared with bipolar energy devices (Alkatout et al., 2012; Entezari et al., 2007). Additional reported advantages of these devices include less tissue necrosis, less instrument traffic (required to perform coagulating and cutting), absence of electrical current and therefore no electrical current passage to the patient, and no foreign material left behind after the procedure (Entezari et al., 2007). Harmonic Scalpel shearing instruments allow for a tension free application and in some studies have demonstrated better healing compared with electrosurgery and lasers for certain applications, as well as improved visualization (Alkatout et al., 2012).

Some evidence demonstrates that ultrasonic shears, particularly Harmonic Scalpel devices, are more effective than other advanced energized surgical tools for cutting through thicker tissue, generating safer as well as less smoke, and potentially offering greater precision. Furthermore, lower rates of tissue damage and wound complications have been reported for ultrasonic surgical energy when compared with electrocautery (standard electrosurgery) (Sinha, 2014). In kidney surgical procedures, ultrasonic shears are advantageous for tumor excision without vascular occlusion, thereby reducing the possibility of renal ischemic damage (Binsaleh, 2011).

From: (Bittner et al., 2012)

Table 2-7: Differences Between Electrosurgical Devices and Ultrasonic Shears

Category	Electrosurgery	Ultrasonic Shears
Grounding electrode	Yes	No
Smoke generation	Yes	No

Category	Electrosurgery	Ultrasonic Shears
Electrocardiogram, pacemaker interference	Yes	No
Current travels through patient	Yes	No
Heat generation	Constant	Time dependent
Thermal spread	Moderate	Minimal
Cost	Low/intermediate	Intermediate/High
Complications	Current concentration Direct coupling Capacitive coupling Tissue sticking	Thermal injury

Disadvantages and Risks of Ultrasonic Shears

The main disadvantages of the Harmonic Scalpel include the high cost, the FDA cleared maximum vessel diameter 3 mm, a temperature of 80–100°C required to achieve sealing in vessels with a 2–3 mm diameter (Entezari et al., 2007), and operational limitations when performing coagulation (Sinha, 2014). The Harmonic Scalpel is associated with more thermal spreading than clips (Entezari et al., 2007). The friction produced by ultrasonic energy devices generates heat, rendering these instruments hot enough to cause unintended tissue burning. The burns can be caused by tissue inadvertently touching the hot tip or by heat delivered from the surgical site via thermal conduction (Baggish, 2012). Although the Harmonic Scalpel can achieve effective coagulation, it cannot be maneuvered as easily as conventional electrosurgical devices, such that it takes longer to cut and coagulate tissue (Sinha, 2014). Unlike electrosurgical devices that can be used to coagulate bleeding tissue at any time during the procedure, the Harmonic Scalpel can coagulate only as it cuts (Sinha, 2014).

Surgical risks associated with use of the Harmonic Scalpel include the formation of aerosolized fatty droplets from target tissue, which can interfere with visualization through a laparoscope (Alkatout et al., 2012). According to some published reports, ultrasonic dissectors produce less surgical plume than do other energized surgical technologies during laparoscopic procedures. However, ultrasonic shears still release particles from the friction of the blades and tissue attached to the laparoscope, thus generating a significant amount of vapor or spray during use (Messenger et al., 2017).

Risks associated with this surgical vaporized plume include compromised visualization of the operative field, which may require the surgeon to remove obstructing particles, including aerosolized fatty droplets, from target tissue (Alkatout et al., 2012; Devassy et al., 2015). Plume aerosol produced by ultrasonic shears typically consists of tissue, blood, and blood products and can be identified up to 40 cm from the point of production (Devassy et al., 2015). In one study, compared with surgical plume produced from electrocautery, the aerosolized plume associated with an ultrasonic scalpel contained large quantities of cellular debris (> 1 x 107 particles/mL), but about 25% of the amount of particle concentration (Devassy et al., 2015).

In kidney surgical procedures, the risks of ultrasonic shears include tissue charring, which causes tissue to adhere to the device, creating an inexact line of parenchymal incision with poor visualization of the tumor bed. Additionally, some, though not necessarily all, ultrasonic energy surgical devices are inadequate when used as the exclusive hemostatic agent for controlling major renal parenchymal bleeding (Binsaleh, 2011).

2.2.1.2.1.5 Argon Beam Tissue Coagulators

Background

Argon beam tissue coagulators, also known as argon gas coagulation units, argon beam coagulation systems, and argon-enhanced coagulation electrosurgical units, are monopolar electrocautery instruments designed to enhance coagulation for vessel sealing. Argon-enhanced monopolar ESU's contain a system for delivery of monopolar current through a flow of ionized argon gas. The argon beam coagulator conducts a RF current to the tissue along a jet of inert, noncombustible argon gas. Argon gas has a lower ionization potential than air and therefore directs the flow of the current. It may also blow away blood and other liquids on the tissue surface or the surgical field, enhancing visualization of operative area.

The electrosurgical current delivered via a monopolar device forms an ionized channel, or arc, within an argon gas stream that flows between the active electrode and the tissue surface. In argon coagulation, there is no contact of the active electrode with the tissue, and the distance between the surgical instrument and the tissue in open surgery is up to about 5 mm, and in endoscopic surgery up to about 3 mm. The thermal effect occurs at the time when a spark jumps from the active electrode tip to the tissue. The length of the plasma arc between the probe tip and the tissue depends on the selected power, resistance of the target tissue, and argon flow rate. The distance between the active electrode and the tissue is usually 3 to 5 mm, depending on the selected coagulation parameters. When using argon coagulation, precautions for standard monopolar coagulation should be observed (Emed, 2015).

Advantages and Benefits of Argon Beam Tissue Coagulators

Control of capillary bleeding in renal parenchyma was initially achieved using the argon beam coagulator. Since the argon beam tissue coagulator leaves a more uniform coagulated surface after blowing away blood and debris from the surgical field, it is considered adequate for minor capillary bleeding after dissection. It is a highly effective form of hemostasis and therefore is still sometimes used in procedures involving major blood loss (Klingler et al., 2006). Because the beam concentrates the electrosurgical current, the resulting eschar produced during the procedure is smoother and more pliable than that resulting from other electrosurgical techniques. Blood is dispersed by the gas, reportedly improving visualization of the operative field. Also, less smoke is produced due to the heavier argon displacing some of the oxygen at the operative site (Brill, 2011).

Argon beam coagulation has broad application in local treatment of cancer, both in the case of advanced tumor resection and in the treatment of benign or pre-cancerous lesions (Emed, 2015).

Argon coagulation is often used during procedures performed for oncological indications and various non-oncological indications, such as endoscopic bleeding control and destruction of vascular lesions in the gastrointestinal tract, and general surgery (Emed, 2015).

Disadvantages and Risks of Argon Beam Tissue Coagulators

The argon beam coagulator by itself cannot be used for tissue dissection and is unsuitable for control of significant bleeding or larger vessels. The insolubility of argon gas in blood puts patients at risk for significant complications such as argon gas embolism, both non-fatal and fatal, as well as pneumothorax even when the device is used correctly, particularly in the presence of unfavorable anatomical conditions (Klingler et al., 2006; Sankaranarayanan et al., 2013). The selected flow rate for argon should be as low as possible to decrease the risk of argon gas embolism. Direct contact of the tool tip on the target anatomical region should be avoided, and the electrode tip should be held at an oblique angle. Furthermore, since this device uses electricity, there is a risk of interference with surgical equipment.

2.2.1.2.1.6 Laser Surgery

Background

Several lasers have been developed specifically for surgical applications of cutting or vaporizing tissue while leaving a coagulated field. The efficacy of these devices to coagulate or excise tissue is regulated by a specific wavelength, energy, or power setting and mode of operation (i.e. continuous or pulsed) (Binsaleh, 2011). The first use of lasers in laparoscopic surgery was recorded in 1979, with regular use of laparoscopic laser surgery underway as early as 1982. In a short span of time, lasers became very widespread in the medical field, ranging from cosmetic treatments to highly complicated surgeries such as atrial fibrillation treatment. Their utilization has faded, however, and currently lasers are relegated primarily to gynecological procedures (Sankaranarayanan et al., 2013) and urologic applications (Lerner and Rajender, 2015).

Lasers generate heat by applying a concentrated beam of light. In a laser system, electromagnetic or light waves are amplified multiple fold in an optical resonator (which contains mirrors and a gain medium) and passed out in the form of high intensity light waves. The amount of amplification in the resonator determines the amount of energy transmitted by the light waves which are then absorbed by the tissue. This energy absorbed by the tissue then manifests itself into heat which cuts and coagulates the tissue. The frequency of the laser determines the width of the beam generated (the higher the frequency of the wave, the lower the diameter of the beam). Most commercial lasers use infra-red to ultraviolet frequencies for medical applications (Sankaranarayanan et al., 2013).

The energy delivered by the laser, whose intensity can be modulated, can cut, destroy, or alter the cellular or extracellular structure of biological tissue. Laser treatment of benign prostatic hyperplasia (BPH) using enucleation techniques has grown in the field of urology (Lerner and Rajender, 2015). Laser enucleation of the prostate (LEP) is a transurethral procedure that utilizes several different types of

lasers to dissect the adenoma from the surgical capsule in a retrograde fashion. Contemporary laser prostate enucleation techniques include Holmium-LEP (HoLEP), Thulium-LEP (ThuLEP), Greenlight-LEP (GreenLEP) and Diode-LEP (DiLEP) applications. Each laser device used for prostate enucleation is intended to remove the adenoma from the surgical capsule, but each laser has unique characteristics (i.e. wavelength, absorption rates) that must be understood by the practicing surgeon (Lerner and Rajender, 2015).

Advantages and Benefits of Laser Surgery

Laser applications have the advantage of reducing the risk of infection and promoting healing. Various LEP techniques have demonstrated similar, if not superior, postoperative results to transurethral resection of the prostate (TURP), the current gold standard in the treatment of BPH (Lerner and Rajender, 2015). Lasers utilized in laparoscopic surgery include the Nd:YAG KTP 532 and carbon dioxide lasers, most commonly employed in gynecologic procedures. The carbon dioxide laser is considered the safest device for intra-abdominal use due to its wavelength and ability for precision and control (Baggish, 2012). Energy from the carbon dioxide laser is effectively absorbed by water. This allows for efficient hydro dissection that can backstop the carbon dioxide laser beam in strategic locations, helping to prevent injury to surrounding structures. Since, lasers are not conducted in tissue they are advantageous for vaporizing endometrial implants and cutting adhesions (Baggish, 2012)

Disadvantages and Risks of Laser Surgery

Although laser surgery was once widely used in many laparoscopic procedures such as cholecystectomy, the high cost of these devices has limited their use in contemporary medicine primarily to gynecologic, urologic, and dermatologic applications. Laser surgery is currently integrated into certain surgical procedures for improved focus and precise cutting, but it holds risks for pregnant women and has contra-indications when used in patients receiving photosensitizing drugs (Legres et al., 2014). Lasers and argon beam coagulation are linked with more reported cases of mortality-related complications than are any other forms of energized surgery. Other drawbacks to using laser surgery is the need for advanced training in laser and laparoscopic surgery (Sankaranarayanan et al., 2013).

Additional risks associated with laser surgery include fire from flammable materials ignited by lasers and increased operative time. The extended sedation period resulting from prolonged surgical time also means a lengthened recovery time. Cellular damage may occur around the area of laser impingement, depending upon the size of the laser tip. Other complications associated with the use of laser surgical energy source are potentially fatal air embolism, injury to the hepatic artery with pseudoaneurysm formation and hemobilia during laparoscopic cholecystectomy, and hemorrhage (Sankaranarayanan et al., 2013).

2.3. Comparative Studies

The purpose of the literature review was to assess the performance and safety of the subject devices in relation to these parameters in alternative therapies and devices used to achieve the same surgical

goals. In order to leverage the highest level of available evidence on comparisons between surgical energy instruments, the SOA literature evaluation focused on systematic reviews/meta-analyses that compared outcomes of various pairs of energy devices. The goal was to use published data on each of the four categories of energy devices compared with non-energy devices, with each other or with argon beam or laser devices. There were multiple possible combinations of head-to-head to comparisons. Not all the possible combinations of comparative studies were available in the included literature. Due to the limited amount of data available on certain comparisons of paired energy devices, the SOA literature evaluation included two RCTs and two comparative studies that compared monopolar electrosurgical devices either with conventional, non-energized techniques of cutting and/or hemostasis (i.e., cold dissection/blunt dissection) or with standard bipolar electrosurgical devices.

While the investigations pertained to a wide array of surgical procedures, including both laparoscopic and open approaches, the data analysis has been organized by head-to-head paired comparisons of energy devices, whenever possible, rather than by procedure type or anatomical region. A few studies presented data for three-way comparisons between energy instruments, the results of which were teased apart for analysis of direct two-way comparisons, where possible. The four types of energy devices evaluated in the comparative literature spanned the four categories of target therapies to which potential ETHICON subject devices belong: (1) monopolar electrosurgical devices, (2) bipolar electrosurgical devices, (3) advanced bipolar electrosurgical devices, and (4) ultrasonic energy surgical devices.

A conventional electrosurgical device, also known as a radiofrequency dissecting sealer (RFDS), can be used in either monopolar electrosurgery or standard bipolar electrosurgery. Some studies in this literature review that examined conventional electrosurgery did not differentiate between monopolar and bipolar electrosurgical devices, and therefore the results of these studies were grouped together as RFDS or conventional (ES) electrosurgical devices rather than as separate monopolar or bipolar instruments.

The majority of studies assessed in this document reported on multiple comparisons of various energy devices used in surgical cutting and/or hemostasis, largely, but not exclusively, between advanced bipolar instruments and ultrasonic energy devices. Relatively fewer studies focused on monopolar or bipolar electrosurgical devices, particularly compared to each other. A small number of studies explored head-to-head comparisons of various energized devices with a variety of traditional non-energized techniques, such as clamp-and-tie or suturing, used to achieve hemostasis or, in some cases, cutting or dissection.

Although argon beam therapy and laser therapy fall under the rubric of energy devices employed in surgical coagulation and cutting, respectively, none of the studies included in the SOA Report evaluated the use of these devices in surgical procedures. Laparoscopic laser cholecystectomy was a popular procedure nearly two decades ago, but it is rarely used for this indication in the current medical climate (Sankaranarayanan et al., 2013). While lasers are still widely utilized in various gynecological

treatments such as endometriosis (Sankaranarayanan et al., 2013), this indication was not addressed in any study that presented "higher level evidence" (i.e., systematic review and/or meta-analysis. Despite its association with complications, argon beam coagulation is sometimes coupled with electrosurgery to improve coagulation. However, no studies with "higher level evidence" that were identified through the literature screening utilized argon beam coagulation as an ancillary strategy to promote hemostasis.

Abbreviations for Literature Data Analysis Tables 8 – 17.

- Cold Dissection/Blunt Dissection: CD
- Monopolar electrosurgery: MES
- Bipolar electrosurgery, conventional / standard: BES
- Conventional electrosurgery (ES) / Radiofrequency Dissecting Sealer (RFDS) (monopolar and/or bipolar): ES/RFDS
- Advanced bipolar electrosurgery (Electrothermal/electrosurgical bipolar vessel sealer): EBVS *
- Ultrasonic energy surgery: UES
- Primary Outcomes: OT (operating time/surgical duration), BL (blood loss), AEs (adverse events), PP (postoperative pain), LOS (length of hospital stay)
- TURP: Transurethral resection of the prostate
- M-TURP: Monopolar electrosurgical TURP
- B-TURP: Bipolar electrosurgical TURP

**EBVS is used in this SOA report because it is a more common clinical term than advanced bipolar electrosurgical device.*

Monopolar Electrosurgery versus Conventional Dissection or Hemostasis

Bukhari 2007 et al. compared the outcomes of monopolar electrodissection with cold dissection (blunt dissection) in 100 pediatric patients who underwent tonsillectomy using a different surgical procedure on each tonsil (Bukhari and Al-Ammar, 2007). As noted previously, some confusion exists in the literature regarding the terminology of electrosurgery versus diathermy. Bukhari et al. labeled the technique they evaluated as monopolar diathermy, but the terms electrodiathermy (including electrocauterization) and electrosurgery are sometimes used interchangeably, particularly in some of the older literature.

The NICE Guidance document on tonsil conditions published in December 2005 titled "Electrosurgery (diathermy and coblation) for tonsillectomy: Interventional procedures guidance [IPG150]," (https://www.nice.org.uk/guidance/ipg150) illustrates that diathermy is categorized by at least some professional societies as a form of electrosurgery (NICE, 2005). Based on this rationale, Bukhari et al.'s article has been included in the SOA literature analysis (see Table 2-8). This study demonstrated that

compared with traditional blunt dissection performed with a scalpel, electrodissection was associated with performance and safety outcomes that were not inferior and furthermore that showed significant benefit. These findings are consistent with the reported advantages of RF energy-based systems, the first of which consisted of monopolar electrosurgical devices, as compared with traditional manual surgical dissection instruments and methods.

Table 2-8: Monopolar Electrosurgery (MES) (Diathermy) vs Cold Dissection (CD) (Blunt Dissection)

	No statistically significant difference in outcome between MES and CD
	MES had a statistically significant better outcome than CD
	CD had a statistically significant better outcome than MES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Patients	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Bukhari and Al-Ammar, 2007) Comparative clinical study (100 pediatric patients; 200 tonsils	Tonsillectomy Operative time (<3 mins >3), intraoperative bleeding, post-operative bleeding, pain Monopolar electrosurgery: Right side (n=81 patients), Left side (n=19 patients) Cold technique: right side (n=19 patients), Left side (n=81 patients)	*p*=0.0011	No p value provided				Monopolar dissection tonsillectomy was found to be a safe technique that significantly reduced operative time and intra-operative blood loss. It caused more pain on 1st postoperative day, but no significant difference in pain was observed on remaining days until 10th postoperative day.

Monopolar Electrosurgery vs Bipolar Electrosurgery

Four studies on monopolar electrosurgery vs bipolar electrosurgery compared outcomes of monopolar transurethral resection of the prostate (TURP), a common monopolar electrosurgical procedure, with those of bipolar TURP, a standard bipolar electrosurgical modality. These studies included a systematic review and meta-analysis of randomized controlled trials (RCTs) (Mamoulakis et al., 2009), two RCTs (Lin et al., 2006; Singh et al., 2005), and a retrospective comparative clinical study (Srivastava et al., 2016). One study concluded that the two techniques achieved comparable effectiveness, but the other three investigations demonstrated relatively more advantageous outcomes for the bipolar technique (See Table 2-9).

In both a systematic review and an RCT, the International Prostate Symptom Score (IPSS), QoL, postvoid residual urine volume (PVR), and Q-max showed similar improvement in B-TURP and M-TURP (Lin et al., 2006; Mamoulakis et al., 2009). However, the between-group differences in these outcomes were not significant in the retrospective comparative study (Srivastava et al., 2016). The difference in the postoperative serum sodium level and the mean sodium change were significantly greater with bipolar electrosurgery, which was associated with a lower risk of TUR syndrome (Srivastava et al., 2016), shorter catheterization duration, shorter hospital stay, and fewer complications (Lin et al., 2006). Although the rates of complications, including blood clot retention, were lower in the B-TURP groups than in the M-TURP groups, the differences were neither significant (Lin et al., 2006) nor highly

significant (Singh et al., 2005). However, the duration of irrigation and catheterization was significantly longer with M-TURP than with B-TURP (Mamoulakis et al., 2009; Srivastava et al., 2016). Based on these results, the authors of these studies concluded that the use of B-TURP was preferable in TURP procedures. Yet, comparable efficacy was achieved in one study (Singh et al., 2005) and no significant differences in adverse events overall occurred in most studies.

Table 2-9: Monopolar Electrosurgery (M-TURP) vs Bipolar Electrosurgery (B-TURP) in Transurethral Resection of the Prostate (TURP)

	No statistically significant difference in outcome between M-TURP and B-TURP
	B-TURP had a statistically significant better outcome than M-TURP
	M-TURP had a statistically significant better outcome than B-TURP
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Patients	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Lin et al., 2006) Prospective RCT of transureth-ral resection of the prostate (TURP)	Transurethral resection of the prostate (TURP) International Prostate Symptom **Score (**IPSS**),** urinalysis, serum creatinine, serum PSA, peak flow rate (Qmax), serum sodium, hemoglobin, resection time, blood loss, Monopolar TURP (M-TURP (n=18) vs Bipolar TURP (B-TURP) (n=22) AE: postoperative serum sodium level			p< 0.001			The devices described in the study appear to be electrosurgical instruments that function with an ESU. The bipolar electrocautery device was safer than the traditional monopolar device for the TURP procedure. The bipolar device decreased the risk of TUR syndrome and produces results similar to those obtained with the monopolar device at 6-month and 1 year follow-ups.

(Singh et al., 2005) RCT	Transurethral resection of the prostate (TURP) Resection time, amount of tissue resected, irrigant amount, blood loss, fluid absorption, and change in serum sodium and hemoglobin Bipolar TURP (n=30) vs Monopolar TURP (n=30) AE: Fall/change in serum Na (mEq/L); Postoperative dysuria was less common with bipolar resection (no p value) Pain: Based on analgesic requirement			p < 0.001 0.0011		p= 0.019	Operative time was divided into resection and coagulation times. Coagulation time was higher (p = 0.019) in the bipolar group ((5.6 *v* 4.6 minutes). Data presented in this table are for resection time and total operative time (no difference between the groups). Improvement in symptom and QoL scores and Qmax were similar in the two groups. Bipolar resection of the prostate is as effective as monopolar TURP. It does not lead to any change in serum Na and causes less postoperative dysuria compared with monopolar resection.
(Srivastava et al., 2016) Retrospective comparative clinical study	Transurethral resection of prostate (TURP) International Prostate Symptom Score (IPSS), quality of life (QoL) scores, PVR, serum creatinine and Q-max at baseline,1, 3, 6 and 12 months Group 1: Monopolar TURP (M-TURP) (n=72 patients) vs Group 2: Bipolar TURP (BP-TURP) (n=81 patients) Group 3: Open prostatectomy (OP): Data not the focus of this analysis. n=52 patients	G1 > G2 > G3; B-TURP p<0.001		G1 > G2 = G3 B-TURP (p=0.04)			Operative time was shorter for bipolar TURP than for monopolar TURP. Statistical values for outcomes were for Group 1 vs Group 2 vs Group 3.

(Mamoulakis et al., 2009) Systematic Review and Meta-analysis of 16 RCTs 1406 patients	Transurethral resection of prostate (TURP Efficacy (maximum flow rate [Qmax], International Prostate Symptom Score [IPSS]) Bipolar TURP (B-TURP) vs Monopolar TURP (M-TURP) # patients varied across outcomes assessed. Bipolar technique involved PlasmaKinetic TURP, an advanced bipolar electrosurgical technology.						No clinically relevant differences in short-term (12-mo) efficacy were detected (Qmax: weighted mean difference [WMD]: 0.72 ml/s; 95% confidence interval [CI], 0.08–1.35; p = 0.03). However, B-TURP is preferable due to a more favorable safety profile (lower TUR syndrome (post-TURP hyponatremia) and clot retention rates) and shorter irrigation and catheterization duration.

Monopolar Electrosurgery vs Advanced Bipolar Electrosurgery (aka Electrosurgical Bipolar Vessel Sealer) (EBVS)

Monopolar electrosurgical devices were compared with LigaSure, an advanced bipolar tissue sealing and cutting device, in a systematic review (Janssen et al., 2012) and in two RCTs (Martucci et al., 2015; Parlakgumus et al., 2011). Although Janssen et al.'s systematic review included 7 studies, the data for monopolar instruments pertained to only two laparoscopic RCTs. The operative time was significantly shorter for LigaSure than for the monopolar instrument in all three systematic reviews. No statistically significant differences between monopolar techniques and Ligasure were reported for the volume of blood loss, rate of complications, or length of hospital stay (Table 2-10).

Table 2-10: Monopolar Electrosurgical (MES) Device vs. Advanced Bipolar Device (Electrosurgical Bipolar Vessel Sealer) (EBVS)

	No statistically significant difference in outcome between EBVS and MES
	EBVS had a statistically significant better outcome than MES
	MES had a statistically significant better outcome than EBVS
	Mixed or inconsistent results across studies
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Janssen et al., 2012) Systematic review 7 RCTs with 554 patients	Colectomy Dissection time, blood loss, postoperative complications, Data for monopolar electrosurgery were based on 2 laparoscopic colectomy RCTs: Hubner et al., 2008 and Targarona et al. 2005. (Use of monopolar device as conventional electrosurgery was not verified in Targarona et al.'s study. Full article was unavailable). Hubner et al: MES (n=20 patients) vs EBVS (n=21 patients)	$P < 0{\cdot}001$					Considering the relatively low number of complications, all hemostatic devices used may be considered relatively safe. Vessel-sealing devices may be considered safe and their use may reduce costs due to reduced blood loss and shorter operating time in some abdominal surgical procedures compared to mono- or bipolar electrothermal devices. In 2 laparoscopic colectomy RCTs, operating time was significantly shorter with LigaSure device compared to monopolar electroscissor and bipolar electrothermal devices.
(Martucci et al., 2015) Pilot RCT with 119 patients	Open Pulmonary Lobectomy Postoperative atrial fibrillation LigaSure™ tissue fusion (n=57 patients) vs electrosurgical pencil (standard hemostatic procedure) (n=62 patients)	P = 0.017					There was no statistically significant difference between LigaSure and electrosurgical pencil in terms of postoperative atrial fibrillation (P = 0.31).

(Parlakgumus et al., 2011) Prospective RCT with 128 patients	Pilonidal Sinus Surgery Surgical site infection, early wound failure (dehiscence), and unhealed wound rate Monopolar electrosurgical device (Aesculap GN 300) (group ME) n=64) vs advanced bipolar tissue sealing-cutting device (LigaSure V 20 cm Instrument [LS1520]) (group TSD) (n=64)	ME3 (P<0.01)		Mixed results wound dehiscence (P=0.02). Abd of ND	EBVS / LS		The efficacious use of devices with low thermal energy spread reduces seroma and infection rates. Despite the long operation time, TSDs may be a method of choice in surgery for pilonidal sinus because of their positive effects on patient outcomes, especially in the early postoperative period.

Monopolar Electrosurgery vs Ultrasonic Energy

Head to head comparisons of monopolar electrosurgical devices vs ultrasonic energy devices were reported in two meta-analyses (Jiang et al., 2017; Xiong et al., 2012) and one retrospective comparative cohort study of laparoscopic cholecystectomy (Zanghi et al., 2014). These three studies had a total of 3175 patients. Compared to the monopolar instruments, the ultrasonic surgical devices were advantageous in terms of a statistically significant shorter operating time, less blood loss, and fewer complications (Jiang et al., 2017; Xiong et al., 2012; Zanghi et al., 2014). Jiang et al.'s performed a meta-analysis and trial sequential analyses of 19 studies with 1955 patients on outcomes of monopolar electrosurgery versus ultrasonic dissection in laparoscopic cholecystectomy (Jiang et al., 2017).These authors concluded that compared to the electrosurgery device, the ultrasonic device could be superior because it showed greater clinical effectiveness. The specific ultrasonic instruments were not identified by manufacturer in each study, but the Harmonic ultrasonic shears resulted in shorter operative time ($P < 0.00001$), less blood loss $P = 0.004$, fewer gallbladder perforations 0.00001, shorter hospital stay ($P = 0.002$), and fewer abdominal pains (Table 2-11). However, the relative risk (RR) or mean differences (MDs) for these outcomes was based on a small number of trials, many of which included only 2 to 3 studies (Jiang et al., 2017).

The length of hospital stay was significantly shorter for ultrasonic surgical devices compared with monopolar electrosurgery ($P = 0.002$ - 0.01) in the two meta-analyses (Jiang et al., 2017; Xiong et al., 2012). No significant difference between the groups was reported for pain or for length of hospitalization in the retrospective comparative cohort study (Zanghi et al., 2014).

Table 2-11: Monopolar Electrosurgical Device (MES) vs Ultrasonic Energy Device (UES)

	No statistically significant difference in outcome between MES and UES
	UES had a statistically significant better outcome than MES
	MES had a statistically significant better outcome than UES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Jiang et al., 2017). Meta-analysis and trial sequential analyses; 19 studies with 1955 patients	Laparoscopic Cholecystectomy Operative time (1006 in ultrasonic device group and 949 in electrosurgical [ES] device group)	P < 0.00001	P = 0.004	P < 0.00001	P < 0.0001	P = 0.002	Compared with the electrosurgery device, the ultrasonic device could be superior with more clinical effectiveness. The trial sequential analysis demonstrated that further studies to confirm the superior operative time associated with the ultrasonic device were not needed.
(Xiong et al., 2012) Meta-analysis 8 high-quality RCTs with 1056 patients	Laparoscopic Cholecystectomy Mean operation time, mean blood loss, mean hospital stay Number of patients varied across outcomes measured; ranged from 413-1280 in all studies and from 2113-925 in high quality studies	P < .00001	P < .00001			P = .01	Ultrasonic energy is as safe and effective as electrosurgical energy and potentially might be safer in laparoscopic cholecystectomy. However, the financial implications of this technical modality need to be established in cost-effectiveness analysis. In 6 studies, no statistically significant difference was found between the two groups (OR, 0.75; 95% CI, 0.33–1.67; P = .48. AEs refer to pooled results for gallbladder perforation: In 6 studies, the pooled result favored the ultrasonic dissection (OR, 0.31; 95% CI, 0.22–0.44; P < .00001).

(Zanghi et al., 2014) Retrospective comparative cohort study with 164 patients	Laparoscopic Cholecystectomy Mean operative time, rate of gallbladder perforation, intraoperative volume blood loss Monopolar coagulation (n=121 patients) vs Harmonic ACE (n=43 patients)	UES $p < 0.0001$	UES $p < 0.0001$	UES $p < 0.05$			The Harmonic Scalpel shows some statistically significant advantages (i.e., duration of the operation, rate of gallbladder perforation, intraoperative bile leaks or escapes, volume of blood loss), but no statistical differences were observed in remaining intraoperative (i.e., amount of drainage, visceral injuries conversion rates) or postoperative (i.e., hospital stay and morbidity), complications. These factors, combined with the US cost, show that harmonic scalpel does not offer sufficient advantages to make it the reference technique.

Conventional (Mono- or Bipolar) Electrosurgery (ES/RFDS) vs Conventional Clamp-crushing (CC) Technique

In a systematic review and meta-analysis of various energy devices used in liver resection, Alexiou et al. reported on outcomes of a radiofrequency dissecting sealer (RFDS) compared with other energy surgical instruments (Alexiou et al., 2013) (Table 2-12). The study included 8 RCTs and 7 nonrandomized studies that evaluated 1539 patients. The RFDSs referred to either monopolar or bipolar electrosurgical devices, but the exact type of instruments used in the studies was not revealed. There were no statistically significant differences between the patients treated with a RFDS device and those who underwent conventional clamping to achieve hemostasis in the outcomes of blood loss, rate of adverse events, and length of hospitals stay. The data showed that RFDS did not exhibit any significant advantage over conventional clamp-crushing (Alexiou et al., 2013).

Table 2-12: Monopolar/Conventional Bipolar Electrosurgical (ES/RFDS) Device vs Conventional Clamp-crushing (CC) Technique

	No statistically significant difference in outcome between ES/RFDS and CC
	ES/RFDS had a statistically significant better outcome than CC
	CC had a statistically significant better outcome than ES/RFDS
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Alexiou et al., 2013) Systematic Review and Meta-analysis; 15 trials [8 RCTs and 7 non-randomized studies) with 1539 patients	Liver Resection Blood loss Sample sizes varied across 2-way and 3-way comparisons; and across outcome analyses RFDS: Monopolar or bipolar electrosurgical devices (not differentiated) RFDS (ES) vs Conventional Clamp-crushing Technique (CC)						RFDS did not exhibit any significant advantage over the Conventional Clamp-crushing Technique (CC)

Conventional (Mono- or Bipolar) Electrosurgical Devices (ES/RFDS) vs Advanced Bipolar (Electrosurgical Bipolar Vessel Sealer) (EBVS) or Ultrasonic Surgical (UES) Devices

There were no direct head-to-head comparisons of outcomes between a standard bipolar electrosurgical device and either an advanced bipolar electrosurgical vessel sealer or an ultrasonic energy device in the included SOA literature. However, as shown in Table 2-13 and Table 2-14, Allaix et al.'s systematic review of laparoscopic colorectal resection compared outcomes of unspecified conventional electrosurgical devices (either monopolar or bipolar) with advanced bipolar electrosurgical devices (such as Ligasure or Enseal vessel sealing systems) as well as a multifunctional ultrasonic surgical dissector-sealer, the Cavitron Ultrasonic Surgical Aspirator (CUSA) (Allaix et al., 2016). Since no meta-analysis was performed, the findings were summarized for individual studies (Allaix et al., 2016). Both types of advanced vessel sealing systems were found to be advantageous in terms of less blood loss compared with conventional electrosurgical devices. The operative time for the vessel sealing systems was significantly shorter in one study (Hubner et al., 2007), but not in the other. There were no statistically significant differences between the conventional electrosurgical devices and

Cavitron Ultrasonic Surgical Aspirator (CUSA) in operative time and intraoperative blood loss in three studies. The authors concluded that ultrasonic surgical devices and advanced bipolar vessel systems are advantageous in terms of less blood loss and/or a shorter operative time compared with conventional electrosurgical devices. However, they noted that the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection (Allaix et al., 2016). Given this information, ES/RFDS devices still remain state of the art depending on surgical circumstances, surgeon training / surgeon choice, healthcare reimbursement and several other factors, as demonstrated by the clinical evaluation contained herein.

Table 2-13: Monopolar/Conventional Bipolar Electrosurgical Device ES/RFDS vs Advanced Bipolar Electrosurgical (Electrosurgical Bipolar Vessel Sealer) (EBVS) Device

	No statistically significant difference in outcome between ES/RFDS and EBVS
	EBVS had a statistically significant better outcome than ES/RFDS
	ES/RFDS had a statistically significant better outcome than EBVS
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Janssen et al., 2012) Systematic review (no meta-analysis) 7 RCTs with 554 patients	Abdominal Surgery Dissection time, blood loss, postoperative complications, (Hubner et al., 2007) In 2 laparoscopic colectomy RCTs: Ligasure (36 patients) vs 31 patients received MES or BES (n=31 patients) in laparoscopic colectomy	EBVS	EBVS	10/20 vs 6/20			In 2 laparoscopic colectomy RCTs, operating time was significantly shorter with LigaSure vs monopolar electroscissor and bipolar electrothermal devices. Outcomes analyzed in this table are for Hubner, et al., 2008. Considering the relatively low number of complications, all hemostatic devices used may be considered relatively safe. Vessel-sealing devices may be considered safe and their use may reduce costs due to reduced blood loss and shorter operating time in some abdominal surgical procedures compared to mono- or bipolar electrothermal devices.

(Allaix et al., 2016) Systematic Review (no meta-analysis)	Laparoscopic Colorectal Resection Operative time 7 studies; 6 comparative studies with 615 patients. Cohort sizes varied across paired comparisons.						No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. In 2 studies, operative time was shorter with EBVS compared with ES; blood loss was lower with EBVS compared with ES Although US and EBVS have the advantages of less blood loss and/or a shorter operative time compared with ES, the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

Table 2-14: Monopolar/Conventional Bipolar Electrosurgical ES/RFDS Device vs Ultrasonic Energy (UES) Device

	No statistically significant difference in outcome between ES/RFDS and UES
	UES had a statistically significant better outcome than ES/RFDS
	ES/RFDS had a statistically significant better outcome than UES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Jiang et al., 2017) Meta-analysis and trial sequential analyses; 19 studies with 1955 patients	Laparoscopic Cholecystectomy Operative time UES (n=1006 patients) vs ES (n=949 patients)	P < 0.00001	P = 0.004	P < 0.00001	P < 0.0001	P = 0.002	Compared with the electrosurgery device, the ultrasonic device could be superior with more clinical effectiveness. The trial sequential analysis demonstrated that further studies to confirm the superior operative time associated with the ultrasonic device were not needed.

(Allaix et al., 2016) Systematic Review (no meta-analysis) 7 studies; 6 comparative studies with 615 patients	Laparoscopic Colorectal Resection Operative time One RCT: ES (n=7 patients2) vs UES (n=74 patients) (Morino et al.		p< 0.05			No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. Although ultrasonic surgical devices (US) and electrothermal bipolar vessel sealers (EBVS) have the advantages of less blood loss and/or a shorter operative time compared with conventional electrosurgery (ES), the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

Advanced Bipolar Electrosurgical Devices vs Conventional Hemostatic Techniques or Conventional Excisional Techniques

Ten studies, including 7 systematic reviews and 3 RTCs, compared advanced bipolar electrosurgical device (particularly, an advanced bipolar vessel sealer) with conventional methods of hemostasis, such as suturing and clamp-and-tie, or excision (see Table 2-15). Compared with traditional techniques, advanced bipolar electrosurgical devices resulted in statistically significant better outcomes in surgical time in meta-analyses of thyroidectomy, including an assessment of LigaSure (n=813 patients) vs conventional hemostasis (n=2735) patients (Luo et al., 2017); an evaluation of LigaSure vs "clamp-and-tie" (11 studies) (Garas et al., 2013); and an examination of LigaSure vs conventional hemostasis (7 trials, with 730 patients) (Contin et al., 2013). Statistically significant lower amounts of blood loss were associated with LigaSure in some, though not all, studies on thyroid surgery (Luo et al., 2017)(Chavez et al., 2017).

Reduced surgical time when compared with traditional techniques was also reported for an advanced bipolar electrosurgical device in an RTC of female patients who underwent thyroidectomy with either an advanced bipolar electrosurgical instrument (the Enseal G2 Curved Tissue Sealer, one of the subject devices) (n=21 patients) or traditional tie and suture (n=20 patients) (Chavez et al., 2017). The use of an advanced bipolar device in thyroid operations decreased operative time by >30 minutes when compared with the traditional tie and suture technique (Chavez et al., 2017).

Pain was decreased with the use of an advanced bipolar vessel sealer in one study and hospital stay was shorter in another study, but the differences associated with the two types of energized surgical devices were not significant for several outcomes. In some cases, the benefit was minimal. For example, the use of a bipolar vessel sealing system in performing axillary node dissection for breast cancer was safe and feasible, but offered marginal advantages when compared to the conventional technique (Nespoli et al., 2012).

Variable outcomes were reported for other studies that compared electrosurgical with conventional excision, resection, or suturing. Pergialiotis et al.'s meta-analysis of 8 RCTs evaluated outcomes of electrosurgical bipolar vessel sealing systems (EBVS) (advanced bipolar devices) versus conventional

suture ligation in 772 female patients who underwent vaginal hysterectomy (Pergialiotis et al., 2014). Six studies used Ligasure and two studies used BiClamp as the EBVS. There was no overall significant difference in operative time or rate of complications between patients treated with EBVS (n=386) and traditional suture ligation (n=386). However, EBVS were associated with significantly lower intraoperative blood loss (Pergialiotis et al., 2014).

The findings demonstrated that EBVS seemed to produce less intraoperative blood loss during vascular clamping without significantly lowering intraoperative time or complication rate. However, the authors cautioned against drawing firm conclusions due to factors such as heterogeneous recruitment of participants, inconsistent inclusion of patients with vaginal prolapse, and the lack of a definition of randomization (Pergialiotis et al., 2014). In addition, it is not clear if the different types of EBVS devices, including Ligasure and BiClamp, could have affected the outcomes. Six of the RCTs in Pergialiotis et al.'s meta-analysis utilized LigaSure whereas two studies used BiClamp (Pergialiotis et al., 2014). In Zubke et al.'s multicenter RCT, BiClamp (n= 88 patients) resulted in a significantly shorter operative time and significantly less blood loss than conventional suture ligation (n= 88 patients) (Zubke et al., 2009). Postoperative pain was decreased in the BiClamp group, but not significantly. The authors concluded that BiClamp was easier to use and more cost effective than conventional suture ligation (Zubke et al., 2009).

Milito et al., conducted a meta-analysis with 608 patients that compared the use of advanced bipolar devices (LigaSure) with conventional excisional techniques, circular stapling and Harmonic Scalpel in patients with symptomatic hemorrhoids (Milito et al., 2010). Compared with conventional excisional hemorrhoidectomy, Ligasure hemorrhoidectomy was found to be a fast procedure characterized by a shorter operation time ($P < 0.001$) limited postoperative pain ($P < 0.001$), short hospitalization, and fast wound healing and convalescence (Milito et al., 2010). However, there was no significant difference between the two groups in blood loss. Anal stenosis and hemorrhoids relapse incidence were significantly lower in the Ligasure group than in other excisional treatments ($P = 0.024$). No case of recurrence was reported in either groups. Also, there was no significant difference in the proportion of patients cured after Ligasure hemorrhoidectomy or other excisional techniques ($P > 0.05$) (Milito et al., 2010). Nonetheless, the series was limited and had a short term follow-up of no longer than 12 months (Milito et al., 2010).

In Alexiou et al.'s meta-analysis, 220 patients in 3 RCTs and 3 nonrandomized studies underwent liver resection using either Ligasure (n=110 patients) or conventional clamping (n=110 patients). While there was no significant difference between the two groups in surgical time, Ligasure seemed to offer significant benefit over standard conventional clamping in terms of total blood loss (p=0.01), incidence of postoperative bile leak (p=0.010), and shorter total hospital stay (p=0.0001). These results provide further support for the advantage of an advanced bipolar electrosurgical device in sealing both biliary and vascular structures. Nonetheless, the generalization of the findings was limited by the scarcity and clinical heterogeneity of the published literature (Alexiou et al., 2013).

Macario et al.'s systematic review of 29 RCTs with 2186 patients evaluated safety and performance outcomes who underwent EBVS-LigaSure) (n=1107 patients) or clamping with suture ligation/electrocauterization (n =1079 patients) in various procedures (Macario et al., 2008). The conventional mechanical hemostatic methods included suture, clips, vascular/circular stapler, and/or monopolar diathermy. EBVS decreased surgical time by about 25% for diverse surgeries. Compared with the traditional techniques, EBVS resulted in a significantly shorter operative time ($P < .0001$), less blood loss ($P = .02$), fewer complications ($P = .02$), and lower pain scores ($P = .02$) (Macario et al., 2008).

Table 2-15: Advanced Bipolar Electrosurgical (Electrosurgical Bipolar Vessel Sealer) (EBVS) Device vs Conventional Clamp-crushing (CC) Technique or Conventional Hemostats or Excision Techniques

	No statistically significant difference in outcome between EBVS and CC/conventional hemostats/excision
	EBVS had a statistically significant better outcome than CC/conventional hemostats/excision
	CC/conventional hemostats/excision had a statistically significant better outcome than EBVS
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Alexiou et al., 2013) Systematic Review and Meta-analysis EBVS vs CC: 3 RCTs and 3 nonrandomized studies	Liver Resection Blood loss Sample sizes varied across 2-way and 3-way comparisons; and across outcomes analyses Vessel sealing systems (VSSs—LigaSure) (EBVS) vs Conventional Crush-clamping (CC) (Patient counts differed across outcomes)		p=0.01			p=0.0001	Of the 3 modalities used in liver resection (VSS/EBVS, Cavitron Ultrasonic Surgical Aspirator [CUSA], and RFDS), only (VSS/EBVS appeared to offer significant benefit over standard CC in terms of total blood loss, incidence of postoperative bile leak, and shorter total hospital stay. Findings may support LigaSure's advantage in the ability to seal both biliary and vascular structures. However, the generalization of our findings is limited by the scarcity and clinical heterogeneity of the published studies.

(Milito et al., 2010) Meta-analysis 8 studies with 608 patients	Hemorrhoidectomy (open and closed) Ligasure vs conventional excisional hemorrhoidectomy Patient counts per cohort were not reported.	P < 0.001			P < 0.001		Conventional excisional hemorrhoidectomy techniques used in this study consisted of diathermy hemorrhoidectomy, Harmonic Scalpel hemorrhoidectomy and Ferguson procedure. There was no significant difference in the proportion of patients cured after Ligasure hemorrhoidectomy or other excisional techniques (P > 0.05). The meta-analysis showed that Ligasure hemorrhoidectomy is a fast procedure characterized by limited postoperative pain, short hospitalization, fast wound healing and convalescence. (No quantitative data were presented on the number of hours by which LS reduced hospitalization.)
(Pergialiotis et al., 2014) Meta-analysis 8 RCTs with 772 patients	Vaginal Hysterectomy Operative duration EBVS (n=386 patients) vs traditional suture ligation (n=386 patients)		*p* < 0.001				This meta-analysis showed that application of EBVS systems during vaginal hysterectomies may significantly limit intraoperative blood loss when compared with traditional ligation of vascular pedicles. Neither operative duration nor intraoperative and postoperative complications seem to be affected from usage of such systems. The limitations of the meta-analysis included heterogeneous recruitment of participants, inconsistent inclusion of patients with vaginal prolapse, no definition of randomization, concern over criteria for predetermining
(Zubke et al., 2009) Multicenter RCT with 175 patients (Also included in Pergialiotis et al.'s study 2014	Vaginal Hysterectomy Postoperative pain Bipolar vessel sealing (BVS; BiClamp®) (EBVS) (n = 88) vs conventional suture ligation (VSL) (n = 87)	*P* = 0.00	*P* < 0.00				Postoperative pain was decreased in the BVS group, but not significantly. The BiClamp® procedure proved superior or similar to conventional ligation, particularly with regard to intraoperative blood loss, operating time and postoperative pain, although statistical significance was not attained for postoperative pain. Moreover, BVS was easier to use and more cost effective.

(Contin et al., 2013) Meta-analysis 34 RCTs with 3875 patients	Open Thyroidectomy Operation time LigaSure (LS) (EBVS) (7 trials, 882 patients total in 2-way and 3-way designs)						This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices.
(Chavez et al., 2017) RTC with 41 patients	Thyroidectomy Surgical time Advanced bipolar device (ABD) (n=21 patients) vs traditional tie and suture n-(20 patients) All patients were women	P = .006			P = .015		The use of an advanced bipolar device in thyroid operation reduces operative time by >30 minutes, with a similar postoperative outcome profile when compared with the traditional tie and suture technique.
(Nespoli et al., 2012) RCT with 116 women with breast cancer	Thyroidectomy Total volume of fluid collected in the axillary drain Conventional node dissection surgical technique (scalpel and monopolar cautery (n = 58 patients) vs electrothermal BVSS (Ligasure Precise) (EBVS) (n = 58 patients)	P = 0.03					The use of a bipolar vessel sealing system in performing axillary node dissection for breast cancer is safe, feasible, and offers marginal advantages when compared to the conventional technique. There were significant benefits in terms of earlier drain removal and reduction of lymph aspirated percutaneously

(Garas et al., 2013) Network meta-analysis 35 RCTs with 2,856 Total patients	Thyroid Surgery Hypoparathyroidism (permanent) Pair-wise comparisons within RCTs: Ligasure (EBVS) vs "clamp-and-tie" (11 studies)	p=0.03* p<0.01**				p<0.01* p= 0.01**	Of the three modalities, ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Conversely, ultrasonic coagulation demonstrated the highest risk for RLN paralysis whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile but was followed by "clamp-and-tie" and finally Ligasure. These results can contribute to establishing guidelines for thyroid surgery. AE refers to Hypoparathyroidism Pair-wise comparisons * Network meta-analysis ** Jadad score (meta-regression analyses of direct comparisons)
(Luo et al., 2017) Meta-analysis 47 RCTs with 6219 patients	Thyroidectomy LigaSure vs Conventional Hemostasis Operation time 2671 patients received Harmonic Scalpel, 813 patients received LigaSure, 2735 patients were treated with conventional hemostasis	p<0.001	p<0.023	P=0.011			The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods. Recorded Results in this table were based on pair-wise comparison. Harmonic scalpel decreased operation time compared with the conventional hemostasis. Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal paralysis compared with conventional hemostatic methods.

(Macario et al., 2008) Systematic review and meta-analysis 29 RCTs with 2186 patients:	Various Procedures/Diverse Anatomical Regions Operative time EBVS-LigaSure (n=1107 patients); clamping with suture ligation / electrocauterization (n =1079 patients), ultrasonic energy (e.g., Harmonic Scalpel) (patient count not reported)	13 studies: *P* < .0001	13 studies: *P* =.02	*P* =.02	*P* <.0001		The meta-analysis of 26 studies indicates that when compared with conventional mechanical hemostatic methods (such as suture, clips, vascular/circular stapler, and/or monopolar diathermy), EBVS reduces operative time by about one fourth for a variety of surgeries. This use is not associated with increased blood loss, pain scores, or complications.

Advanced Bipolar Devices (Electrosurgical Bipolar Vessel Dissector-Vessel Sealers) vs Ultrasonic Surgical Devices

Some studies included in the SOA provided three-way comparisons of various energy surgical devices, with the most revealing data often pertaining to either direct or indirect comparisons between EBVS and ultrasonic instruments. For example, Contin et al.'s three-way comparison of conventional techniques for hemostasis with ultrasonic systems (e.g. UltraCision® or Harmonic Focus® devices) and LigaSure in thyroid surgery showed a significant reduction of operation time of Harmonic Focus and LigaSure compared with conventional hemostasis and a marginal benefit of Harmonic Focus for several safety outcomes (Contin et al., 2013). The postoperative morbidity was not affected by employing energized devices (Contin et al., 2013).

Garas et al.'s network meta-analysis was designed to evaluate the incidence of a postoperative adverse event, permanent hypoparathyroidism, following thyroid surgery (Garas et al., 2013). The meta-analysis overall encompassed 35 RCTs with 2,856 total patients. Outcomes were assessed via various comparisons of paired energy surgical devices, including an evaluation of Ligasure vs "clamp-and-tie" in 11 studies (patient count was not provided) (Garas et al., 2013). Ligasure showed a significantly shorter operative time ($p<0.01$) and shorter length of hospitalization ($p= 0.01$), but there were no significant differences in blood loss and adverse events compared to the traditional hemostatic technique. Although Ligasure exhibited a more favorable profile in terms of outcomes than "clamp-and-tie", the outcomes associated with ultrasonic coagulation were superior to the other two techniques (Garas et al., 2013)

A total of 13 studies, primarily meta-analyses, provided data on head-to-head comparisons of outcomes associated with advanced bipolar vessel sealing devices (mainly LigaSure) vs ultrasound (primarily Harmonic Scalpels) in a variety of procedures, such as liver resection (Scatton et al., 2015), laparoscopic colorectal resection (Allaix et al., 2016; Di Lorenzo et al., 2012), hemorrhoidectomy (Milito

et al., 2010), thyroid surgery (Cannizzaro et al., 2016{Contin, 2013 #607; Garas et al., 2013; Lang et al., 2013; Luo et al., 2017; Pastore et al., 2013; Upadhyaya et al., 2016) and other operations in diverse anatomical regions (Macario et al., 2008) (see Table 2-16). Of the studies that reported data on surgical time, ultrasonic surgical devices showed a significant advantage over EBVS in laparoscopic colorectal surgery (Di Lorenzo) and thyroid surgery (Garas et al., 2013; Luo et al., 2017), including open thyroidectomy (Contin et al., 2013; Upadhyaya et al., 2016) and total thyroidectomy (Cannizzaro et al., 2016; Lang et al., 2013). However, in one of the RCTs in Milito et al's meta-analysis, the operative time for hemorrhoidectomy was significantly shorter with LigaSure than with the ultrasonic surgical instrument ($P < 0.001$) (Milito et al., 2010). In regard to volume of blood loss, LigaSure (EBVS) was favored in two studies (Allaix et al., 2016; Scatton et al., 2015), whereas ultrasonic surgical devices were favored in one study (Lang et al., 2013), with the majority of studies reporting no significant differences. Lower levels of pain were recorded for LigaSure compared with ultrasonic surgical devices in a meta-analysis of hemorrhoidectomy (Milito et al., 2010) and a meta-analysis of a variety of procedures (Macario et al., 2008). Some studies demonstrated the advantages of electrothermal bipolar vessel sealing over ultrasonic energy in procedures such as laparoscopic colorectal surgery (Di Lorenzo et al., 2012), hemorrhoidectomy (Milito et al., 2010) and laparoscopic radical prostatectomy (Pastore et al., 2013).

In a systematic review, Janssen et al. performed a direct head-to-head comparison of outcomes between LigaSure (an advanced bipolar electrosurgical device) and ultrasonic energy device in laparoscopic colectomy (Janssen et al., 2012). Although no meta-analysis was performed, outcomes were reported for two of the laparoscopic colectomy RCTs (Janssen et al., 2012). LigaSure device was associated with a significantly shorter operating time and significantly less blood loss compared with the bipolar electrosurgery device. The overall rate of adverse events was 50% for standard bipolar devices and 30% for the advanced bipolar instrument (LigaSure). The authors concluded that vessel-sealing devices such as LigaSure may be considered safe and their use may decrease costs due to their advantages in reduced surgical time and amount of blood loss. (Janssen et al., 2012).

In several studies of thyroid surgery, the Harmonic Scalpel exhibited superiority over advanced bipolar vessel sealing devices such as LigaSure in surgical time (Garas et al., 2013; Lang et al., 2013; Luo et al., 2017; Upadhyaya et al., 2016), but not necessarily in lower volume of blood loss. Janssen et all's. meta-analysis included a direct head-to-head comparison of 673 patients treated with an advanced bipolar electrosurgical device vs ultrasonic energy device in thyroid surgery (Janssen et al., 2012). The meta-analysis provided a reduction in operation time by 9.3 minutes when using Harmonic Scalpel (95% CI, [−17.8, −0.8]; $P = 0.032$; 6 studies. When the one study that used the Ligasure instrument (LF121) (which was relatively newer at the time of publication) was removed, both the overall result and the "total thyroidectomy" subgroup results became statistically significant. For total thyroidectomies, the use of the Ligasure was slower by 7.1 min compared with the Harmonic Scalpel (95%CI, [−11.1, −3.0] ($P < 0.001$); and in 2 studies and overall, LigaSure resulted in a decrease in surgical time reduction by 12.3 minutes [−20.4, −4.2]; $P = 0.003$; 5 studies (Janssen et al., 2012). According to the authors, the amount of time saved in operative time when using Harmonic Scalpel devices could be beneficial for high

volume centers conducting many thyroidectomies a day, but not for institutions with a low surgical volume (Contin et al., 2013; Upadhyaya et al., 2016).

Other evidence suggests that the performance outcomes of these two types of energy surgical instruments may be comparable, particularly in total thyroidectomy (Cannizzaro et al., 2016; Lang et al., 2013). Compared to Ligasure, Harmonic Scalpel when used in total thyroidectomy significantly reduced blood loss and operating time. However, the overall mean difference appeared small, and with the wider availability of a more recent version of LigaSure, this difference may become even smaller such that it is not clinically relevant. There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices in Lang et al.'s meta-analysis of total thyroidectomy (Lang et al., 2013). Cannizzaro et al found no significant differences in complications between the Harmonic Scalpel, such that the choice of the device may be determined by cost (Cannizzaro et al., 2016).

Recent published evidence, therefore, suggests that there is no appreciable difference in clinical outcomes associated with these two types of "advanced energy surgical devices" (Cannizzaro et al., 2016). As noted previously, Allaix et al. concluded that while ultrasonic surgical instruments and advanced bipolar electrosurgical devices (EBVS) are both advantageous in terms of less blood loss and/or a shorter surgical time compared with conventional surgical devices, the data do not show the superiority of one these multifunctional instruments over the other in laparoscopic colorectal resection (Allaix et al., 2016). The anatomical region and type of procedure, including minimally invasive vs traditional open operations, as well as multiple patient characteristics may affect outcomes.

Table 2-16: Advanced Bipolar Device (Electrosurgical Bipolar Vessel Sealer) (EBVS) vs Ultrasonic (UES) Surgical Energy Device

	No statistically significant difference in outcome between EBVS and UES
	EBVS had a statistically significant better outcome than UES
	UES had a statistically significant better outcome than EBVS
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Scatton et al., 2015) Systematic Review 30 heterogeneous studies (1 RCT in data analysis)	Liver Resection Blood loss No meta-analysis data reported Data reported for I RCT: (Campagnacci et al., 2007) LS (100 patients) vs HS (100 pt)		EBVS p < 0.001 - 0.002				No meta-analysis of pooled data was presented. Results were qualitative except for the 1 RCT (Campagnacci et al.). Due to the low quality and heterogeneity of the studies, no firm conclusion can be drawn, but meticulous dissection of vessels does not usually lead to vascular damage. Campagnacci et al., 2007 (RCT): LigaSure Hepatectomy is safe and effective with less blood loss than occurs with an ultrasound surgical device.
(Allaix et al., 2016) Systematic Review (no meta-analysis) 7 studies; 6 comparative studies with 615 patients	Laparoscopic Colorectal Resection Operative time US (n=102) versus EBVS (n=106): 3 Studies Targarona et al. Hubner et al. Rimonda et al.		EBVS p < 0.001, p = 0.002				No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. Although US and EBVS have the advantages of less blood loss and/or a shorter operative time compared with ES, the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

(Di Lorenzo et al., 2012) Meta-analysis 4 studies (including 2 RCTs) with 397 patients were included in final analysis	Laparoscopic Colorectal Surgery Operative time, blood loss EBVS (n=200 patients) vs. UES (n=197 patients)	EBVS p<0.05	EBVS p<0.05				The meta-analysis indicated that electrothermal bipolar vessel sealing is associated with a shorter operative time and less blood loss than ultrasonic energy in laparoscopic colorectal surgery.
(Macario et al., 2008) Systematic review and meta-analysis 29 RCTs with 2186 patients	Various Procedures / Diverse Anatomical Regions Operative time Electrothermal bipolar vessel sealing system (EBVS-LigaSure) (n=1107 patients); clamping with suture ligation / electrocauterization (n =1079 patients), ultrasonic energy (e.g., Harmonic Scalpel) (patient count not reported)						The meta-analysis of 26 studies indicates that when compared with conventional mechanical hemostatic methods (such as suture, clips, vascular/circular stapler, and/or monopolar diathermy), EBVS reduces operative time by about one fourth for a variety of surgeries. This use is not associated with increased blood loss, pain scores, o outcomes associated with the Harmonic Scalpel).
(Milito et al., 2010) Meta-analysis 8 studies with 608 patients	Hemorrhoidectomy (open and closed) 1 RCT: Ligasure (n=24) vs Ultracision (n=255 (ultrasonic surgical device)	EBVS P < 0.001			EBVS P < 0.001		Conventional excisional hemorrhoidectomy techniques used in this study consisted of diathermy hemorrhoidectomy, Harmonic Scalpel hemorrhoidectomy and Ferguson procedure. There was no significant difference in the proportion of patients cured after Ligasure hemorrhoidectomy or other excisional techniques (P > 0.05). The meta-analysis showed that Ligasure hemorrhoidectomy is a fast procedure characterized by limited postoperative pain, short hospitalization, fast wound healing and convalescence. (No quantitative data were presented on the number of hours by which LS reduced hospitalization.)

(Cannizzaro et al., 2016) Systematic review and meta-analysis 14 RCTs with 2293 patients:	Total Thyroidectomy Operating time Five studies: Focus Harmonic Scalpel (n=238 patients with) vs LigaSure Precise (EBVS) (n=236 patients)					UES p = .005	In total thyroidectomy, the Focus Harmonic scalpel is a reliable and safe tool. There was no appreciable difference between the Focus Harmonic scalpel and the LigaSure Precise Vessel Sealing System. No significant differences were found in complications and when compared with the LigaSure Precise, so the choice of the device may be determined by cost.
(Lang et al., 2013) Systematic Review and Meta-analysis 8 studies (5 RCTs, 3 retrospective studies) with 963 patients	Total Thyroidectomy Total operating time, volume of blood loss Harmonic Scalpel (n=433 patients) vs (EBVS/Ligasure (n=530 patients)	UES SMD = -0.28, 95 %CI = -0.42-0.15 UES SMD = -0.28, 95 %CI = -0.42 to -0.15 -0.38 to -0.02					Compared with Ligasure, Harmonic Scalpel when used in total thyroidectomy significantly reduced blood loss and operating time. However, the overall mean difference appeared small, and with the availability of the newer version of LS this difference may become even smaller, and therefore may not be clinically relevant There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices.
(Upadhyaya et al., 2016) Meta-analysis 7 RCTs with 981 patients	Open Thyroidectomy Surgical time UES n=492 patients0 vs LS/EBVS N=489 patients)	UES P=0.02					The meta-analysis indicated superiority of Harmonic Scalpel only in terms of surgical time compared with LigaSure hemostasis techniques in open thyroid surgery. The postoperative morbidity was not affected. The results of the present study may be useful for high-volume centers performing numerous thyroidectomies every day.
(Contin et al., 2013) Meta-analysis 34 RCTs with 3875 patients in final meta-analysis	Open Thyroidectomy Operation time RTCs had three-arm or two-arm parallel group design: HS vs. LS (3 trials, 471 patients)	UES P =0.032					This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices. The 23 min saved in operative time associated with HS may be beneficial for high volume centers performing many thyroidectomies a day, but not for institutions with a low operation volume.

(Garas et al., 2013) Meta-analysis 35 RCTs with 2,856 Total patients	Thyroid Surgery Hypoparathyroidism (permanent) Pair-wise comparisons within RCTs: ultrasonic coagulation vs Ligasure (5 studies)	UES p= 0.01*					Ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Ultrasonic coagulation demonstrated the highest risk for RLN paralysis whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile These results can contribute to establishing guidelines for thyroid surgery. AE refers to hypoparathyroidism. Pair-wise comparisons * Network-adjusted score (meta-regression analyses of direct comparisons)
(Luo et al., 2017) Meta-analysis 47 RCTs with 6219 patie**nts**	Thyroidectomy Operation time 2671 patients received Harmonic Scalpel vs 813 patients received LigaSure, 2735 patients were treated with conventional hemostasis	UES (significant, but no P value)					The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods Recorded results were based on pair-wise comparison. Harmonic Scalpel decreased operation time compared with the conventional hemostasis, Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal paralysis compared with conventional hemostatic methods. Pair-wise meta-analysis * Subgroup analysis via pair-wise comparison**
(Pastore et al., 2013) Prospective RCT with 132 men	Laparoscopic Radical Prostatectomy Recovery of urinary Continence (ICIQ-UI score at 180-day follow-up, recovery of erectile function (IIEF-5 score at 180-day follow-up) Group A (LigaSure radiofrequency [RF] scalpels) (n = 66) vs group B (ultrasound [UES] scalpels (n = 66)						In RF group vs US group, recovery of urinary continence at 180 days occurred in 53 (80%) vs 41 (62%) patients (P = 0.048); recovery of erectile function at 180 days occurred in 56 (84%) vs 41 (62%) patients (P = 0.009) At postoperative day 180, better functional outcomes (recovery of continence and erectile function) were found in the RF group (LigaSure) compared with the US group (UltraCision).

Ultrasonic Energy Device vs Conventional Crush-clamping Technique

In comparisons of ultrasonic energy device and conventional clamping (see Table 2-17), the Harmonic Scalpel generally outperformed traditional hemostatic techniques in the clinical outcome of operative time during thyroid surgery (Contin et al., 2013; Garas et al., 2013; Luo et al., 2017). Meta-analyses of thyroid surgery also showed that Harmonic Scalpel was also associated with lower intra-operative blood loss (Garas et al., 2013; Luo et al., 2017) and had the lowest risk of definitive recurrent laryngeal paralysis when compared with conventional hemostatic methods (Garas et al., 2013).

The liver crush clamp technique is used In hepatic parenchymal transection to crush liver tissue without destroying hepatic vascular or ductal structures of the liver, thereby reducing excessive blood loss (Aragon and Solomon, 2012). The surgeon uses basic surgical clamps to crush the hepatic parenchyma as he grasps the tissue between his fingers, enabling him to expose and isolate small vessels and biliary radicals. The crush-clamp method is viewed as a point of reference for all other hepatic parenchymal transection techniques (Aragon and Solomon, 2012). In a comparison of the Cavitron Ultrasonic Surgical Aspirator (CUSA), a multifunctional instrument, vs the crush-clamp technique, CUSA did not exhibit any significant advantage over crush-clamping. No differences were observed between the two groups of patients who underwent these techniques in operating time, complications, or length of hospital stay (Alexiou et al., 2013).

Table 2-17: Ultrasonic Energy (UES) Device vs Conventional Crush-clamping (CC) or Other Conventional Hemostatic Technique

	No significant statistical difference in outcome between UES and CC
	UES had a statistically significant better outcome than CC
	CC had a statistically significant better outcome than UES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Alexiou et al., 2013) Systematic Review and Meta-analysis (15 trials [8 RCTs and 7 non-randomized studies) with 1539 patients	Liver Resection Blood loss during the operation and/or the transection Clamp-crushing technique (CC) (n=111 patients) vs Cavitron Ultrasonic Surgical Aspirator (CUSA) (n=111 patients)						CUSA did not exhibit any significant advantage over CC
(Cannizzaro et al., 2016) Systematic review and meta-analysis Total: 14 RCTs with 2293 patients:	Open thyroidectomy Operating time Focus Harmonic scalpel (FHS) versus conventional techniques (classic ligation with/without electrocoagulation): 12 studies: 968 patients with FHS (968 patients) vs classic ligation w/wo electrocoagulation (n=952 patients)	UES p = .000	UES p = .000			UES p = .000	Outcomes were recorded for both Focus Harmonic scalpel vs conventional techniques (knot and tie with/without electrocoagulation); and for Focus Harmonic scalpel vs classic ligation with/without electrocoagulation. In total thyroidectomy, the Focus Harmonic scalpel is a reliable and safe tool. This meta-analysis confirmed that its use is more effective than conventional techniques in terms of operative time, blood loss, and length of stay, with a statistically and clinically difference in results.

(Contin et al., 2013) Meta-analysis 34 RCTs with 3875 patients in final meta-analysis	Open Thyroidectomy Operation time RTCs had three-arm or two-arm parallel group design: HS vs. LS (3 trials, 471 patients)	UES P < 0.001					This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices. The 23 min saved in operative time associated with HS may be beneficial for high volume centers performing many thyroidectomies a day, but not for institutions with a low operation volume.
(Garas et al., 2013) Network meta-analysis 35 RCTs with 2,856 Total patients	Thyroid Surgery Hypoparathyroidism (permanent) Pair-wise comparisons within RCTs: ultrasonic coagulation vs "clamp-and-tie" (24 studies)	UES p= p=0.03	UES p<0.01				Of the three modalities, ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Conversely, ultrasonic coagulation demonstrated the highest risk for RLN paralysis whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile but was followed by "clamp-and-tie" and finally Ligasure. These results can contribute to establishing guidelines for thyroid surgery. AE refers to hypoparathyroidism.
(Luo et al., 2017) Meta-analysis 47 RCTs with 6219 patients	Thyroid Surgery Harmonic Scalpel vs Conventional Hemostasis Operation time 2671 patients received Harmonic Scalpel, 2735 patients were treated with conventional hemostasis	UES 95 % CI -28.11 to -20.44 min, P<0.001	UES 95 % CI -56.011 to -16.329 ml, P<0.001	UES OR 0.275, 95 % CI 0.102–0.745, P = 0.011			The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods. Recorded results were based on pair-wise comparison. Harmonic scalpel decreased operation time compared with the conventional hemostasis, Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal paralysis compared with conventional hemostatic methods.

Comparative Studies: Conclusions

The critical analysis of the clinical data within this CER (see Benefit/Risk Analysis in Section 7 as well as the analysis provided within this section sufficiently determines and supports each of the four main types of energy-based therapies, which are represented by the subject devices, as state of the art tools for surgical cutting, dissection, and coagulation. All energy-based devices exhibited overall advantages over conventional non-energized techniques of cutting, dissection, and coagulation in terms of surgical time, blood loss, and a majority of complications.

Both advanced bipolar devices and ultrasonic surgical instruments, as the two representatives of advanced energized devices, were generally associated with superior clinical safety and performance outcomes relative to conventional electrosurgical devices. However, there is no consensus over which advanced energy-based device is superior overall in vessel sealing across a wide range of traditional and minimally invasive surgical procedures. The Harmonic Scalpel appeared to result in more favorable outcomes when compared to advanced bipolar vessel sealing devices, particularly LigaSure, in multiple studies of thyroid surgery. However, other evidence supported the superiority of electrothermal advanced bipolar vessel sealing devices over ultrasonic energy surgical devices in laparoscopic colorectal surgery (Di Lorenzo et al., 2012) and laparoscopic radical prostatectomy (Pastore et al., 2013).

The reviewed comparative studies on energy-based systems demonstrated an overall advantage in terms of safety and performance outcomes for bipolar electrosurgery in tonsillectomy and TURP and for ultrasonic energy in cholecystectomy, when these techniques were compared with monopolar electrosurgery. Jiang et al.'s meta-analysis of studies on laparoscopic cholecystectomy reported superior outcomes for ultrasonic surgery compared with monopolar electrosurgery, but the merit of these results might be limited because many of the trials included only three or fewer studies. Furthermore, despite the benefits of ultrasonic surgery, the higher cost of ultrasonic instruments compared with standard electrosurgical devices may make their use prohibitive for numerous surgeons and health care centers (Jiang et al., 2017). Additionally, ultrasonic surgical devices generate aerosol plume, which poses a health hazard for both patients and OR staff.

In patients who underwent hepatic resection, there was no difference in clinical outcomes of surgical time, complications and length hospitalization in patients treated with the crush-clamp technique versus the Cavitron Ultrasonic Surgical Aspirator (CUSA) (Alexiou et al., 2013). It is not known if a different ultrasonic surgical dissector would have yielded different outcomes.

The clinical outcomes of the included studies seem to suggest that bipolar and advanced bipolar technologies, as well as ultrasonic surgical devices, are superior to conventional monopolar electrosurgery. However, this conclusion might be misleading because it does not take into account the many evidence-based benefits of standard monopolar technology, including its established longer history of use, preference by numerous clinicians, similar rates of overall efficacy compared with advanced bipolar electrosurgery in some studies, relatively low re-operation rates, and continually decreasing rates of the complication of TUR syndrome in prostate surgery.

TUR syndrome, or dilutional hyponatremia, resulting from irrigation using hypotonic/hypo-osmolar nonconductive fluids, is traditionally one of the most important disadvantages of monopolar electrosurgery. In bipolar electrosurgery, there is minimal if any risk of TUR syndrome because irrigation is performed in a conductive rather than nonconductive medium. Although this difference is often used as a rationale for utilizing bipolar technologies in prostate procedures, the literature reveals that TUR syndrome can still occur in B-TURP, since bipolar electrosurgery does not prevent fluid absorption. Moreover, TUR is statistically not necessarily a high risk for most monopolar electrosurgical

procedures, as evidenced in some studies that compared M-TURP with B-TURP (Singh et al., 2005; Srivastava et al., 2016). TURP remains the reference standard, and according to some sources, the gold standard, for the operative treatment of benign prostatic hyperplasia (BPH) due to the longevity of outcomes and overall low occurrence adverse events (Muslumanoglu et al., 2012).

Compared with cold/blunt dissection, electrodiathermy (electrosurgery) was associated with a significantly shorter surgical time and considerably less blood loss in patients who underwent tonsillectomy. The benefits of monopolar electrosurgery underscore the maturity of a technology that has advanced considerably beyond manual cutting that has been used in surgical operations for millennia. One of the primary advantages of monopolar electrosurgery is the ease with which it can be used, its familiarity to many operators, and its relatively low cost, rendering equipment affordable to individual surgeons and to surgical clinics. The current literature review demonstrates that standard electrosurgery is associated with overall acceptable rates of performance, efficacy, and safety in regard to multiple surgical tasks across different anatomical therapeutic areas, including tonsillectomy, TURP, and laparoscopic cholecystectomy.

Advanced energized surgical devices, consisting of EBVS and ultrasonic instruments, utilized in contemporary surgery, are associated with a significantly shorter operating time, lesser

perioperative bleeding, and lesser postoperative pain. It bears repeating that the findings reported across studies do not consistently demonstrate the superiority of one form of energized surgery tool over the other. As in the utilization of monopolar and standard bipolar electrosurgical devices, the selection of a particular advanced energized surgical devices may ultimately depend on surgeon preference, based on factors such as cost, skill in using the instrument, type of surgical operation, and patient characteristics.

Hemostasis in various surgeries such as thyroidectomy remains a paramount goal after preserving vital structures. Advanced electrothermal bipolar vessel sealing technology and ultrasonic dissectors have been shown to significantly decrease surgical times without increasing costs or complications (Materazzi et al., 2017). While these instruments result in a significant elevation of temperature in the tissues, the temperatures they produce are never as high as those of standard monopolar electrosurgery. In clinical scenarios where small bleeding occurs in close proximity to critical structures, energy devices pose considerable risk. The use of clamp and tie may not always be technically feasible in these anatomical regions, making adjunctive hemostatic agents the preferred method of controlling bleeding in these cases (Materazzi et al., 2017).

Overall, however, energized surgical devices, in general, and advanced bipolar and ultrasonic energized devices, in particular, have dramatically enhanced the surgeon’s armamentarium with options for safely and effectively achieving hemostasis in a wide range of both open and laparoscopic surgical procedures. Although conventional electrosurgical devices, including monopolar and standard bipolar instruments, performed less efficiently than advanced energy devices in coagulation for sealing larger vessels (> 3mm), basic electrosurgical instruments were adequate and sometimes the preferred modality for tissue cutting and dissection in some studies. Monopolar electrosurgical devices are

therefore an appropriate option for physician and surgeon use in the appropriate therapeutic spaces based on their experience, patient needs, and surgical requirements for tissue dissection, coagulation, and in the case of the Endopath Probe Plus II and Megadyne All-In-One, for surgical irrigation, and fluid evacuation.

When assessing multiple surgical functions across diverse therapeutic areas, the literature supports the safety and performance of the four categories of subject devices in comparison to alternate therapies utilized within the same surgical spaces and intended use.

GUIDELINES

The use of energy-generating equipment, including electrosurgical units (ESUs), lasers, and argon beam coagulators used for tissue dissection and coagulation poses a risk for unintended injury if these items are used incorrectly. Some guidelines, including the Association of periOperative Registered Nurses (AORN) "Guideline for safe use of energy-generating devices" provide guidance on the use and maintenance of devices that deliver energy in the forms of radiofrequency waves, ultrasound waves, or lasers (Eder, 2017). Electrosurgical equipment used in perioperative settings potentially can cause thermal injuries (including burns to surgical and nursing staff), interfere with implanted devices, ignite fires and generate detrimental plume that can adversely affect both patients and perioperative personnel.

Therefore, current evidence-based guidelines on energy-based devices address precautions to mitigate the risk associated with electrosurgical units, particularly during minimally invasive surgery; fire safety practices the safe use of these instruments in patients who have an implanted electronic device; and actions to take following an injury or equipment failure during the use of an energy-generating device (Eder, 2017).Published guidelines for energy-based devices are limited and primarily include publications issued by AORN on the use of energy-generating devices for Perioperative RNs. These guidelines are applicable to a wide range of health care practitioners and surgical technicians who work in the presence of a large number of energy generating devices used in the OR. However, only some of the guidelines identified in the current literature are based on systematic literature reviews as described below (see **Table 2-18**).

Table 2-18: Examples of Current Guidelines for Energy-based Surgical Devices

Tonsillectomy using ultrasonic scalpel Interventional procedures guidance [IPG178] Published date: June 2006	AORN Recommended Practices for Electrosurgery	AST Standards of Practice for Use of Electrosurgery (AST, 2012).
Published in June 2006	Effective July 1, 2009. Originally published March 1985, *AORN Journal.*	2012

Tonsillectomy using ultrasonic scalpel Interventional procedures guidance [IPG178] Published date: June 2006	AORN Recommended Practices for Electrosurgery	AST Standards of Practice for Use of Electrosurgery (AST, 2012).
Makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund the procedure	These recommended practices provide guidance to perioperative nurses in the use and care of electrosurgical equipment, including high frequency, ultrasound, and argon beam modalities.	To support healthcare facilities (HCF) and reinforce best practices related to electrosurgery safety in the perioperative setting. The purpose of the Standards is to provide an outline that surgical team members can use to develop and implement policies and procedures for electrosurgery safety. The Standards are presented with the understanding that it is the responsibility of the HCF to develop, approve and establish policies and procedures for electrosurgery safety, per established HCF protocols
The medical literature was searched to identify studies and reviews relevant to ultrasonic scalpel for tonsillectomy. Searches were conducted via the following databases, covering the period from their commencement to August 2005 MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.	These recommended practices address all of these technologies and do not endorse any specific product.	Measurable criteria include educational standards as established by the Core Curriculum for Surgical Technology.
Narrative literature review with expert conclusions based on current evidence on the safety and efficacy of tonsillectomy using ultrasonic scalpel appears adequate to support the use of this technique provided that normal arrangements are in place for consent, audit and clinical governance.	These recommended represent what is believed to be an optimal level of practice.	The publication consists of 14 **Standards of Practice** researched and written by the Association of Surgical technologists (AST) Education and Professional Standards Committee.
The Specialist Advisers did not have any particular concerns about the efficacy of this procedure but noted that the evidence base was still small and that a number of the studies had methodological limitations. The Specialist Advisers stated that the	Electrical Surgical Units (ESUs)and accessories should be selected based on safety features that minimize patient and personnel injury. the risk of alternate site injuries. the risk of insulation failure and capacitive coupling injuries, the	"CSTs are knowledgeable of the risks, patient and surgical personnel hazards and safety principles associated with the use of ESU and accessory items."

Tonsillectomy using ultrasonic scalpel Interventional procedures guidance [IPG178] Published date: June 2006	AORN Recommended Practices for Electrosurgery	AST Standards of Practice for Use of Electrosurgery (AST, 2012).
safety is much the same as for any other method of tonsillectomy, however it appeared that there is a slight increase in postoperative hemorrhage compared with cold steel dissection.	risk of unintentional activation.	
-Nine comparative studies, including three randomized between-patients' comparisons and three within-patient comparisons -Six studies assessed pain following tonsillectomy using ultrasonic scalpel, cold steel dissection or diathermy. Return to normal diet or appetite was assessed in four studies.	66 References were cited; no further information provided.	Risk factors identified with the use of electrosurgery included fire, patient burns, surgical personnel injuries, and biological hazards, such as plume, which are addressed by safety standards.

2.4. Maturity of Technology

Energy-based systems involving monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, ultrasonics, and hybrid configurations of two or more of these systems have become the standard of care in cutting, dissection, coagulation, and in some cases, additional functions required for MIS in diverse anatomical regions. Energy-based instruments are commonly used to perform various gastrointestinal as well as hepatic, gynecologic, thoracic, urologic, and spinal procedures. These technologies collectively provide state-of-the-art interventions whose safety and efficacy have been demonstrated in multiple studies, as discussed in Section 2.3.

Historically, the origins of electrosurgery can be traced to the first use of electrocautery in the early 1800s. The predecessor of the contemporary electrosurgical devices was invented in the 1920s and used therapeutically until a smaller unit was manufactured in the 1960s. In current clinical practice, electrosurgery, including electrosurgical instrumentation, plays a critical role in laparoscopic surgery, utilizing various devices inserted into the surgical field, sometimes through a trocar sleeve. These instruments are used routinely in surgical operations, both traditional open and minimally invasive, to provide essential functions of tissue cutting, dissection, and coagulation (Rozner and Jones, 2012).

Laparoscopic surgery often requires drainage of fluids and irrigation of wound surfaces in order to render them clean and sufficiently visible to the surgeon (Ferreira, 2015). In traditional electrosurgery, an irrigator is used to clear debris or blood from bleeding, whereas a suction pump or central vacuum supply system may be employed to remove irrigation fluid or intraperitoneal air and smoke. Alternatively, a large suction-irrigation probe may be utilized to remove blood clots in cases of abrupt bleeding. Only a limited number of electrosurgical combined suction-irrigation devices are currently on

the market that simultaneously perform versatile functions, including blunt dissection, coagulation, irrigation, and fluid suction (e.g., the Endopath Probe Plus II and Megadyne All-in-One, two subject devices of this SOA Report, and the GORDTS/CAMPO coagulating suction and irrigation cannula by Karl Storz).

Monopolar electrosurgical devices such as the Ethicon Endopath Electrosurgery Probe Plus II and Megadyne All-In-One perform multiple functions of tissue dissection, coagulation, irrigation, and fluid evacuation (resulting in desiccation), which are essential for laparoscopic surgical procedures. The Endopath Electrosurgery Probe Plus II operates with electrosurgical generators and has high frequency maximum voltage of 5750 Volts peak. The device leverages seven interchangeable shafts of different lengths and two types of interchangeable handles that allow for a variety of handle/shaft configuration to meet the surgeon's needs. The shafts are designed for use through a 5 mm, 10 mm, or larger diameter trocar with a 5 mm reducer. Shaft EPS13 permits the introduction of a non-conductive flexible device, such as a laser, through the side port of shaft (IFU P40237P13).

Table 2-19: Ethicon & Megadyne Energy-based Surgery Subject Devices

Ethicon & Megadyne Energy-based Surgical Products as categorized on Website
Monopolar Electrosurgery
Ethicon Endopath Probe Plus II
Megadyne All - In One® Hand Control Device
Megadyne Ace Blade 700 Soft Tissue Dissector
Megadyne E-Z Pen™
Megadyne Mega 2000, Mega Soft, Universal, Universal Plus Reusable Patient Return Electrodes
Megadyne Disposable Patient Return Electrodes
Megadyne Suction Coagulators
Megadyne Mega Power Generator with ACE Mode
Bipolar Electrosurgery
Megadyne Reusable Electrosurgical Bipolar Forceps
Advanced Bipolar Electrosurgery
Enseal
Ultrasonic Surgery
Harmonic Scalpel

As a multifunctional monopolar energy-based device, the Endopath Electrosurgery Probe Plus II can be used with irrigation and suction devices that are compatible with monopolar electrosurgery units. Shaft EPS11 allows increased capacity of suction (10 mm) with irrigation and without electrosurgery (IFU P40237P13). Ergonomics for user control includes a pistol or pencil grip as well as options for foot control or hand control. Cutting and coagulation can be achieved with the use of the appropriate configuration of electrodes, including the Hook Electrode, Spatula Electrode, Curved Dissector Electrode, and L-hook Electrode, placed with either a 29 cm length or 34 cm length shaft (IFU P40237P13).

The various capabilities of electrosurgical devices are typically achieved using electrodes of three basic shapes: needle tip, spatula, and L-hook or J-hook. Electrodes with hooks or narrow tips allow concentration of current and power and are therefore generally used in tissue vaporization and cutting (Munro, 2012). Active electrodes characterized by a slightly larger surface area, ball-shape, or grasper-shape are suitable for achieving hemostasis (Munro, 2012). An electrode with a wide surface is advantageous for initiating coagulation, the effect of which can be increased by physical maneuvers to decrease the amount of tissue to coagulate (Dargent and Sergio, 2005). The versatility of electrodes in this subject device provides multiple options for performing crucial surgical tasks.

The Megadyne All - In One® Hand Control Device is designed as a hand controlled monopolar electrosurgical tool that provides irrigation, aspiration and electrosurgery in a single device. This instrument is intended to conduct monopolar electrosurgical energy from an electrosurgical generator to target tissue. It is suitable for use whenever monopolar electrosurgical cutting and coagulation are indicated. The modified tips of this device are totally insulated. The Megadyne All-In-One® Hand Control Device is configured for use with Coated Laparoscopic Electrodes that resist splitting up to 700° and minimize risk of damage to surrounding tissue. These features are designed to save surgeons time during a procedure. A damp sponge wipe is sufficient for cleaning the electrode (IFU 3000016-02).

Megadyne Electrosurgical Pencils have an ergonomic and lightweight design that is comfortable and minimizes fatigue. The water-resistant construction minimizes electrical shocks and inadvertent activations. The device is equipped with cords that are flexible and "memory-free" for easier handling of the pencil. With the option of a Push Button or Rocker Switch configuration, Megadyne Electrosurgical Pencils are available with E-Z Clean or stainless steel blade electrodes. The product line includes the Megadyne Reusable E-Z Pen™ with an innovative safety lockout mechanism that prevents usage after 12 applications. The 12-use life span promotes cost efficiency. The E-Z Clean PTFE coating on the Megadyne Reusable E-Z Pen™ lasts longer and requires less cleaning than other coatings (IFU 3000009-02).

Other Megadyne monopolar electrosurgical products include Patient Return Electrodes and Suction Coagulators. The Patient Return Electrodes eliminate the small disposable sticky pad that can damage the patient’s skin. The Suction Coagulators provide precise coagulation with controlled fluid evacuation and feature an ergonomic handle combined with a flexible, kink-resistant cannula to maximize suction. The ergonomic configuration allows the surgeon to customize the instrument to the specific procedure at hand. While the ergonomic handle reduces fatigue over time, the bendable shaft facilitates precise application and the integrated guard prevents user shocks (IFU 3000137-01).

The Megadyne portfolio of energized surgical products includes a novel monopolar device, the Megadyne Ace Scalpel, that provides a fourth mode of electrosurgical cutting called the Advanced Cutting Effect (ACE). This device achieves a scalpel like cutting effect that results in little to no thermal necrosis as well as no hemostasis. It utilizes proprietary software to maintain a constant voltage at the tip of the electrode rather than constant power like traditional Cut modes (IFU 3000158-01).

The importance of smoke evacuation during electrosurgery was discussed in Section 2.2.1.2.1.1. To help meet this need, Megadyne manufactures or distributes multiple smoke evacuation systems designed to remove smoke from the OR during either open or laparoscopic surgery. These devices include the Mega Vac smoke Evacuator (2100), Mega Vac PLUS Smk Evac, Laparoscopic Mode (2200), Charcoal Filter Mega Vac Smoke Evacuator (2220), Mini Vac Smoke Evacuators 120v (ECVV120), Fluid Trap Mini Vac Smoke Evacuator 220V (ECVV220), and RF Sensor Mini Vac Smoke Evacuator (MGEZLINK01).

Megadyne also produces Smoke Evacuation Pencils for electrosurgery intended for use with various smoke evacuators. These devices facilitate precise electrosurgery while minimizing the hazards of inhaling surgical smoke. The Zip Pen™ Smoke Evacuation Pencil provides surgeons with three ergonomic use options to maximize comfort and functionality. The Zip Pen has ergonomic features that promote significantly less torque on the back end of the pencil compared with both standard smoke evacuation pencils and standard non-smoke evacuation pencils. The lightweight design helps to minimize hand fatigue, while allowing surgeons to experience both comfort and precision.

The Zip Pen incorporates the Megadyne patented E-Z Clean® coated electrode technology designed to decrease eschar buildup during surgery, thereby potentially increasing the safety of the OR environment. In addition, Zip Pen is equipped with large activation buttons for ease of use, full 360 degree swivel capabilities for maximum procedural flexibility and a safety grip for comfort and control. The buttons have a tactile “pop” which provides positive and instant feedback for activation and deactivation of electrosurgical energy. An innovative “one-size-fits-most” connector allows the ZIP Pen to easily connect to smoke evacuators.

The Megadyne Reusable Electrosurgical Bipolar Forceps is a bipolar electrosurgical device intended to provide improved safety and performance compared to traditional bipolar electrosurgical instruments. In addition to state-of-the-art cutting functions, this device has a disposable suction coagulator that allows precise coagulation in conjunction with controlled fluid evacuation. Substantial re-bleeding and scarring are common adverse events triggered by tissue adherence during surgery. To help mitigate this problem, the Megadyne Reusable Electrosurgical Bipolar Forceps are crafted with highly polished tips designed to reduce tissue adherence. The light closing force causes less fatigue for the surgeon over time. This device is manufactured from lightweight, highly durable stainless steel and coated with a nylon material that resists abrasion and provides superb insulation. It has a precision tip alignment to aid fine control and it greatly reduces the risks of user error or equipment malfunction. This capacity for precision potentially may reduce the threat of removing coagulum from sealed vessel (NR7 4001 Rev C 2012-11).

The Megadyne Mega Power® Generator is an innovative electrosurgical unit (ESU) that provides a Proprietary Advanced Cutting Effect (ACE) mode. Built to work in tandem with the ACE Blade, it is designed to provide a scalpel-like cutting effect for minimal thermal necrosis and reduced scarring. This device can be used with the Monopolar Footswitch (3-meter cable), Bipolar Footswitch (3-meter cable), and /or Monopolar Adapter that comes with the Generator. The unit is equipped with Constant Control

Technology installed to automatically monitor tissue impedance and adjust power output to diminish tissue damage and drag. The Megadyne Mega Power® Generator is intended to facilitate smooth, clean, accurate cutting effect at the lowest possible setting for maximum patient safety (IFU 3000158-01).

Advanced bipolar instruments can quickly achieve consistent vessel sealing within seconds at seal bursting pressures significantly above physiologic blood pressure levels (Park and Porteenier, 2012). By alerting the surgeon when the desired tissue effect has been achieved, the audio signaling system helps to mitigate against potential device-related injuries. These types of alert systems have been credited with minimizing charring (and grasper sticking during release) and lateral thermal spread that may be associated with prolonged device activation (Law et al., 2014). One of the defining features of state-of-the-art advanced bipolar electrosurgical devices, is impedance monitoring with grasper designs that optimize mechanical pressure delivery to the vascular pedicle. This configuration optimizes the vessel-sealing capabilities of advanced bipolar electrosurgical devices. The Ethicon Enseal Seal Tissue Sealing and Hemostasis System includes multiple advanced bipolar electrosurgical devices that employ nanotechnology to control energy at the electrode–tissue interface. The jaws contain a temperature-sensitive matrix with embedded conductive carbon spherules that “sense” tissue characteristics. These technologically advanced graspers utilize extremely high jaw compression to create uniform tissue effects. Ethicon Enseal Seal Tissue Sealing devices do not require a dedicated electrosurgical unit for use. Instead, the adapter allows it to function with most generators (P40632P01, P40627P04).

Ethicon EndoSurgery Harmonic Scalpel Devices are multifunctional ultrasonic surgical dissector-shears used to perform coagulation and transection of tissue, vessel sealing, and fluid evacuation. These devices employ ultrasound technology (high-frequency ultrasonic transducer - 55,000 cycles/second) to cut tissues while simultaneously sealing the edges of the cut. They are used in open and/or endoscopic procedures, depending upon the specific Harmonic device. Clinical evidence reveals that the Harmonic Scalpel seals vessels ≤5mm with decreased operating time and intraoperative blood loss. The Harmonic ACE+7, another product in this line, has received FDA clearance for sealing of vessels up to 7mm (IFU P000162P01).

The Ethicon Endo-Surgery (EES) Generator for HARMONIC® and ENSEAL® has a universal connector and automatic instrument recognition. It has a universal connector, automatic instrument recognition, a touchscreen for easy setup and operation, and a high-resolution display with wider viewing angles. Software updates to ensure that the system is operating optimally are available via USB memory stick. The compact design that takes up less space in the OR, promoting the spatial economy of this device (HARH23).

From: (Sankaranarayanan et al., 2013), Manufacturers' Marketing Literature

Table 2-20: Examples of Energy Devices in Open and/or Minimally Invasive Surgery

Type	Product Name
Monopolar Electrosurgery	▪ Covidien / Valleylab Opti4™ ▪ Encision AEM™ ▪ Ethicon Endopath Probe Plus II ▪ Megadyne All - In One® Hand Control Device ▪ Megadyne Ace Scalpel ▪ Megadyne E-Z Pen™ Electrosurgical Pencils ▪ Megadyne Suction Coagulators ▪ Megadyne Mega Power Generator with ACE Mode ▪ Covidien SURGIWAND™ ll ▪ Stryker StrykeFlow 2
Bipolar Electrosurgery	▪ Megadyne Reusable Electrosurgical Bipolar Forceps ▪ Gynecare Versapoint Bipolar Electrosurgical Hysteroscopic System ▪ Ethicon Endopath Bipolar Forceps ▪ Olympus Gyrus Medical PKS Cutting Forceps
Advanced Bipolar Electrosurgery	▪ Covidien LigaSure™ Olympus PKS Bipolar System – Laparoscopic Loop (BiLL), HALO PKS Cutting Forceps, PKS™ Cutting Forceps, PKS PlasmaSord, PKS Omni, PKS SEAL Open Forceps ▪ Ethicon EnSeal™
Ultrasonic Energy	▪ Ethicon Ultracision Harmonic Scalpel ▪ Ethicon Harmonic ACE ▪ Ethicon Harmonic FOCUS ▪ Olympus SonoSurg ▪ US Surgical Corp / Covidien AutoSonix ▪ Covidien Sonicision™ Cordless Ultrasonic Dissection Device
Laser Energy	▪ Most commonly referred to their type than a product name. ▪ Nd: YAG laser (neodymium-doped yttrium aluminum garnet) ▪ Argon laser ▪ CO_2 laser
Argon Beam Coagulator	▪ System 7550™ ABC® ▪ Cardioblate®
Radio Frequency (RF) Energy	▪ RF 3000® Radiofrequency Ablation System ▪ StarBurst® ▪ Cardioblate®

2.5. Summary of Safety and Performance within the SOA

Since its inception and widespread use almost a century ago, energy-based surgery has been improving steadily with the myriad of surgical techniques and variants with a focus on performing the essential functions of tissue cutting, dissection, and coagulation. This is especially needed in the laparoscopic field where non-energy-based surgical instruments alone prove to be difficult to use in dissection. However, the risks inherent in the nature of the technology used continue to persist even into the current era, such as electrothermal injury due to accidental direct application of the device. These risks have since been mitigated steadily through improved technologies and improvements in device designs. Indeed, advanced versions of these electrosurgical instruments are already being developed and with some being already in use to answer the shortcomings of the current technology (Law et al., 2014).

The key safety and performance safeguards summarized in the state-of-the-art literature review in Section 2 concludes that use of electrosurgical devices provided the following benefits:
(Bukhari and Al-Ammar, 2007) (Lin et al., 2006) (Singh et al., 2005) (Srivastava et al., 2016)

- Decreased Blood Loss
- Increased Wound Healing
- No Adverse Events (AE's)
- Decreased Operative Time
- Decreased Complications

Additionally, the state-of-the-art literature review found that technologies and advanced device designs are further reducing the inherent risks involved in the use of the subject devices thus increasing performance outcomes with:

- Warning systems: audio signaling, visual display, auto shut off
- Temperature controls
- Minimized use of power to minimize patient injury while performing its intended effects

The state-of-the-art Section 2.2.1 Therapeutic Alternatives/Treatment Options states:

> More than 80% of surgical procedures performed in the current clinical environment utilize advanced devices such as electrosurgical instruments (Meeuwsen et al., 2017).

The state-of-the-art Section 2.3 Comparative Studies Conclusion states:

> The current literature review demonstrates that standard electrosurgery is associated with overall acceptable rates of performance, efficacy, and safety in regard to multiple surgical tasks across different anatomical therapeutic areas, including tonsillectomy, TURP, and laparoscopic cholecystectomy.

3. SUBJECT DEVICE DESCRIPTION

3.1. Design and Specifications – Both Subject Devices (Equivalent)

According to the Device Master Records for the subject devices (ENG-DMR-015, ENG-DMR-008, **Windchill**), the Megadyne Electrosurgical Generators have application in open and laparoscopic procedures and are intended as a general-purpose electrosurgical generator. The generators are designed to produce radio frequency (RF) current for cutting and coagulation, to be delivered to target tissue through an accessory electrode. The Megadyne Electrosurgical Generators are high frequency and are microprocessor controlled with isolated output. The generators have the ability to perform both monopolar cutting and coagulation and bipolar coagulation of tissue in a wide range of surgical applications.

The new footswitch accessory (purchased separately) is intended to provide a foot control option (in addition to hand control) for bipolar outputs only.

For reference, the Equivalence Table 4-2 in Section 4 compares in detail the design specifications and function of the new line extension Ethicon Megadyne Electrosurgical Generator to the existing Megadyne Mega Power Electrosurgical Generator.

3.1.1. Megadyne Electrosurgical Generators - Design and Function

The Megadyne Mega Power® Electrosurgical Generator and Ethicon Megadyne Electrosurgical Generator are both microprocessor controlled, isolated output, high frequency generators designed for use in cutting and coagulating of tissue. The Generators have the ability to perform both monopolar cutting and coagulation and bipolar coagulation of tissue in a wide range of surgical applications (ENG-DMR-008, ENG-DMF-015, **Windchill**).

The Megadyne Electrosurgical Generators are designed to provide the surgeon with a wide series of power, voltage, current, and frequency within the optimal range for each compatible instrument and the associated electrosurgical surgical modes. The front panel user interface has been incorporated to provide the operator with information, control, and feedback during use. The generator provides electrical power to the radiofrequency to the surgical instruments (electrodes) for optimal direct application to tissues.

Instrument hand-switch inputs and an optional footswitch are provided to the surgeon to control power activation. The round Bipolar pedal in blue activates power for BIPOLAR modes for coagulation of tissues.

3.1.1.1. Primary Functions and Features

The primary functions and features for both subject devices are presented below. The slight differences in nomenclature and/or function between the equivalent subject devices are also included in the IFU/Owner's Manual documentation (3000158-01 and 3000315-01, **Windchill**) below:

Isolated Output – The system output and return path are isolated from earth ground. This insures that the safety of the patient and the user are maintained and that burns are not going to occur.

Three Monopolar CUT Modes - The CUT mode has three settings, GEM (Geometric Electron Modulation), PURE, and BLEND.

- The Megadyne Mega Power Generator CUT mode also has three settings, Advanced Cutting Effect (ACE), Pure CUT, and Blend. *(These are different from the Ethicon Megadyne Generator in name only.)*

Four Monopolar COAG Settings – Four COAG modes are available, COAG 1, COAG 2, SOFT and SPRAY.

- **SOFT COAG - New on the Ethicon Megadyne Generator:** SOFT COAG desiccates tissue at a slower rate with deeper thermal penetration
- *The Megadyne Mega Power Generator does not have SOFT Monopolar COAG Mode.*

Two Bipolar Coagulation Settings – The Bipolar mode shall have two settings, MICRO and MACRO. The Bipolar mode can be operated by either the foot switch or the hand switch on the bipolar instrument.

Bipolar Current Monitor – The current flow through the bipolar instrument is monitored and displayed on a bar graph current meter. The decreasing current is an indication that the tissue is becoming desiccated. There is a frequency change in the optional audible tone that occurs when the current flow reaches a minimum value.

AUTO Bipolar – New on the Ethicon Megadyne Generator: The Auto Start and Stop feature are available with both micro and macro bipolar functions. When selected, the generator senses when the surgeon has contacted tissue with the bipolar forceps and will automatically activate. There are three delay options, none, short and long that are selectable by the user. The auto stop is programmed into the generator and will discontinue the bipolar output when the impedance increases, and the tissue is desiccated.

- *The Megadyne Mega Power Generator does not have AUTO Bipolar function.*

Push button Power Adjustment – The power adjustment of each mode, monopolar CUT, monopolar COAG and BIPOLAR is easily adjusted with the press of a button.

Contact Quality Monitoring (CQM) – Although Megadyne recommends the use of the Mega Soft® family of reusable return electrodes, the CQM system allows use of standard dual foil or single foil disposable return electrodes. The CQM system continuously monitors the patient to pad contact of a dual foil return electrode and will sound an alarm and deactivate the output if an unsafe condition occurs. Likewise, the CQM system will monitor the cable integrity of any return electrode, sound an alarm and deactivate the output if there is a break in either one or both of the conductors of the return electrode cable.

Setup Retention – When the Generator is turned off, the microcontroller retains the last power settings in the memory of the electronics. When the unit is turned on it will start at null settings and can be returned to the last settings used by pressing the Recall button.

Foot Control – An accessory foot control can be purchased for either monopolar (two pedal) or bipolar (single pedal).

- The generator has two connectors for monopolar, one for channel A and one for channel B, and one connector for bipolar.
- The monopolar footswitch will activate the electrode that is either mounted in the pencil or in the foot control receptacle.
- The monopolar footswitch has two pedals, the CUT (LEFT) in yellow activates power for the CUT modes while the COAG (RIGHT) pedal in blue activates the power for COAG modes.
- The footswitch requires more than 10 N to activate each pedal.
- The footswitch weighs 2.91 kg and has a non-skid material on the bottom to minimize sliding.
- The bipolar footswitch activates the bipolar instrument.
- There are two types of Bipolar Footswitch: The Bipolar pedal (1450J) is blue and activates power for Bipolar modes.
- The footswitch requires more than 10 N to activate and weighs 1.67 kg and has a non-skid material on the bottom to minimize sliding.
- **New on the Ethicon Megadyne Generator:** The round Bipolar pedal (1459J) is blue and activates power for the Bipolar modes.
- The footswitch requires more than 10 N to activate and weighs 0.7 kg and has a non-skid material on the bottom to minimize sliding.
- This footswitch is functionally the same as the square shaped Bipolar pedal. The only difference between the two is ergonomic.

3.1.1.2. Operation of Megadyne Electrosurgical Generators

The Megadyne Electrosurgical Generators are non-sterile devices. In use, the generators will stand on a cart or a designated shelf near the operating room table.

Required Accessories

The use of the generator requires the addition of electrosurgical accessories. The required accessories for the operation of bipolar electrosurgery are a set of bipolar forceps (electrodes) and a bipolar footswitch (single pedal for COAG mode only) or a set of hand switching bipolar forceps. For monopolar electrosurgery, the required accessories for operation are the handswitch or footswitch (bipedal for CUT and COAG modes) with their respective active electrodes and a passive return electrode. The existing footswitches (monoploar, bipolar) for the existing Mega Power Generator are compatible with both subject device generators. The new footswitch (1459J) is currently only compatible with the new Ethcion Megadyne Generator.

Operation

The input power switch is an intuitive switch on the front of the generator that is marked with the international symbols for ON and OFF. The modes of operation for CUT and COAG are designated by color codes that are internationally recognized, yellow for CUT and blue for COAG. The bipolar mode is marked in green for the Mega Power Generator and blue for the Ethicon Megadyne Generator. The power settings for these modes are adjusted by touching one of two arrows (there are membrane switches under the arrows). There is an up arrow/button for increasing the power and a down arrow/button for decreasing the power. The plug receptacles for the accessories are unique to each type of accessory.

The Megadyne Electrosurgical Generators performs the operator interaction function by responding to the operator's footswitch and/or hand switch presses, button presses, and by displaying the machine status to the operator. Waveform generation refers to the production of a logic-level waveform that is amplified by device hardware to produce the desired effect. Output control involves real-time feedback control of the Generator output. It adjusts the commanded RF level in accordance with predefined algorithms to produce the best effect consistent with existing load conditions. RF Power Amplification is checked as output current and voltage levels are monitored and limited to prevent injury to the patient or component damage.

3.2. Required and Adjunctive Devices and Accessories Not Included in CER Scope - Identical

The electrosurgical generators for this CER, are a single component of an integrated electrosurgical system, that includes a generator (subject devices), an active electrode and a dispersive/return electrode (monopolar only). The required, adjunctive devices include active electrodes and dispersive return electrodes and are not included within this Megadyne Electrosurgical Generator CER. The Active Accessories are the monopolar hand switching pencils, electrodes, monopolar foot cords, and bipolar cords. Also, there are non-required accessories (footswitches and carts) available for purchase for use with the Electrosurgical Generators. These required and adjunctive devices and accessories are not included with this CER but within their own accessories and electrodes CER's.

3.3. Generator Software

The international standard IEC 62304 for medical device software is a standard which specifies life cycle requirements for the development of medical software and software within medical devices. The software safety class shall initially be assigned based on severity as follows:

- Class A: No injury or damage to health is possible
- Class B: Non-SERIOUS INJURY is possible
- Class C: Death or SERIOUS INJURY is possible

The software classification for the Megadyne Electrosurgical Generators is: Class C, (ENG-WI-005-existing, ENG-SWS-009-new, **Windchill**) based on the software not contributing to a hazardous situation which leads to risk of death or serious injury related to the possible effects on the patient, operator, or other people resulting from a HAZARD to which the SOFTWARE SYSTEM can contribute. There is no risk of death or serious injury arising from a software failure. This falls in line with the ISO Software Classification of acceptability and particularly the IEC 62304:2006 standard.

Electrosurgical Generator Software Applications

Software is incorporated in the microprocessor controlled Megadyne Electrosurgical Generators, including constant controlled technology circuitry. This feature monitors tissue impedance and automatically adjust power output to reduce tissue damage and drag for a smooth, clean, accurate cutting effect at the lowest possible settings. The software is not designed or intended for user interaction.

The Megadyne Electrosurgical Generators are designed for special purpose applications in the domestic and international markets. In serving these applications, the Generator allows the operator to select and adjust the power of three different modes of operation.

1. Monopolar CUT
2. Monopolar COAG
3. Bipolar

To provide these three operating modes, the Megadyne Electrosurgical Generators performs four major functions:

1. Operator Interaction
2. Dosage Control
3. Waveform Generation
4. RF Power Amplification Monitoring Megadyne Electrosurgical Generators

3.3.1. Role of Software in the Device

3.3.1.1. Megadyne Mega Power Electrosurgical Generator Software

The software for the Megadyne Electrosurgical Generators are located in four micro controllers:

1. Master
2. Watchdog
3. Frequency
4. Front Panel

The *Master Controller* is responsible for:

- CQM Analog to Digital Conversion
- High Voltage Power Supply Management
- Output Relay Control
- Relay Sensors
- RF Output Activation
- Activation and Alarm Tones
- PFC Shutdown Sensor
- Front Panel Controller Reset
- RF Mode Control
- Voltage and Current Feedback Analog to Digital Conversion
- Power Control Algorithm
- Serial Peripheral Interface Bus Controller
- RS-232 Communications

The *Watchdog Microcontroller* is tasked with monitoring the Master Controller. All of the analog inputs are wired, in parallel, to the Master and Watchdog (WD). The Watchdog has independent RF shutdown control for the Electrosurgical Generator.

The Watchdog Controller is responsible for:

- CQM analog to digital conversion monitoring
- High Voltage Power Supply monitoring
- Output relay control monitoring
- Relay sensor monitoring
- RF output activation
- RF mode control monitoring
- Voltage and current feedback analog to digital conversion monitoring
- Communications with Master Controller via SPI Bus

The role of the *Front Panel Controller* is to manage the front panel displays. This controller sends out signals to Master Controller to coordinate the actual power output with the displayed settings. This software also has error monitoring capabilities.

The *Front Panel* is responsible for:

- Power Display CUT
- Mode Display
- Bipolar Current Meter display
- CQM Alarm display
- Power LED display

- Display of all Errors
- Communications with Master Controller via SPI Bus

The role of the *Frequency Controller* is to generate square wave patterns that drive the output to create the various waveforms.

Further details regarding the software requirements for the Megadyne Electrosurgical Generators can be found in the Software Requirements documents (ENG-WI-005)

3.3.1.2. Ethicon Megadyne Electrosurgical Generator Software

The software for the Ethicon Megadyne Electrosurgical Generator (ENG-SWS-009, **Windchill**) is located in one micro controller, and is responsible for the following tasks:

- CQM analog to digital conversion
- High Voltage Power Supply management
- Output relay control
- Relay sensors
- RF output activation
- Activation and alarm tones
- PFC shutdown sensor
- RF mode control
- Voltage and current feedback analog to digital conversion
- Power Control Algorithm
- Serial Peripheral Interface Bus Controller
- RS-232 communications
- USB communication
- Power Display CUT
- Mode Display
- Bipolar Current Meter display
- CQM Alarm display
- Power LED display
- Display of all Errors

3.3.1.3. Megadyne Electrosurgical Generator's Software Communication To External Devices

Both Megadyne Electrosurgical Generators have an RS232 port provided for external communications used for data acquisition and calibration. Access to this communication port is located in the back panel behind a removable plate.

Also, a new USB port is provided on the Ethicon Megadyne Generator also located in the back panel, behind a removable plate. The USB port is used for: access to error log, access to activation log and Software updates.

Both communication ports (RS232 and USB) are provided for use by authorized service centers or authorized personnel only. Details of these external communication ports are provided in Software Requirement documents: ENG-SWS-009, **Windchill** (existing device) and ENG-WI-005, **Windchill** (new device).

3.4. Materials and Biocompatibility

3.4.1. Biocompatibility - NA for Subject Devices

The subject device generators are manufactured in accordance with International Standard, EN ISO 10993-1 which states that the biocompatibility of finished medical devices should be evaluated and the devices are considered to be biocompatible when used as intended, based on chemical characterization and biological test results, if applicable. The exact testing required is dictated by several factors, one of which is the tissue contact and duration of contact.

Both subject device generators, including the footswitch (1459J) are non-patient, contact devices. Per the requirements of iso 10993-1, *biological evaluation of medical devices- part 1: guidance on selection of tests,* no biocompatibility testing is required.

3.4.2. Materials – Electrosurgical Generator Subject Devices (Equivalent)

3.4.2.1. Materials for Megadyne Mega Power Electrosurgical Generator

The Mega Power Electrosurgical Generator (equivalent subject device) is an electrical medical device that produces high frequency energy. The materials of construction are electrical components, circuit boards, metal chassis, sheet metal bottom, molded plastic enclosure, membrane switch front panel and electrical cords. The external metal components are grounded when the unit is plugged in whether the power is on or not. This prevents any electrical shock hazard to the user. The electrical components and circuitry reside inside of an enclosure. The enclosure is an aluminum sheet metal enclosure with a reaction injection molded polyurethane cover and a laminated plastic display panel (ENG-DMR-008, **Windchill**). Table 3-1 below lists the materials of construction included in the manufacture of the Megadyne Mega Power Generator.

Table 3-1: Materials of Construction for the Mega Power Electrosurgical Generator

1000 – Mega Power Electrosurgical Generator		
Part Number	**Description**	**Material**
6020062-01	CHASSIS, ESU, W/ARTWORK, REAR CONNECTOR	Coated Aluminum
5600007-04	SCREW, PHILLIPS, FLAT HEAD 6T-32X ½”	Stainless steel
5600008-02	SCREW, PHILLIPS, PAN HEAD, SEMS 6-32X5/16”	Stainless steel
3151269-01	LABEL, ESU OUTPUT CONNECTION INSTRUCTION	Polycarbonate
4600092-01	SWITCH, POWER, FRONT PANEL	Polycarbonate
6020165-01	FRONT COVER WITH ARTWORK	Solid Polyurethane

5600007-05	SCREW, PHILLIPS, FLAT HEAD 6-32X 3/8”	Stainless steel
5800025-01	TOP COVER, ESU	Solid Polyurethane
5600006-04	SCREW, PHILLIPS, PAN HEAD, 8-32 x 5/8”	Stainless steel
4600042-03	WASHER, FLAT #8	Stainless steel
4600023-01	FOOT, RUBBER, 1.0 DIA, 1.0 HIGH	SBR

The Megadyne Mega Power Electrosurgical Generator design for RoHS Compliance was verified with Test Results, Mega Power Electrosurgical Generator, RoHS (ENG-RPT-338, **Windchill**) based on the Megadyne Mega Power Electrosurgical Generator RoHS Compliance Protocol (#1150744-10, **Windchill**). The materials selected for the construction of these devices, with their additives, are fit for their intended purpose with regard to the characteristics and properties of the materials (chemical, toxicological, physical, electrical, morphological and mechanical) required for manufacture of the electrosurgical generator. Functional laboratory tests (per ISO 10993-1:2009 Annex A) were performed per protocol to provide verification that the following generator components meet RoHS ISO 10993-1:2009 Annex A:

- Motherboards
- Power Conversion Boards
- Richco Shoulder Washer
- Monopolar Hand Switch
- Bipolar Hand Switch
- Fan Control
- Foot Control
- Isolated Supplies

The Mega Power Generator RoHS Compliance testing outcomes, supported by more than a decade of clinical use, demonstrate a safe history of use in its physical form when used as intended and reveals no significant potential biological or material hazards.

3.4.2.2. Materials for Ethicon Megadyne Electrosurgical Generator

The Ethicon Megadyne Electrosurgical Generator (MEGEN1) is an electrical medical device that produces high frequency energy. The materials of construction are electrical components, circuit boards, metal chassis, sheet metal bottom, molded plastic display, membrane switch front panel and electrical cords. The external metal components are grounded when the unit is plugged in whether the power is on or not. This prevents any electrical shock hazard to the user. The electrical components and circuitry reside inside of an enclosure. The enclosure is a coated aluminum sheet metal enclosure with a coated aluminum top cover and an acrylic polyvinyl chloride display panel (ENG-DMR-015, **Windchill**). Table 3-2 below lists the materials of construction included in the manufacture of the Ethicon Megadyne Electrosurgical Generator.

Form (Non-PPE) 100503977 Rev3
Quality System CO: 100610371
Franchise Clinical Evaluation Report Template (Shared)

Table 3-2: Materials of Construction for the Ethicon Megadyne Electrosurgical Generator

Protocol	Report	Test Description	Test Category	Results
ENG-PRT-501	ENG-RPT-596	Report, Software Verification/Validation Ethicon Megadyne™ ESU	Software	Pass
ENG-PRT-498	ENG-RPT-611	Electromagnetic Compatibility, Ethicon Megadyne Electrosurgical Generator	IEC Safety	Pass
ENG-PRT-514	ENG-RPT-613	Thermal Testing, Ethicon / Megadyne Electrosurgical Generator, MEGEN1	Design	Pass
ENG-PRT-515	ENG-RPT-614	Ethicon Megadyne ESU Shipping Test	Shipping	Pass
N/A	ENG-RPT-615	Ethicon Megadyne ESU IEC 60601-1 Report	IEC Safety	Pass
ENG-PRT-516	ENG-RPT-617	Ethicon Megadyne ESU Product Specification Verification Report	Design	Pass
ENG-PRT-517	ENG-RPT-618	Ethicon Megadyne ESU Cleaning Report	Design	Pass
ENG-PRT-518	ENG-RPT-619	Ethicon Megadyne ESU Footswitch Specification Verification Report	Design	Pass
ENG-PRT-524	ENG-RPT-625	Summative Usability and Design Validation, Ethicon Megadyne Electrosurgical Generator	Design	Pass
ENG-PRT-529	ENG-RPT-635	Report, Ethicon Megadyne ESU, Thermal Effects on Tissue	Design	Pass
ENG-PRT-536	ENG-RPT-647	Report, Ethicon Megadyne ESU, Labeling Verification	Design	Pass
ENG-PRT-548	ENG-RPT-660	Report, Incremental Software Verification/Validation, Ethicon Megadyne ESU	Software	Pass
ENG-PRT-599	ENG-RPT-689	Ethicon Megadyne ESU Rev H Software Verification Report	Software	Pass
ENG-PRT-611	ENG-RPT-698	Golden Gate Reliability Report	Design	Pass
ENG-PRT-639	ENG-RPT-737	Report, 1459J Round Bipolar Footswitch Shipping Test	Shipping	Pass
ENG-PRT-560	ENG-RPT-673	MEGEN1 ESU Process Validation Report	Process	Pass
500438089	500438090	Golden Gate Auto Bipolar Test Report	Design	Pass

The Ethicon Megadyne Electrosurgical Generator (new subject device) is equivalent to the Megadyne Mega Power Electrosurgical Generator (equivalent subject device) as documented in Section 4. EQUIVALENCE below.

The RoHS Compliance Memorandum (500430815, **Windchill**) for the Ethicon Megadyne Electrosurgical Generator dated 25 April 2018, documents and confirms that the new Ethicon Megadyne Electrosurgical Generator (MEGEN1) and footswitch (1459J) complies with the latest RoHS standards for the EU. The data used to ensure the EU compliance includes certifications, testing results and all documentation required by the EU RoHS based off of the equivalent subject device Test Report, Mega Power, Electrosurgical Generator, RoHS Compliance Master Document (ENG-RPT-338, **Windchill**). EU RoHS compliance is also required to receive the CE Mark for the new subject device.

3.5. Intended Purpose - Identical

The Ethicon Megadyne Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000315-01, **Windchill**).

The Megadyne Mega Power Electrosurgical Generator is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000158-01, **Windchill**).

3.6. Clinical Claims – N/A

There are no clinical claims for the subject devices found in the IFU’s or promotional material.

3.7. Indications - Identical

The Ethicon Megadyne Electrosurgical Generator (new) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000315-01, **Windchill**).

The Megadyne Mega Power Electrosurgical Generator (existing) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000158-01, **Windchill**).

3.8. Contraindications – Identical

There are no contraindications for either subject device per the IFU’s.

3.9. Adverse Events / Side Effects – N/A

Adverse Events / Side Effects

There are no adverse events / side effects for the subject devices described within the IFU's.

3.10. Warnings and Precautions – Similar

The Warnings and Precautions found in both of the Megadyne Electrosurgical Generator's IFU's are nearly the same (highly similar). The Ethicon Megadyne Electrosurgical Generator IFU (3000315-01, **Windchill**) Warnings and Precautions are presented below and the differences, when compared to the Megadyne Mega Power Generator (IFU 3000158-01, **Windchill**), are documented for ease of comparison.

3.10.1. Warnings: Ethicon Megadyne Electrosurgical Generator

- Use the lowest possible power settings to achieve the desired effects. Certain devices or accessories may present a safety hazard at low power settings. For example, with argon beam coagulation, the risk of gas embolism rises if there is insufficient high frequency power to produce a rapid impermeable eschar on the target tissue.
- When the generator is operational, keep active accessories away from the patient and return electrode when not in use, or store in an electrically isolated container in a clean, dry, highly visible area. Inadvertent contact with the patient may result in burns.
- The use of flammable anesthetics or oxidizing gases such as nitrous oxide (N_20) and oxygen shall be avoided if a surgical procedure is carried out in the region of the thorax or the head, unless these agents are aspirated from the area.
- Non-flammable agents should be used for cleaning and disinfection wherever possible.
- Flammable agents used for cleaning or disinfecting, or as solvents of adhesives, should be allowed to evaporate before the application of high frequency Electrosurgery. There is a risk of pooling of flammable solutions under the patient or in body depressions such as the umbilicus, and in body cavities such as the vagina. Any fluid pooled in these areas should be mopped up before high frequency surgical equipment is used. Attention should be called to the danger of ignition of endogenous gases. Some materials, for example cotton, wool and gauze, when saturated with oxygen may be ignited by sparks produced in normal use of the high frequency surgical equipment.
- Laparoscopic procedures may result in gas embolism due to insufflation of gas in the abdomen.
- For surgical procedures where the HF current could flow through parts of the body having a relatively small cross sectional area (e.g. circumcisions), the use of bipolar techniques may be desirable in order to avoid unwanted tissue damage.
- Do not operate the electrosurgical generator with the cover removed.

➢ Cautery tips that are activated or hot from use can cause a fire. ***The surface of the electrode may remain hot enough to cause burns after the RF current is deactivated.*** *(Bolded sentence newly added to Ethicon Megadyne Electrosurgical Generator IFU.)*

- Do not place them near or in contact with flammable materials and substances (e.g. drapes, flammable gases, endotracheal tubes, etc.).
- Failure of the high frequency surgical equipment could result in an unintended increase of output power.
- The use of accessories other than those specified in the approved accessory list may result in increased emissions or decreased immunity of the Ethicon Megadyne™ ESU. The accessory RF voltage rating should be ≥ 4.0 kV peak. If accessories do not meet this rating, please refer to accessory manufacturer's instructions for recommended rated voltage. Power settings may need to be limited to accommodate accessory voltage ratings.
- To avoid risk of electrical shock, use grounded AC outlets when connecting the generator power cord.
- As with all medical systems generating high RF, the Ethicon Megadyne™ ESU may interfere or affect the functionality of other electronic equipment. Precautions should be taken during equipment installation to reduce this condition. Ethicon recommends moving other electronic equipment away from the generator and separating cables within the room from the RF carrying cables.
- No modification to this equipment is allowed.

➢ ***When using HF current there is a risk of neuromuscular stimulation, especially with modes which produce electrical arcs between the active electrode and tissue****. (Newly added to Ethicon Megadyne Electrosurgical Generator IFU.)*

- Use of equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, the equipment and the other equipment should be observed to verify that they are operating normally.
- Portable RF communications equipment (including peripherals such as antenna cables and external antennae) should be used not closer than 12 inches (30 cm) to any part of the generator including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.

Additional Warnings: (Newly Added to Ethicon Megadyne Electrosurgical Generator IFU)

- ➢ For patients with cardiac pacemakers, electrically conductive or other active implants, a possible hazard exists due to the concentration or re-direction of HF currents. The pacemaker or other active implant may be damaged due to the interference of HF currents. In case of doubt, approved qualified advice should be obtained from the device manufacturer
- ➢ Electrosurgical cables should be positioned to minimize contact with the patient and avoid contact with other leads to avoid adversely influencing the operation of other electronic equipment.
- ➢ Studies indicate smoke generated during Electrosurgery may be harmful to surgical staff. Use of a surgical mask and proper smoke ventilation as provided by a surgical smoke evacuation system is recommended.
- ➢ Connect adapters and accessories to the Ethicon Megadyne™ ESU only when the energy is off. Failure to do so may result in an injury or electrical shock to the patient or operating room personnel.

3.10.2. Cautions: Ethicon Megadyne Electrosurgical Generator

- Read all instructions prior to use.
- Federal (USA) law restricts this device to sale by or on the order of a physician.
- Do not place containers of fluids on the generator or allow fluids to spill on the generator.
- Do not operate the generator without adequate clearance for ventilation. The space between the bottom of the feet and floor of the generator should be clear of obstruction. At least two inches of air should separate sides, back, and top of the generator from any ventilation-obstructing surface.
- Removal of the generator cover may create the risk of an electrical shock. Please contact Ethicon, or your local representative for proper servicing.
- The clinical use of Electrosurgery is by nature intermittent. This system should be operated intermittently as well. Prolonged use may cause overheating.
- Failure of the electrosurgical generator could result in an unintended increase of output power.
- Inspect electrode cables and endoscopically used accessories for possible damage prior to use. Connect accessories (e.g. pencil, foot cord, bipolar instruments, return electrode, etc.) to the proper receptacle. Use connectors designed for the intended purpose. Follow the instructions for use provided by accessory manufacturers.
- All associated equipment and active accessories should be inspected to determine the rated accessory voltage prior to use.
- The maximum permissible length of any accessory connected to the generator, including its cord shall not exceed 15 feet (4.57 meters).
- Apparent low power output or failure of the electrosurgical equipment to function correctly at normal settings may indicate faulty application of the dispersive electrode or failure of an electrical lead. Do not increase power output before checking for obvious defects or misapplication. For monopolar surgery, effective coupling between the patient and the dispersive electrode must be verified whenever the patient is repositioned.
- If a compatible monitoring neutral electrode is not used with a contact quality monitor, loss of safe contact between the neutral electrode and the patient will not result in an auditory alarm.
- ~~For patients with cardiac pacemakers, electrically conductive or other active implants a possible hazard exists due to the concentration or re-direction of HF currents. The pacemaker or other active implant may be damaged due to the interference of HF currents. In case of doubt, approved qualified advice should be obtained from the device manufacturer.~~ (Removed from Ethicon Megadyne Electrosurgical Generator IFU.)
- The cables to the surgical electrodes should be positioned in such a way that contact with the patient or other leads is avoided.

- ***The Mega Cart is recommended if the Ethicon Megadyne™ ESU is moved out of the operating room. Maintain control of the generator and cart when moving over thresholds or on incline surfaces.*** *(Newly added to the Ethicon Megadyne Electrosurgical Generator IFU.)*
- Patient monitoring electrodes should be placed as far from the surgical electrodes as possible. Needle monitoring electrodes should be avoided. Patient monitoring systems using high frequency current-limiting devices are recommended. Follow manufacturers' recommendations for proper application of monitoring electrodes.
- When practical, the patient should not be allowed to come into contact with earthed metal parts or parts with appreciable capacitance to earth (e.g. operating table supports, etc.). Use of antistatic sheeting recommended for this purpose. It is recognized that this recommendation may not be practical during certain procedures, however, to maximize patient safety during the use of electrosurgical devices, such practices should be minimized.
- Skin-to-skin contact (i.e., between the arms and body of the patient) should be avoided. Insertion of non-conductive materials between the skin-to-skin contact sites is recommended.
- The use and proper placement of a dispersive electrode is a key element in the safe and effective use of monopolar Electrosurgery, particularly in the prevention of pad site burns. Follow manufacturer's directions and recommended practices for the preparation, placement, surveillance, and use of dispersive electrodes.
- For disposable, adhesive type ("sticky") return electrodes the entire area of the return electrode should be reliably attached to the patient's body and as close to the operating field as possible. Place the adhesive type return electrode over good muscular, vascular, tissue. Avoid areas of hair, fat, bony prominences and metal implants.
- For the Mega Soft® family of Reusable Patient Return Electrodes, maximize the patient weight bearing area on the pad and minimize the materials placed between the pad and patient.
- Regularly inspect electrosurgical accessories for damage. In particular, electrode cables and endoscopic accessories should be checked for damaged insulation.
- Avoid high frequency output settings where the maximum output voltage may exceed the rated accessory voltage.
- Do not activate an electrode until it is in contact with (for desiccation and the GEM Mode), or in close proximity (for fulguration) to the target tissue.
- Do not coil electrosurgical accessory cords, and do not wrap electrosurgical accessory cords around metal objects. This may induce current flow to unintentional areas causing, shocks, burns, or fires.
- ***In the Auto Bipolar setting, activation may occur with contact of any material and without the use of a switch sensor. When not in use, place electrosurgical instruments in a safety holster or safely away from patients, the surgical team, and flammable materials.*** *(Newly added to the Ethicon Megadyne Electrosurgical Generator IFU.)*

- ***Bipolar forceps should not be set down while Auto bipolar is active. Contact with any material may cause activation. Turn off Auto bipolar before releasing an instrument.*** *(Newly added to the Ethicon Megadyne Electrosurgical Generator IFU.)*
- ~~*Studies indicate smoke generated during Electrosurgery may be harmful to surgical staff. Use of a surgical mask and proper smoke ventilation as provided by a surgical smoke evacuation system is recommended.*~~ *(Removed from Ethicon Megadyne Electrosurgical Generator IFU.)*

3.11. Device Lifetime / Duration of Use - Identical

3.11.1. Service Life – Identical

The service life of the Ethicon Megadyne Electrosurgical Generator is 10 years. The service life of the Footswitch (1459J) is 12 years (ENG-DMR-015, **Windchill**).

The service life of the Mega Power Generator is 10 years (ENG-DMR-008, **Windchill**).

3.11.2. Power Duty Cycle – Identical

Under maximum power conditions, the Ethicon Megadyne™ ESU is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour (ENG-DMR-015, **Windchill**).

Under maximum power conditions, the Mega Power generator is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour (ENG-DMR-008, **Windchill**).

3.11.3. Duration of Use - Identical

The subject devices are used during a single surgical procedures with no stated limitations as to the duration/length of the procedure time when operated within the identical safety limits of the power duty cycle as described above. The devices are intended for multiple use within the scope of its anticipated service life, also stated above.

3.12. Magnetic Resonance Imaging (MRI) Compatibility – N/A

MRI - Not Applicable

The Ethicon Megadyne Electrosurgical Generator and Megadyne Mega Power Electrosurgical Generator are not designed for use during MRI nor is the subject device implantable.

3.13. Sterility – N/A

Sterilization - Not Applicable

Sterilization is not required for the subject devices including footswitch (1459J) as these are non-patient contact devices.

3.14. Principles of Operation

3.14.1. Principles of Electrosurgery[1]

Electrosurgery: the electrical current heats the tissue. The current must pass through the tissue to produce the desired effect. Alternating current flows through the patient. Current enters the body at a high density and leaves the body at a low density.

Tissue Heating: As electrical current enters tissue, the ions within the cells become excited and begin to go into motion releasing kinetic energy. As this action increases or is prolonged, the cells begin to heat.

The temperature rise in tissue is directly proportional to:

- the resistance of the tissue
- the current density
- the power output
- the time of current application.

If a substance is an excellent conductor it will allow easy passage of current and offer very little resistance; therefore, the heat generated will be very little. The resistance to current flow in living tissues is inversely proportional to the water content. The more water present the greater current flow through that tissue because of the lower resistance. Therefore, current flow is greatest in tissues of high water content, such as blood, and least in those of low water content, such as bone. Electrical current flows preferentially through blood, then nerve, then muscle, then adipose tissue and finally bone.

Monopolar: (monoterminal) is an electrosurgical technique in which the tissue effect takes place at a single active electrode and is dispersed (circuit completed) by a patient return electrode. A patient return pad or electrode for monopolar electrosurgery functions as the pathway the current takes back to the generator. Some of the pads are flexible sticky pads that have polymer covering a conductive foil. These pads are referred to as sticky pads because of the adhesive edge that holds the pad in direct contact with the patient.

The pad must be large enough to keep the current density low as the electrical energy exits the patient; otherwise, heat will build up under the pad resulting in a burn. If the contact area is reduced because the pad is too small or is not in full contact such as with tenting, heat will increase. Surface area impedance can also be compromised with sticky pads if the site of application is impaired. Excessive hair, bony prominences, fluid, scar and adipose tissue and prostheses are some of the situations that can interfere with dispersive needs.

[1] Reference Electrosurgery Book 4 by Megadyne Inc.

Three unique problems related to monopolar electrosurgery use during endoscopic procedures are direct coupling, insulation failure and capacitive coupling.

Bipolar: (biterminal) is an electrosurgical technique in which the electrosurgical effect takes place between paired electrodes placed across the tissue to be treated. No patient return electrode is needed. Typically, bipolar forceps are utilized for this technique.

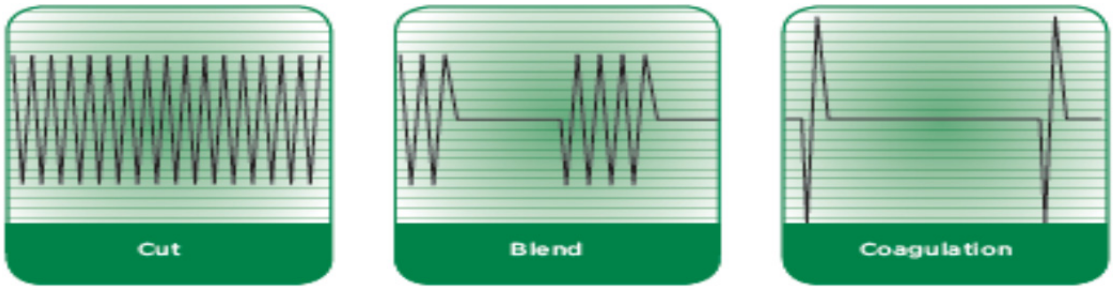
The distance between the active and return electrodes in a bipolar circuit is very small since both electrodes are adjacent to each other. The distance the current flows is limited and is contained in the vicinity of the two electrodes. As current passes through the tissue from one electrode to the other, the tissue is desiccated, and the resistance increases. As resistance increases current flow decreases. The LEDs on the electrosurgical generator indicate current flow when bipolar instruments are used.

3.14.2. Subject Device(s) Principles of Operation – Electrosurgical Generators[2]

In surgery, the generator converts the electricity to high frequency waveforms and creates the voltage for flow of current. 60 cycle current is increased to over 300,000 cycles per second by the generator. The high "radio" frequency eliminates nerve and muscle stimulation and electrocution that occurs at 60 cycle current.

Electrosurgical Waveforms:

Electrosurgical generators can produce a variety of waveforms and each waveform creates different tissue results.



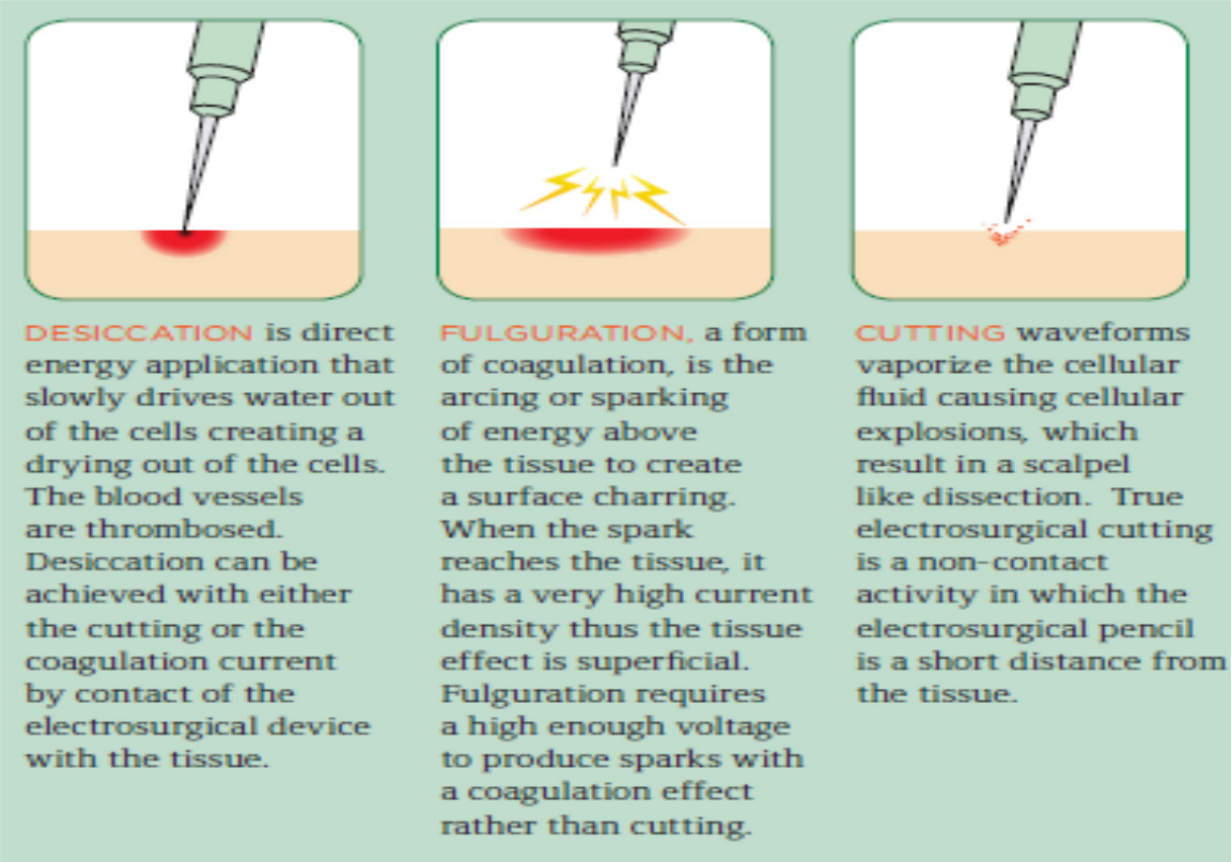
The cutting current will cut the tissue but provides little hemostasis. The coagulation current provides coagulation but does not allow for smooth cutting. The blend current is an intermediate current between the cutting and coagulation currents but is not a combination of the two as the name might imply. It is a cutting current in which the duty cycle (time current is actually flowing) is reduced from 100 percent of the time to approximately 50 percent of the time (depends on manufacturer). The "off" time allows the tissue to cool creating some hemostasis. It is important to know that the "Blend" currents in ESUs are delivered only when the cut button/footswitch is activated. Depressing the coag button/footswitch will deliver the coag or spray coag current.

[2] Reference Electrosurgery Book 4 by Megadyne Inc.

Tissue Responses:

Given the versatility of waveforms available with modern generators, surgeons have the opportunity to create a multitude of tissue responses and results. Figure 3-1 illustrates the three types of surgical application modes resulting from electrosurgical waveforms created by the generator: Desiccation, fulguration and Cutting.

Figure 3-1: Tissue Responses Derived from Electrosurgical Waveforms



End – Section 4.13. Principles of Operation.

4. EQUIVALENCE

4.1. Equivalent Subject Device Description

The existing Megadyne Mega Power Electrosurgical Generator is the equivalent subject device for the new Ethicon Megadyne Electrosurgical subject device. The existing subject device has been on the market for 15 years. Both subject devices have the same Clinical, Technical and Biological outcomes

	Subject Device: Ethicon Megadyne Electrosurgical Generator / Megadyne Medical Products, Inc.	**Equivalent Device: Megadyne Mega Power Electrosurgical Device / Megadyne Medical Products, Inc.**
Regulatory Status:	• CE Mark (#640176) New Product - Pending • 510(k) (#K193145) 24 March 2020 (included new bipolar footswitch accessory -1459J)	• CE Mark (#640176) 12 May 2005 • FDA 510(k) (#K050579) 24 August 2005
Technical Documentation:	• 500441224 Ethicon Megadyne Electrosurgical Generator Technical File • ENG-DMR-015 Ethicon Megadyne Electrosurgical Generator Device Master Record	• ENG-DMR-008 Mega Power ESU Device Master Record
Variant Descriptions	The Ethicon Megadyne Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000315-01, **Windchill**). The footswitch accessory (purchased separately) is intended to provide a foot control option (in addition to hand control) for bipolar outputs only (ENG-DMR-015, **Windchill**).	The Ethicon Mega Power Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures (IFU 3000158-01, **Windchill**).

Note 1: Refer to Table 4-1: Megadyne Electrosurgical Generators Variants for footswitch image. Generator images in Table 4-2 below.

Note 2: Refer to Appendix for Product Codes

4.2. Equivalence Table – New Line Extension Subject Device vs Existing Subject Device

Table 4-2: Equivalence Table

	New Line Extension Subject Device: Ethicon Megadyne Electrosurgical Generator	Equivalent Subject Device: Megadyne Mega Power Electrosurgical Generator	
Picture (include pictures of all component types)			
A. Clinical Parameters- Intended use– Equivalence means used for the same clinical condition (including when applicable similar severity and stage of disease, same medical indication), for the same intended purpose, at the same site in the body, in similar populations (including age, gender, anatomy, physiology); and not foreseen to deliver significantly different performances (in the relevant clinical performances such as the expected clinical effect, the specific intended purpose, the duration of use, etc.)			
Intended Purpose	IFU 3000315-01 The Ethicon Megadyne Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.	IFU 3000158-01 The Mega Power® Electrosurgical Generator is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.	Identical
Indication(s) / Clinical Condition	IFU 3000315-01 The Ethicon Megadyne Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.	IFU 3000158-01 The Ethicon Mega Power® Electrosurgical Generator (ESU) is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.	Identical

	New Line Extension Subject Device: Ethicon Megadyne Electrosurgical Generator	Equivalent Subject Device: Megadyne Mega Power Electrosurgical Generator	
Contra - indications	IFU 3000315-01 There are no contraindications per the IFU.	IFU 3000158-01 There are no contraindications per the IFU.	Identical
Anatomic Areas of Use	IFU 3000315-01 There are no limits to anatomical areas of use. The Megadyne Electrosurgical Generator is used during open and laparoscopic surgical procedures.	IFU 3000158-01 There are no limits to anatomical areas of use. The Megadyne Electrosurgical Generator is used during open and laparoscopic surgical procedures.	Identical
Conditions of Use	IFU 3000315-01 The Megadyne Electrosurgical Generator is for use by qualified medical personnel skilled in the particular techniques and procedures to be performed. The Ethicon Megadyne ESU is intended for use in an operating theatre or surgical setting only. It is not intended for home use, in ambulances or in hospital transport.	IFU 3000158-01 This Mega Power electrosurgical generator is intended for use by qualified medical personnel skilled in the particular techniques and procedures to be performed. The Mega Power is to be used in an operating theatre or a surgical setting only. It is not to be used for home use, in ambulances, during hospital transport or wall mounted.	Identical
Patient Population	IFU 3000315-01 The Megadyne Electrosurgical Generator is intended for use on the general population with no patient age limit.	IFU 3000158-01 The Mega Power Electrosurgical Generator may be used on the general population (with multiple patients) with no patient age limit.	Identical
Duration of Application	IFU 3000315-01 Power Duty Cycle This equipment rated for intermittent duty at maximum output 10 seconds on and 30 seconds off, according to IEC 60601-2-2. Under maximum power conditions, the Mega Power generator is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour.	IFU 3000158-01 Power Duty Cycle This equipment rated for intermittent duty at maximum output 10 seconds on and 30 seconds off, according to IEC 60601-2-2. Under maximum power conditions, the Mega Power generator is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour.	Identical

	New Line Extension Subject Device: Ethicon Megadyne Electrosurgical Generator	Equivalent Subject Device: Megadyne Mega Power Electrosurgical Generator	
Expiration/Shelf-Life/Service Life Data	ENG-DMR-015 The service life of the Generator is 10 years.	ENG-DMR-008 The service life of the Generator is 10 years.	Identical
B. Technical Parameters – Equivalence means be of similar design; used under same conditions of use; have similar specifications and properties; use similar deployment methods (if relevant); have similar principles of operation and critical performance requirements. *(NOTE: Break out key parameters into new rows as warranted)*			
Design Parameters (Physical Characteristic)	IFU 3000315-01 Width: 36.8 cm (14.5 inches) Depth: 43.9 cm (17.3 inches) Height: 17.9 cm (7.1 inches) Weight: 7.71 kg (17 lbs)	IFU 3000158-01 Width: 40.5 cm (15.9 inches) Depth: 40.5 cm (15.9 inches) Height: 20 cm (7.9 inches) Weight: 8.65 kg (19 lbs)	Equivalent: Varies slightly in size and weight.
Specifications, Properties			
Equipment Classification	Equipment Classification: IEC 60601-1 Class I	Equipment Classification: IEC 60601-1 Class I	Identical
Equipment Type	Equipment Type: IEC 60601-1 Edition 3.1, Type CF	Equipment Type: IEC 60601-1 Edition 3.1, Type CF	Identical

	New Line Extension Subject Device: Ethicon Megadyne Electrosurgical Generator	Equivalent Subject Device: Megadyne Mega Power Electrosurgical Generator	
Degree of protection against ingress of water	IEC 60601-1 Edition 3.1 IEC 60601-2-2 Edition 6.0 Ingress Protection of Footswitch: IP68 (ref. on drawing) Patient Circuit: Isolated from Earth Ground Cooling: Natural Convection, Modulated Internal Fans	IEC 60601-1 Edition 3.1 IEC 60601-2-2 Edition 6.0 Ingress Protection of Footswitch: IP68 (ref. on drawing) Patient Circuit: Isolated from Earth Ground Cooling: Natural Convection, Modulated Internal Fans	Identical
Operating Environment	The Ethicon Megadyne ESU is designed and tested to operate within the following environmental parameters. • Temperature Range: +10°C (+50°F) to +40°C (+104°F) • Humidity Range: 15% to 75% Non-condensing • Atmospheric Pressure: 700 hPa (10.2 psi) to 1060 hPa (15.37 psi)	The Ethicon Megadyne ESU is designed and tested to operate within the following environmental parameters. • Temperature Range: +10°C (+50°F) to +40°C (+104°F) • Humidity Range: 15% to 75% Non-condensing • Atmospheric Pressure: 700 hPa (10.2 psi) to 1060 hPa (15.37 psi)	Identical
Warm-up Requirements	If the Ethicon Megadyne ESU is stored outside of the above range, allow the unit to stabilize at room temperature for a minimum of one hour before use.	If the Ethicon Megadyne ESU is stored outside of the above range, allow the unit to stabilize at room temperature for a minimum of one hour before use.	Identical
Storage Environment	The Ethicon Megadyne ESU is designed and tested for storage within the following environmental parameters. • Temperature Range: -40°C (-40°F) to +70°C (+158°F) • Humidity Range: 10% to 95%, Condensing • Atmospheric Pressure: 500 hPa (7.25 psi) to 1060 hPa (15.37 psi)	The Ethicon Megadyne ESU is designed and tested for storage within the following environmental parameters. • Temperature Range: -40°C (-40°F) to +70°C (+158°F) • Humidity Range: 10% to 95%, Condensing • Atmospheric Pressure: 500 hPa (7.25 psi) to 1060 hPa (15.37 psi)	Identical

	New Line Extension Subject Device: Ethicon Megadyne Electrosurgical Generator	Equivalent Subject Device: Megadyne Mega Power Electrosurgical Generator	
Audio Frequencies	GEM Cut, Pure CUT and Blend 840 Hz ± 10% Coag 1, Coag 2, and Spray Coag 520 Hz ± 10% Micro and Macro Bipolar 480 Hz ± 10% Alarms: Power Limit (One beep) 1 1980 Hz ± 10% Errors (Two beeps) 1980 Hz ± 10% CQM (Three Beeps) 2550 Hz ± 10% The volume of the CUT, COAG and BIPOLAR active signals can be adjusted up and down. They have a minimum volume of 40 dB at a distance of one meter. The alarm volume is fixed to exceed 65 dB at a distance of one meter per the requirements of IEC 60601-2-2.	ACE Cut, Pure CUT and Blend 840 Hz ± 10% Coag 1, Coag 2, and Spray Coag 520 Hz ± 10% Micro and Macro Bipolar 480 Hz ± 10% Alarms: Power Limit (One beep) 1980 Hz ± 10% Errors (Two beeps) 1980 Hz ± 10% CQM (Three Beeps) 2550 Hz ± 10% The volume of the CUT, COAG and BIPOLAR active signals can be adjusted up and down. They have a minimum volume of 40 dB at a distance of one meter. The alarm volume is fixed to exceed 65 dB at a distance of one meter per the requirements of IEC 60601-2-2.	Identical
Type and Rating of Fuses	2 each F10.0AH/250VAC, Schuster Inc. Type FSF	2 each F10.0A/250VAC, Schuster Inc. Type FSF	Identical
Electrical Properties	Nominal Operating Voltage: 100 – 240 VAC Nominal Operating Frequency: 50-60 Hz	Nominal Operating Voltage: 100 – 240 VAC Nominal Operating Frequency: 50-60 Hz	Identical
Output Power Variation	Output variation as a function of input variation <5%	Output variation as a function of input variation <5%	Identical

Output Power Characteristics MONOPOLAR CUT

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Rated Load (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (Rated Load)	Crest Factor Nominal @ (Rated Load)
Monopolar CUT							
GEM Cut	150	20%	200	860	1.2	400kHz	1.6
Pure Cut	300	20%	300	1500	1.1	400kHz	1.6
Blend	200	20%	300	2500	1.0	400kHz	2.5

** Or 5 watts, whichever is greater*

NOTE 1: GEM Cut, and ACE Cut are identical functions with different names.

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Rated Load (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (Rated Load)	Crest Factor Nominal @ (Rated Load)
Monopolar CUT							
ACE Cut	150	20%	200	1500	1.24	400kHz	1.6
Pure Cut	300	20%	300	3000	1.25	400kHz	1.6
Blend	200	20%	300	4000	1.0	400kHz	3.0

** or 5 watts, whichever is greater*

EQUIVALENT: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0

Output Power Characteristics
MONOPOLAR COAG

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Load Rated (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (RatedLoad)	Crest Factor @ Nominal (Rated Load)
Monopolar COAG							
COAG 1	120	20%	500	5000	1.4	2.5 µs Pulse@ 30kHz	6.9
COAG 2	120	20%	500	5900	1.4	2.5 µs Pulse@ 30kHz	7.1
Spray	120	20%	500	5800	1.4	2.5 µs Pulse@ 22kHz	8.2
SOFT COAG	120	20%	140	470	1.1	400kHz	1.6

** or 5 watts, whichever is greater*

NOTE 1: SOFT COAG –New function for new subject device. SOFT COAG desiccates tissue at a slower rate with deeper thermal penetration.

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Load Rated (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (RatedLoad)	Crest Factor @ Nominal (Rated Load)
	Monopolar COAG						
COAG 1	120	20%	500	5000	1.1	2.5 µs Pulse@ 32kHz	6.9
COAG 2	120	20%	500	5000	1.1	2.5 µs Pulse@ 30kHz	7.1
Spray	120	20%	500	6000	1.1	2.5 µs Pulse@ 22kHz	8.0

** Or 5 watts, whichever is greater.*

EQUIVALENT: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0

Output Power Characteristics Bipolar

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Rated Load (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (RatedLoad)	Crest Factor @ Nominal (Rated Load)
Bipolar							
Micro	80	20%	100	450	1.7	400kHz	1.6
Macro	80	20%	100	590	1.7	400kHz	1.6

** or 5 watts, whichever is greater*

Mode	Power (Watts)	Output Tolerance * (Rated Load)	Rated Load (Ohms)	Max Open Circuit Voltage (Vp-p)	Max Current (Amps)	Operating Freq. (RatedLoad)	Crest Factor @ Nominal (Rated Load)
Bipolar							
Micro	80	20%	100	360	1.7	400kHz	1.6
Macro	80	20%	100	760	1.7	400kHz	1.6

** or 5 watts, whichever is greater*

EQUIVALENT: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0

Low Frequency (50-60 Hz) Leakage Current	• Earth Leakage Current general NC < 300 µA SFC < 1.0 mA • Enclosure NC < 100 µA SFC < 500 µA • Patient Leakage Current NC < 10 µA SFC < 50 µA • Patient Auxiliary Current d.c. NC < 10µA SFC < 50 µA • Patient Auxiliary Current a.c. NC < 100µA SFC < 500 µA	• Earth Leakage Current general NC < 300 µA SFC < 1.0 mA • Enclosure NC < 100 µA SFC < 500 µA • Patient Leakage Current NC < 10 µA SFC < 50 µA • Patient Auxiliary Current d.c. NC < 10µA SFC < 50 µA • Patient Auxiliary Current a.c. NC < 100µA SFC < 500 µA	Identical
High Frequency (RF) Leakage Current	• Monopolar Modes (all settings at the maximum) • Patient Return to Ground <150mA • Active to Ground <150mA • Bipolar Mode (Maximum setting) • Each Lead to Ground < 63mA	• Monopolar Modes (all settings at the maximum) • Patient Return to Ground <150mA • Active to Ground <150mA • Bipolar Mode (Maximum setting) • Each Lead to Ground < 63mA	Identical

Power Consumption	Maximum mains current Idle Cut Coag Bipolar Power Factor Correction Idle Cut Coag Bipolar	100-120 VAC 0.3 A 5.0 A 2.4 A 1.3 A 0.85 0.99 0.98 0.95	220-240 VAC 0.15 A 2.5 A 1.2 A 0.65 A 0.70 0.98 0.97 0.93	Maximum mains current Idle Cut Coag Bipolar Power Factor Correction Idle Cut Coag Bipolar	100-120 VAC 0.3 A 5.0 A 2.4 A 1.3 A 0.85 0.99 0.98 0.95	220-240 VAC 0.15 A 2.5 A 1.2 A 0.65 A 0.70 0.98 0.97 0.93	Identical
Power Cord	• 100V to 120V Supply - Power Cord Rating 150V~, minimum 8A, 16 AWG, 3 conductor type SJT with Hospital Grade Plug, detachable type 4.6m (15 feet) long. • 220V to 240V Supply - Power Cord Rating 250V~, minimum 10A, 1.0 mm^2, 3 conductor, detachable type 4.6m (15 feet) long.			• 100V to 120V Supply - Power Cord Rating 150V~, minimum 8A, 16 AWG, 3 conductor type SJT with Hospital Grade Plug, detachable type 4.6m (15 feet) long. • 220V to 240V Supply - Power Cord Rating 250V~, minimum 10A, 1.0 mm^2, 3 conductor, detachable type 4.6m (15 feet) long.			Identical
Power Duty Cycle	• Under maximum power conditions, the Megadyne generator is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour.			• Under maximum power conditions, the Mega Power generator is designed to operate safely with activation times of 10 seconds on, 30 seconds off for one hour.			Identical

Audio Volume	Mode	Frequency	Volume Adjustability	Mode	Frequency	Volume Adjustability	Identical
	Pure Cut	840 Hz ± 10 %	40 to 65 dB	Pure Cut	840 Hz ± 10 %	40 to 65 dB	
	GEM	840 Hz ± 10 %	40 to 65 dB	ACE	840 Hz ± 10 %	40 to 65 dB	
	Blend	840 Hz ± 10 %	40 to 65 dB	Blend	840 Hz ± 10 %	40 to 65 dB	
	COAG 1	520 Hz ± 10 %	40 to 65 dB	COAG 1	520 Hz ± 10 %	40 to 65 dB	
	COAG 2	520 Hz ± 10 %	40 to 65 dB	COAG 2	520 Hz ± 10 %	40 to 65 dB	
	Coag Spray	520 Hz ± 10 %	40 to 65 dB	Coag Spray	520 Hz ± 10 %	40 to 65 dB	
	Bipolar (Micro and Macro)	480 Hz ± 10 %	40 to 65 dB	Bipolar (Micro and Macro)	480 Hz ± 10 %	40 to 65 dB	
	Bipolar Monitor	480 Hz ± 10 %	40 to 65 dB	Bipolar Monitor	480 Hz ± 10 %	40 to 65 dB	
	Power Limit Alarm (1 Beep)	1980 Hz ± 10 %	> 65 dB non-adjustable	Power Limit Alarm (1 Beep)	1980 Hz ± 10 %	> 65 dB non-adjustable	
	Errors (2 Beeps)	1980 Hz ± 10 %	> 65 dB non-adjustable	Errors (2 Beeps)	1980 Hz ± 10 %	> 65 dB non-adjustable	
	CQM (3 Beeps)	2550 Hz ± 10 %	> 65 dB non-adjustable	CQM (3 Beeps)	2550 Hz ± 10 %	> 65 dB non-adjustable	
Contact Quality Monitor	• Ethicon recommends the use of the Mega Soft Reusable Patient Return Electrode. Due to the built-in safety (self-current limiting) of the Megadyne™ Mega Soft Reusable Patient Return Electrode, the CQM limitation is no longer essential. • Acceptable Resistance Range 0 to 135 ohms • CQM Alarm Activation: If a disposable split pad is used with the Ethicon Megadyne™ ESU, the system will perform as follows. CQM alarm activation occurs in the resistance range from 10 to 135 ohms. An increase in resistance of 40% will cause the CQM indicator to turn red, an alarm tone will sound three times and the RF output will be disabled. The Ethicon Megadyne™ ESU system will remain in this mode until the unsafe condition is corrected.			• Megadyne recommends the use of the Mega Soft Reusable Patient Return Electrode. Due to the built-in safety (self-current limiting) of the Megadyne Mega Soft Reusable Patient Return Electrode, the CQM limitation is no longer essential. • Acceptable Resistance Range: 0 to 135 ohms • CQM Alarm Activation: If a disposable split pad is used with the Mega Power, the system will perform as follows. CQM alarm activation occurs in the resistance range from 10 to 135 ohms. An increase in resistance of 5 ohms or 30%, whichever is greater, will cause the CQM indicator to turn red, an alarm tone will sound three times and the RF output will be disabled. The Mega Power system will remain in this mode until the unsafe condition is corrected.			Identical

External Communication Ports	The communication ports are located in the back panel behind a removable plate. The RS232 and USB Ports are provided for use by authorized Service Centers.	This communication port is located in the back panel behind a removable plate. The RS232 Port is provided for use by authorized Service Centers.	Identical - Enhancement
Conditions of Use	IFU 3000315-01 • The Megadyne Electrosurgical Generator is for use by qualified medical personnel skilled in the particular techniques and procedures to be performed. • The Ethicon Megadyne ESU is intended for use in an operating theatre or surgical setting only. • It is not intended for home use, in ambulances or in hospital transport. • The Ethicon Megadyne™ ESU **and its accessories** are not intended for implant into a patient. • It is intended for use on the general population with no patient age limit. **NOTE 1:** …'and its accessories' wording not included with existing subject device IFU.	IFU 3000158-01 • The Mega Power electrosurgical generator is intended for use by qualified medical personnel skilled in the particular techniques and procedures to be performed. • The Mega Power is to be used in an operating theatre or a surgical setting only. • It is not to be used for home use, in ambulances, during hospital transport or **wall mounted**. • The Mega Power is not to be used as a permanent implant in a patient. • It may be used for use on the general population (with multiple patients) with no patient age limit. **NOTE 1:** 'Wall Mounted' dropped from new subject device IFU.	Highly Similar – 3 words added to new device IFU

Preparation for Use	• The Megadyne ESU is non-sterile. In use, this device will stand on a cart or a designated shelf near the operating room table. • The use of the generator requires the addition of electrosurgical accessories. • The required accessories for bipolar electrosurgery are a set of bipolar forceps and a bipolar footswitch or a set of hand switching bipolar forceps. • For monopolar electrosurgery, the required accessories are the hand switch or footswitch with their respective active electrodes and a passive return electrode. • The generator designed to accept the most common industry configurations including handheld electrosurgical pencils, foot-controlled cables and both single plate and dual plate return electrodes. • The setup of the generator entails the use of simple controls. • The input power switch is an intuitive switch on the front of the generator that is marked with the international symbols for ON and OFF. • The modes of operation for CUT and COAG are designated by color codes that are internationally recognized, yellow for CUT and blue for COAG. • The bipolar mode is marked in blue. • The power settings for these modes are adjusted by touching one of two arrows (there are membrane switches under the arrows). • There is an up arrow/button for increasing the power and a down arrow/button for decreasing the power. • The plug receptacles for the accessories are unique to each type of accessory.	• The Mega Power ESU is non-sterile. In use, this device will stand on a cart or a designated shelf near the operating room table. • The use of the generator requires the addition of electrosurgical accessories. • The required accessories for bipolar electrosurgery are a set of bipolar forceps and a bipolar footswitch or a set of hand switching bipolar forceps. • For monopolar electrosurgery, the required accessories are the hand switch or footswitch with their respective active electrodes and a passive return electrode. • The generator designed to accept the most common industry configurations including handheld electrosurgical pencils, foot-controlled cables and both single plate and dual plate return electrodes. • The setup of the generator entails the use of simple controls. • The input power switch is an intuitive switch on the front of the generator that is marked with the international symbols for ON and OFF. • The modes of operation for CUT and COAG are designated by color codes that are internationally recognized, yellow for CUT and blue for COAG. • The bipolar mode is marked in green. • The power settings for these modes are adjusted by touching one of two arrows (there are membrane switches under the arrows). • There is an up arrow/button for increasing the power and a down arrow/button for decreasing the power. • The plug receptacles for the accessories are unique to each type of accessory.	Identical

	ENG-DMR-015 (Windchill) • Isolated Output – The system output and return path are isolated from earth ground. This insures that the safety of the patient and the user are maintained and that burns are not going to occur. • Three Monopolar CUT Modes - The CUT mode has three settings, GEM (Geometric Electron Modulation), PURE, and BLEND. • Three Monopolar CUT Modes - The CUT mode has three settings, **GEM**[3] (Geometric Electron Modulation), PURE, and BLEND. ➢ Selecting the "GEM" button places the generator in the GEM (Geometric Electron Modulation) cut mode. ➢ The GEM mode automatically controls the output power of the generator to provide the surgeon with a consistent cutting effect. Little hemostasis is achieved in this mode. ➢ The GEM high mode is equivalent to the ACE Cut mode in the Megadyne™ Mega Power™ generator and should be used in place of the ACE mode. • Four Monopolar COAG Settings – Four COAG modes are available, COAG 1, COAG 2, **SOFT (new)** and SPRAY. ➢ **New:** [4]**SOFT COAG** - Pressing the SOFT button places the generator in the SOFT Coag mode. The SOFT mode desiccates tissue at a relatively slower rate with deeper thermal penetration. SOFT mode is typically used with an uncoated electrode. SOFT Coag power delivery takes place at much lower impedance than other Coag modes. • Two Bipolar Coagulation Settings – When the bipolar mode is used the current will flow between the two tips of the instrument and will desiccate tissue. The Bipolar mode shall have two settings, MICRO and MACRO with an **AUTO Bipolar feature (new)**. • **New:** [5]**AUTO Bipolar** – There is an Auto Start and Stop feature available with both micro and macro bipolar functions. When selected, the generator senses (tissue impedance) when the surgeon has contacted tissue with the bipolar forceps and will automatically activate (auto start or stop the delivery of bipolar energy). There are three delay options, none (no delay prior to the onset of energy delivery), short (0.5 second) and long (1 second) that are selectable by the user. The auto stop is programmed into the generator and will discontinue the bipolar output when the impedance increases, and the tissue is desiccated. Bipolar Current Monitor – The current flow through the bipolar instrument is monitored and displayed on a bar graph current meter. The decreasing current is an indication that the tissue is becoming	**ENG-DMR-008 (Windchill)** • Isolated Output - The system output and return path are isolated from earth ground. This ensures that the safety of the patient and the user are maintained and minimizes the risk of thermal damage related to return current. • Three Monopolar CUT Settings - The CUT mode has three settings, Advanced Cutting Effect (ACE™), Pure CUT, and Blend. ➢ Selecting the "ACE" key places the generator in the Advanced Cutting Effect cut mode. ➢ The ACE mode automatically controls the output power of the generator to provide the surgeon with a consistent cutting effect. This is achieved by delivering a stable voltage, pure sine wave current to the surgical site regardless of the impedance to affect the cutting of tissue. Little hemostasis is achieved in this mode. [Highlighted wording dropped from new subject device] ➢ In the ACE mode, power cannot be manually adjusted by using the up and down arrow keys. • Three Monopolar COAG Settings- Three COAG modes are available, COAG 1, COAG 2 and SPRAY ➢ Bipolar Coagulation- The bipolar mode operates on an independent power source from the monopolar power source. This enables one surgeon to use the bipolar coagulation mode at the same time another surgeon is using monopolar CUT or COAG mode. Either the footswitch or the hand switch on the bipolar instrument can activate the bipolar instrument. [Highlighted wording and functionality dropped from new subject device] • Two Bipolar Coagulation Settings – When the bipolar mode is used the current will flow between the two tips of the instrument and will desiccate tissue. The Bipolar mode shall have two settings, MICRO and MACRO. • Bipolar Current Meter- The current flow through the bipolar instrument is [illegible], displayed on a current meter. This meter provides both a visual graph and bipolar tone to provide an indication of the amount of current flow between the tips of the bipolar instrument. The decreasing current is an indication that the tissue is becoming desiccated. There is a frequency change in the audible tone that occurs as the current drops. This current flow meter used for information only and not intended as a diagnostic tool. The bipolar current meter visual indicator is shown in green. • Push button Power Adjustment- The power adjustment of each mode,

[3] Geometric Electron Modulation (GEM™) vs. Advanced Cutting Effect (ACE™) are identical.
[4] New: SOFT COAG-Desiccates tissue at a slower rate with deeper thermal penetration. Highly similar, identical comparison.

Technique / Deployment Method	**THE MEGA POWER ESU CAN BE USED** during open and laparoscopic surgical procedures. The use of the generator requires the addition of electrosurgical accessories. The required accessories for bipolar electrosurgery are a set of bipolar forceps and a bipolar footswitch or a set of hand switching bipolar forceps. For monopolar electrosurgery, the required accessories are the hand switch or footswitch with their respective active electrodes and a passive return electrode.	**THE MEGA POWER ESU CAN BE USED** during open and laparoscopic surgical procedures. The use of the generator requires the addition of electrosurgical accessories. The required accessories for bipolar electrosurgery are a set of bipolar forceps and a bipolar footswitch or a set of hand switching bipolar forceps. For monopolar electrosurgery, the required accessories are the hand switch or footswitch with their respective active electrodes and a passive return electrode.	Identical

[5] New: AUTO Bipolar feature. Auto stop is programed into generator and will stop delivery of energy when increased impedence detected. Auto start provides programable delay options: None, Short, Long. Device enhancement.

[6] CQM vs. RECQM - Same function, different name.

Mode of Action	• Monopolar electrosurgery is the most popular method of electrosurgery because it allows the surgeon to both cut and coagulate tissue. In the monopolar mode, current passes from the active electrode through the patient's body to the patient return electrode and back to the generator to complete the circuit. A break in the circuit will not allow current to flow and electrosurgical effect will not occur. • Cutting and coagulation is achieved by concentrating energy to a very high density at the tip of the active electrode. Burns do not occur at the patient return electrode site because the energy is dispersed over a sufficient area to prevent a significant build-up of heat under the pad. • When the "CUT" switch is activated, a lower voltage, pure sine wave current is delivered to the surgical site to affect the cutting of tissue. The continuous delivery of the current causes the cells to heat, burst, and separate. As a result, the target tissue is cut with no hemostasis. • When the "COAG" switch is activated, higher voltage in an interrupted waveform is delivered through the pencil. This causes the tissue cells to heat and dehydrate, not burst. By dehydrating the cells, a coagulum is formed which creates hemostasis. • A blended waveform is a blending of modified duty cycles of CUT and COAG. Blend delivers a larger percentage of COAG. When the blend mode is selected, the "CUT" switch on the pencil will deliver the blended current, while the "COAG" switch always delivers a pure COAG current.	• Monopolar electrosurgery is the most popular method of electrosurgery because it allows the surgeon to both cut and coagulate tissue. In the monopolar mode, current passes from the active electrode through the patient's body to the patient return electrode and back to the generator to complete the circuit. A break in the circuit will not allow current to flow and electrosurgical effect will not occur. • Cutting and coagulation is achieved by concentrating energy to a very high density at the tip of the active electrode. Burns do not occur at the patient return electrode site because the energy is dispersed over a sufficient area to prevent a significant build-up of heat under the pad. • When the "CUT" switch is activated, a lower voltage, pure sine wave current is delivered to the surgical site to affect the cutting of tissue. The continuous delivery of the current causes the cells to heat, burst, and separate. As a result, the target tissue is cut with no hemostasis. • When the "COAG" switch is activated, higher voltage in an interrupted waveform is delivered through the pencil. This causes the tissue cells to heat and dehydrate, not burst. By dehydrating the cells, a coagulum is formed which creates hemostasis. • A blended waveform is a blending of modified duty cycles of CUT and COAG. Blend delivers a larger percentage of COAG. When the blend mode is selected, the "CUT" switch on the pencil will deliver the blended current, while the "COAG" switch always delivers a pure COAG current.	Identical

C. Biological Parameters – Equivalence means use of same materials or substances in contact with the same human tissues or body fluids / tissues			
Materials / Construction	• Materials Equivalency Memo: 500430815 - Rev. A. Materials Equivalency Document Title: MEGEN1 RoHS Compliance Memorandum verifies functionality of the Ethicon Megadyne Electrosurgical Generator is compliant with the European RoHS Directive 2011/65/EC due to equivalency with existing subject device materials. • ENG-DMR-015: Footswitch 1459J is equivalent to 1450, 1450J. Only difference is the shape of the footswitch.	• ENG-RPT-385 verifies the Mega Power Electrosurgical Generator is compliant with European RoHS Directive 2011/65/EC. • The generator design was verified with Test Results, Mega Power Electrosurgical Generator, RoHS 1151744-10. • ENG-DMR-008: Section 6.3 Performance Specification: Foot Control Cable Materials (only) Connectors: Gold plated brass, Connector insulation material: Santoprene, Cable insulation jacket: Santoprene	Equivalent: Documentation Equivalency
Human Tissue or Body Fluids in Contact with the Device	The Megadyne ESU is non-patient contacting. Per the requirements of ISO 10993-1, *Biological evaluation of medical devices- Part 1: Guidance on selection of tests,* no biocompatibility testing is required.	The Mega Power Generator is non-patient contacting. Per the requirements of ISO 10993-1, *Biological evaluation of medical devices- Part 1: Guidance on selection of tests,* no biocompatibility testing is required.	Identical
Biological Response	The Mega Power Generator EU Class IIb device does not administer medicinal substances nor incorporate any human or animal substances.	The Mega Power Generator EU Class IIb device does not administer medicinal substances nor incorporate any human or animal substances.	Identical

4.3. Equivalence Rationale

4.3.1. Clinical Parameters - Identical

All of the Clinical Parameters for the Megadyne Electrosurgical Generators are Identical as documented in the Equivalence Table above (Table 4-2) and requires no additional documentation.

4.3.2. Technical Parameters – Identical, Highly Similar or Equivalent

The Technical Parameters for the Megadyne Electrosurgical Generators documented in the Equivalence Table above (Table 4-2) contain thirty (30) categories for equivalence comparison. Twenty-four (24) of the (30) Technical Parameter categories are Identical. The remaining six (6) Technical Parameter categories are Highly Similar and/or Equivalent (Electrical) and the differences are documented below.

1. Design Parameters (Physical Characteristics): Highly Similar (Sufficiently the Same to be Equivalent)
   The new (line extension) subject device is:
   a. 3.7 cm (1.4 in) smaller in Width than existing subject device
   b. 3.4 cm (1.4 in) larger in Depth than existing subject device
   c. 2.1 cm (0.8 in) smaller in Height than existing subject device
   d. 0.9 kg (2 lbs) lighter in Weight than existing subject device

2. Output Characteristics for Monopolar Cut: Highly Similar, Equivalent
   a. Max Open Circuit/ Peak-to-Peak Voltage (Vp-p)
   The new subject device has:
      i. 640 Vp-p less voltage than existing subject device for GEM Cut*
      ii. 1500 Vp-p less voltage than existing subject device for Pure Cut*
      iii. 1500 Vp-p less voltage than existing subject device for Blend*

   *Note: The new Ethicon Megadyne Electrosurgical Generator uses voltage and current limiting technology to prevent excessive leakage currents. This technology effects the open circuit voltage measurement but voltages in clinical use are not affected.
   b. Crest Factor Nominal @ (Rated Load)
      i. Blend has 0.5 less than existing subject device
   c. Current Equivalent Electrical Standards: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0
3. Output Characteristics for Monopolar Coag: Highly Similar, Equivalent
   a. Max Open Circuit/ Peak-to-Peak Voltage (Vp-p)
   The new subject device has:
      i. 900 Vp-p more voltage than existing subject device for COAG 2*
      ii. 200 Vp-p less voltage than existing subject device for Spray*

*Note: The new Ethicon Megadyne Electrosurgical Generator uses voltage and current limiting technology to prevent excessive leakage currents. This technology effects the open circuit voltage measurement but voltages in clinical use are not affected.

b. New SOFT Coag: feature has 470 Vp-p voltage. Existing subject device does not have feature
c. Crest Factor Nominal @ (Rated Load)
    i. Spray has 0.2 more than existing subject device
d. Current Equivalent Electrical Standards: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0

4. Output Characteristics for Bipolar: Highly Similar, Equivalent
    a. Max Open Circuit/ Peak-to-Peak Voltage (Vp-p)
    The new subject device has:
        i. 90 Vp-p more voltage for Micro Bipolar Coag than existing subject device
        ii. 170 Vp-p less voltage for Macro Bipolar Coag than existing subject device
    b. Current Equivalent Electrical Standards: IEC 60601-1 Ed3.1 & IEC 60601-2-2 Ed6.0
5. Conditions of Use: Highly Similar
    a. 'and its accessories' wording not present in existing subject device IFU.
    b. 'Wall Mounted' wording dropped from new subject device IFU.
6. Application (e.g. how the device achieves its intended performance): Highly Similar
    a. The ACE mode (existing subject device) automatically controls the output power of the generator to provide the surgeon with a consistent cutting effect. This is achieved by delivering a stable voltage, pure sine wave current to the surgical site regardless of the impedance to affect the cutting of tissue. Little hemostasis is achieved in this mode.
        i. Underlined sentence above was dropped from new subject device IFU
        ii. Functionality of the ACE and GEM modes are identical
            1. Two selectable GEM settings (on the new subject device):
                a. High power GEM setting: maintained from the Mega Power (ACE mode)
                b. Low power GEM setting (approximately 50% of Mega Power ACE mode)
    b. Bipolar Coagulation - The bipolar mode operates on an independent power source from the monopolar power source. This enables one surgeon to use the bipolar coagulation mode at the same time another surgeon is using monopolar CUT or COAG mode. Either the footswitch or the hand switch on the bipolar instrument can activate the bipolar instrument.
        i. Wording and functionality stated above dropped from new subject device
        ii. Mega Power Generator bipolar visual indicator is green, Ethicon Megadyne Generator is blue
        iii. New subject device functionality allows only one modality to be used at time

c. New: SOFT COAG - Pressing the SOFT button places the generator in the Monopolar SOFT Coag mode. The SOFT mode desiccates tissue at a relatively slower rate with deeper thermal penetration. SOFT mode is typically used with an uncoated electrode. SOFT Coag power delivery takes place at much lower impedance than other Coag modes.
    i. SOFT COAG-Desiccates tissue at a slower rate with deeper thermal penetration. Highly similar, device enhancement.
    ii. Existing subject device has 3 Monopolar Coag Modes. The new subject device has 4 Monopolar Coag Modes with SOFT Coag added.
d. New: AUTO Bipolar – There is an Auto Start and Stop feature available with both Micro and Macro Bipolar functions. When selected, the generator senses (tissue impedance) when the surgeon has contacted tissue with the bipolar forceps and will automatically activate (auto start or stop the delivery of bipolar energy). There are three delay options, None (no delay prior to the onset of energy delivery), Short (0.5 second) and Long (1 second) that are selectable by the user. The AUTO stop is programmed into the generator and will discontinue the Bipolar output when the impedance increases, and the tissue is desiccated.
    i. This is a new feature on the new subject device only and involves user selectable, timed delays in addition to the AUTO Start and Stop delivery of power.
e. Contact Quality Monitoring (new) vs. Return Electrode Contact Quality Monitoring System (existing) - Same function, different name.
f. Bipolar Footswitch - Activates the bipolar instrument. There are two types of Bipolar Footswitches:
    i. Square Bipolar Pedal (1450J) is blue and activates power for Bipolar modes. Currently used on existing subject device.
    ii. NEW: Round Bipolar Pedal (1459J) is blue and activates power for the Bipolar modes. Currently used on the new subject device.
    iii. This new footswitch is functionally the same as the existing square shaped Bipolar pedal. The only difference between the two is ergonomic - the new footswitch is round.

4.3.2.1. Summary of Technical Parameters:

- Slight variations in generator size which is slightly smaller overall for the new subject device.
- Slight variations in voltage outputs with 6 variations being lower for the new subject device and three being higher with equivalent electrical standards (IEC 60601-1 Ed3.1, IEC 60601-2-2 Ed6.0) established for both devices.
- Slight changes to the wording of the IFU's with no change in function
- Two new features on the new subject device:

- SOFT Coag for use with Monopolar Coagulation Mode delivers power that takes place at much lower impedance than other Coag modes. This is an enhancement for the new device but highly similar to the existing Coag features.
- AUTO Bipolar for use with Micro and Macro Coag Mode automatically activates and deactivates the bipolar energy. There is a programable setting for None, Short and Long. This is an enhancement for the new device that does not involve any new technical parameters required for function (software) or performance (on/off).

- One new Bipolar Footswitch (1459J) accessory is identical to the existing footswitch (1450J) except for the shape. The new footswitch is round versus square.

4.3.3. Biological Parameters - Identical or Equivalent

The Biological Parameters for the Megadyne Electrosurgical Generators contain three (3) categories two of which are Identical as documented in the Equivalence Table above (Table 4-2). The remaining biologic category is for Materials / Construction and the equivalence documentation is provided below.

1. Restriction of Hazardous Substances: Equivalent
    a. The existing Megadyne Mega Power Electrosurgical Generator is compliant with European RoHS Directive 2011/65/EC. The generator design was verified with document: Test Results, Mega Power Electrosurgical Generator, (RoHS 1151744-10, **Windchill**).
    b. A Materials Equivalency Memo (500430815, **Windchill**) titled: MEGEN1 RoHS Compliance Memorandum documents that the new Ethicon Megadyne Electrosurgical Generator is compliant with the European RoHS Directive 2011/65/EC due to documented equivalency with existing subject device materials.
    c. The new Footswitch (1459J) is equivalent to the existing Footswitch (1450J). The only difference is ergonomic - the shape of the new footswitch is round.

4.4. Equivalence Conclusion

In summary, out of the total number of combined design parameters (Clinical, Technical and Biological) used for determining equivalence between the new subject device and the existing subject device, 83% were identical and 17% were highly similar or equivalent. Table 4-3 below provides the breakdown of equivalence for each category type and the resulting outcome percentages for identical and highly similar/equivalent design specification comparisons between the two subject devices.

Table 4-3: Subject Device's Equivalence Outcomes for Comparable Design Specifications

Equivalence Category	Category Total	Total Identical	Percentage Identical	Total Highly Similar/ Equivalent	Percentage Highly Similar/Equivalent
Clinical Parameters	8	8	100%	0	0%
Technical Parameters	30	24	80%	6	20%

Biological Parameters	3	2	67%	1	33%
Total	**41**	**34**	**83%**	**7**	**17%**

In conclusion, all of the equivalent rationale parameters documented for both subject devices (Clinical, Technical and Biological) have been described above to be either 'Identical' or 'Highly Similar' and/or Equivalent' with electrical compliance standards. Where there are differences (all Highly Similar), it has been demonstrated by the evidence above that these small differences do not have an impact on the safety and performance of the subject devices. Thus, the data from one device may be used to support the other device.

5. DATA SOURCES - IDENTIFICATION AND APPRAISAL (STAGE 1, 2)

5.1. Data Appraisal Plan

Comprehensive methods were utilized to identify and appraise all data sources that are generated and held by Megadyne Medical Products Inc. for the subject devices including evidence from Europe and other countries. The appraisal of each data source is described in Table 5-1 below, with further details in subsequent CER sections for each data source.

Table 5-1 Data Appraisal Sources and CER Appraisal Sections

Data Source	Section (Detailed Appraisal)
Data Appraisal Matrix	Section 6.1
Non-Clinical Data	Section 6.2
Pre-Market Clinical Investigations	Section 6.3
Post-Market Clinical Follow-Up	Section 6.6
Literature	Section 6.7, 6.8
Internal Complaint Data	Section 7.1

For all data sources, suitability and contribution were determined by assessing whether the data were generated on the subject device or other devices considered representative. Data were only included if the reports contained sufficient information to be able to undertake a rationale and objective assessment.

For nonclinical testing (Section 5.2), the test methods/study design were assessed to ensure they were considered representative of the intended use of the subject devices and of the treatment population. More weight was given to representative in vivo (ex vivo) analyses and testing to international / national standards, but all studies were included if the data were of sufficient quality. More weight was given to in vivo studies where the follow-up time was representative of the functional lifetime of the device.

For clinical data from pre-market clinical investigation (Section 5.3) / post-market clinical investigations (i.e. PMCF [Section 5.6.2] / proactive clinical data [Section 5.7), external registries (Section 5.4), and internal registries (Section 5.5), the data were critically appraised to determine whether the outcome measures reflected the intended performance of the subject device, the study design was adequate, whether the intended treatment population reflected the entire target population, how the follow-up time compared with the lifetime of the device, and whether the quality of the data were sufficient to allow a rationale and objective analysis in order to determine the overall weight of the data (as assessed by the aforementioned characteristics).

For clinical data from scientific literature (Section 5.8), the data relevance and contribution were assessed. using the Oxford Centre for Evidence Based Medicine (OCEBM) Levels of Evidence. The level of evidence for each citation was assessed and higher levels (randomized controlled clinical trials, for example) are given more weight towards overall conclusions and assessment of safety and performance when compared against lower level cohort or case reports. Nevertheless, even case reports reflect real-world usage of the subject device. Follow-up times, population characteristics, and device usage (compared against intended use) are all appraised and factor into the presentation and weight of the data

While of lower quality (due to the availability of limited information), post-market surveillance data (Section 0), including complaints and sales, vigilance, CAPA, Escalations, Field Actions, and Alerts; still provides valuable information towards the assessment of safety for the subject devices and reflects real world usage. While the follow-up times and clinical use of the devices relative to the intended purpose cannot easily be ascertained, the data obtained are representative of the treated population and are of sufficient quality to allow a rationale and objective assessment.

Risk management data (Section 7), including identified clinical risks, benefits, and information provided to the user on residual risks are evaluated in comparison to the other data sources and the SOA to determine the acceptability of the known side effects and benefit-risk ratio.

The following matrix (Table 5-2) identifies the data sources being used to support safety and / or performance of the subject devices to support the demonstration of conformity with the relevant Essential Requirements.

Table 5-2: Data Source Contribution

Data Source	Performance / Clinical Benefits	Safety/Clinical Risks	Side-Effect Acceptability	Benefit-Risk Profile Acceptability
MDD ERs	3	1	6	1
Nonclinical				
Bench-Top Data	X	X	X	X
Analytical Data	X	X	X	X
Pre-Clinical Animal Data	X	X	X	X
Complaints / Sales Data	--	X	X	X
Vigilance Data (MDVs, FDA-MDRs)	--	X	X	X
CAPAs, Field Actions, Escalations	--	X	X	X
Clinical				
Post-Market Clinical Follow Up Study Data (PMCF) • **Survey Data**	X	X	X	X
Proactive Clinical Data	X	X	X	X
Published Literature	X	X	X	X

5.2. Non-Clinical Data

The design requirements of the Megadyne Electrosurgical Generators have been investigated and defined in the specification documents used for development. The Ethicon Megadyne Electrosurgical Generator requirements document is titled Input / Output Conformance Test Matrix (ENG-IOM-020, **Windchill**). The requirements and specification documents for the Megadyne Mega Power Electrosurgical Generator includes: ENG-IOM-010, ENG-PS-001, ENG-WI-005, MKT-US-001, and MKT-CMR-009 (**Windchill**).

The design verification activities have been confirmed through examination and provision that the design outputs of device design meet the design requirements (design inputs). The design validation activities have ensured that finished device design and manufacturing, including packaging and labeling, conforms to defined customer requirements (user and patient needs) to allow the specific intended purpose to be consistently fulfilled. The design validation further evaluated the performance of initial production units, lots, batches, or devices justified to be representative under actual or simulated use conditions.

Megadyne Medical Products, Inc., has undertaken all necessary steps to apply standard techniques in designing and manufacturing the subject devices to ensure they are safe and perform as intended. The available non-clinical dataset further substantiates, the Megadyne Electrosurgical Generators as state-of-the-art medical devices, designed to produce radio frequency (RF) current for cutting and coagulation of tissue, in electrosurgical surgical procedures and, also identifies the residual risks from its design and production as specified in this Data Appraisal Plan Section. The subsequent section summarizes the non-clinical datasets where key design requirements (Benchtop Testing and Design Verification and Validation) are provided from the Technical Documentation. Complete details on the ex vivo study follows the Non-Clinical Data Summary's tables.

5.2.1. Non-Clinical Data Documentation

5.2.1.1. Design Requirement Conformance Testing

The physical and performance requirements are defined in the design specification documents used by Megadyne Medical Products Inc. The Non-Clinical data sets for the design verification and validation testing of the Megadyne Electrosurgical Generator requirements are derived from the Input and Output Conformance Matrix's (Mega Power Generator-ENG-IOM-010 and Ethicon Megadyne Generator ENG-IOM-020, **Windchill**).

Design Requirement Categories for Conformance Testing:

- System Requirements
- Electromagnetic Compatibility
- Mechanical Enclosure Requirements
- Mechanical Strength
- Labels

- Connectors and Switches
- Indicators and Alarms
- Displays
- User Controls
- Cables
- Foot Controls
- Cart Requirements
- Electrical Requirements
- General
- Functional Requirements
- Shipping Requirements
- Serviceability Requirements
- Reliability Requirements
- Miscellaneous CMR
- Software Requirements
- Programmable Electrical Medical Systems (PEMS)
- Risk Management Requirements

Design Requirement Test Categories:

The Non-Clinical Data Summaries provided below for both subject devices (Table 5-3 and Table 5-5) provide testing Results/Outcomes from the following Test Categories:

- IEC Safety
- Design
- Marketing Evaluation
- Sterilization
- Software
- Shipping
- Restriction of Hazardous Substances
- Process

Design Requirements Testing for Mega Power Generator Upgrade (2011)

Additionally, Table 5-4 below provides the design requirements testing results for the Mega Power Generator upgrade in completed in 2011. The testing categories included: Mechanical, Electrical/Software, Packaging and Environmental.

5.2.1.1.1. Non-Clinical Data Results/Outcomes

5.2.1.1.1.1 Megadyne Mega Power Electrosurgical Generator

The initial Design History File (DHF) for the existing Mega Power Generator is archived in the Megadyne Document Control System and is titled Project “Gemini I”. An upgrade to the design of the Mega Power occurred in 2011. This upgrade project was performed in accordance with the requirements of ENG-

SOP-005, *Design Control*. The Design History File (DHF) is archived in Document Control and is titled "Mega Power Upgrade" (ENG-DMR-008, **Windchill**).

A summary of the Mega Power Non-Clinical Data is presented in Table 5-3 below. Additionally, Table 5-4 summarizes the Non-Clinical datasets for Input / Output testing related to the Mega Power Generator Upgrade in 2011. Key design requirements and results are provided from the Technical Documentation.

Form (Non-PPE) 100503977 Rev3
Quality System CO: 100610371
Franchise Clinical Evaluation Report Template (Shared)

Table 5-3: Mega Power Electrosurgical Generator Non-Clinical Data Summary (existing subject device)

Protocol	Report	Test Description	Test Category	Results/ Outcome
N/A	ENG-RPT-052	Mega Power EMC Test Report	IEC Safety	Pass
N/A	ENG-RPT-058	Mega Power UL Test Report	IEC Safety	Pass
N/A	ENG-RPT-059	Mega Power CB Test Report	IEC Safety	Pass
ENG-PRT-118	ENG-RPT-193	Test Report Mechanical Testing of Footswitch Cables 1400	Design	Pass
ENG-PRT-119	ENG-RPT-195	Test Report Mega Power Macro Bipolar and Standard Bipolar Marketing Eval	Design/ Marketing Eval	Pass
ENG-PRT-147	ENG-RPT-227	Test Report 0075 Reusable Foot Control Cable New Vendor Qual 0075	Design/ Sterilization	Pass
ENG-PRT-150	ENG-RPT-230	Test Report Mega Power Standard Bipolar Rev T Marketing Eval	Design/ Marketing Eval	Pass
ENG-PRT-155	ENG-RPT-238	Test Report Mega Power Calibration SW Verification Rev J	SW	Pass
ENG-PRT-158	ENG-RPT-240	Test Report Mechanical Testing of 1450 Footswitch Cables	Design	Pass
ENG-PRT-174	ENG-RPT-254	Test Report SW Master Rev V Verification	SW	Pass
ENG-PRT-192	ENG-RPT-281	Test Report SW Master II Rev A Verification	SW	Pass
ENG-PRT-199	ENG-RPT-291	Test Report Mega Power Shipping	Shipping	Pass
ENG-PRT-200	ENG-RPT-292	Test Report Updated Mega Power Performance Testing	Design	Pass
ENG-PRT-204	ENG-RPT-297	Test Report Motherboard Arc Damage Detection Verification	Design	Pass
ENG-PRT-206	ENG-RPT-300	Test Report Anti-Arcing Mega Power Motherboard Layout Verification	Design	Pass
ENG-PRT-096, ENG-PRT-147	ENG-RPT-303	Test Report IEC 60601-2-2 5th Ed Leakage HF and Mains 0075	Design	Pass
ENG-PRT-016	ENG-RPT-321	Test Report Mega Power Foot Pedal Shipping Cycle Test	Shipping	Pass
ENG-PRT-237	ENG-RPT-338	Test Report Mega Power Electrosurgical Generator RoHS Compliance	RoHS	Pass
ENG-PRT-055	ENG-RPT-357	Test Report Mega Power Bipolar Customer Preference Clinical Eval	Design/ Clinical Eval	Pass
N/A	ENG-RPT-371	Test Report Transport and Storage Conditions Test Summary	Shipping	Pass
ENG-PRT-237	ENG-RPT-385	Test Report Mega Power Electrosurgical Generator RoHS Compliance	RoHS	Pass
ENG-PRT-237	ENG-RPT-389	Test Report Mega Power Electrosurgical Generator Assembly RoHS	RoHS	Pass
ENG-PRT-237	ENG-RPT-393	Test Report Mega Power Electrosurgical Generator Assembly RoHS	RoHS	Pass
ENG-PRT-277	ENG-RPT-399	Test Report Mega Power Electrosurgical Generator Motherboard Functional Test	Process	Pass

ENG-PRT-309	ENG-RPT-448	Test Report Mega Power U6/U7 Change to IXYS	Design	Pass
ENG-PRT-313	ENG-RPT-456	Test Report ESU Electrical Safety Test	Design	Pass
ENG-PRT-322	ENG-RPT-466	Test Report HW Verification Motherboard IXYS and Power Resistor Change	Design	Pass
ENG-PRT-446	ENG-RPT-560	Test Report Motherboard Transistor Change Verification	Design	Pass

Table 5-4 below summarizes the Non-Clinical datasets for Input / Output testing related to the Mega Power Upgrade in 2011 (*Design Control*, ENG-SOP-005,**Windchill**).

Table 5-4: Mega Power Electrosurgical Generator Upgrade (2011): Input / Output Test Matrix (existing subject device)

Origin of Input Standards - Internal/External	Design Input	Conformance Method	Output of Conformance	Requirement Status
MECHANICAL				
FMEA 1300013-01 Item 41	Mechanical fit of keypad, front cover and PCB	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS
IEC 60601-2-2 Clause 42	Device operated at stated duty cycle under worse case conditions for 1 hour	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS
ELECTRICAL/SOFTWARE				
CMR 1250010-10	CUT functions PURE, BLEND and ACE have same power curve characteristics as former Mega Power Rev V	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS
CMR 1250010-10	Coag functions: Coag 1, Coag 2 and Spray have same power curve characteristics as former Mega Power Rev V STANDARD, CwC, and SPRAY respectively	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS
CMR 1250010-10	Bipolar functions: Micro and Macro Bipolar have the same power curve characteristics as former Mega Power Rev V.	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS

CMR 1250010-10	Bipolar Tone Button will turn tone on/off. System will start with tone off. Tone will be available in both the Micro and Macro modes for customer preference.	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE / PASS
1010020-10 Software Development SOP and 1020017-10 ESU DMR	Develop Software that controls the ESU properly to meet the DMR	1150557-10 Test Protocol, Software Master II Rev A Verification	1150557-01 Test Report, software Master II Rev A Verification	COMPLETE / PASS
PACKAGING				
1200011-10 Product Specification	The packaging must be tested and approved per ASTM D 4169, D13. After performing the shipping tests the device shall pass functional and safety tests.	1150569-10 Mega Power Shipping Test	1150569-01 Mega Power Shipping Test	COMPLETE / PASS
ENVIRONMENTAL				
IEC 60601-2-2 Clause 44.3	Fluid Ingress Test	1150570-10 Updated Mega Power Performance Test	1150570-01 Test Report, Updated Mega Power Performance Test	COMPLETE/PASS

5.2.1.1.1.2 Ethicon Megadyne Electrosurgical Generator

The initial Design History File (DHF) for the Ethicon Megadyne Electrosurgical Generator is archived in the Megadyne Document Control System and is titled Project “Golden Gate”. A summary of the Ethicon Megadyne Electrosurgical Generator Non-Clinical Data input/output testing is presented in Table 5-5 below.

Form (Non-PPE) 100503977 Rev3
Quality System CO: 100610371
Franchise Clinical Evaluation Report Template (Shared)

Table 5-5 Ethicon Megadyne Electrosurgical Generator Non-Clinical Data Summary (new subject device)

Protocol	Report	Test Description	Test Category	Results
ENG-PRT-501	ENG-RPT-596	Report, Software Verification/Validation Ethicon Megadyne™ ESU	Software	Pass
ENG-PRT-498	ENG-RPT-611	Electromagnetic Compatibility, Ethicon Megadyne Electrosurgical Generator	IEC Safety	Pass
ENG-PRT-514	ENG-RPT-613	Thermal Testing, Ethicon / Megadyne Electrosurgical Generator, MEGEN1	Design	Pass
ENG-PRT-515	ENG-RPT-614	Ethicon Megadyne ESU Shipping Test	Shipping	Pass
N/A	ENG-RPT-615	Ethicon Megadyne ESU IEC 60601-1 Report	IEC Safety	Pass
ENG-PRT-516	ENG-RPT-617	Ethicon Megadyne ESU Product Specification Verification Report	Design	Pass
ENG-PRT-517	ENG-RPT-618	Ethicon Megadyne ESU Cleaning Report	Design	Pass
ENG-PRT-518	ENG-RPT-619	Ethicon Megadyne ESU Footswitch Specification Verification Report	Design	Pass
ENG-PRT-524	ENG-RPT-625	Summative Usability and Design Validation, Ethicon Megadyne Electrosurgical Generator	Design	Pass
ENG-PRT-529	ENG-RPT-635	Report, Ethicon Megadyne ESU, Thermal Effects on Tissue	Design	Pass
ENG-PRT-536	ENG-RPT-647	Report, Ethicon Megadyne ESU, Labeling Verification	Design	Pass
ENG-PRT-548	ENG-RPT-660	Report, Incremental Software Verification/Validation, Ethicon Megadyne ESU	Software	Pass
ENG-PRT-599	ENG-RPT-689	Ethicon Megadyne ESU Rev H Software Verification Report	Software	Pass
ENG-PRT-611	ENG-RPT-698	Golden Gate Reliability Report	Design	Pass
ENG-PRT-639	ENG-RPT-737	Report, 1459J Round Bipolar Footswitch Shipping Test	Shipping	Pass
ENG-PRT-560	ENG-RPT-673	MEGEN1 ESU Process Validation Report	Process	Pass
500438089	500438090	Golden Gate Auto Bipolar Test Report	Design	Pass

5.2.2. Pre-Clinical Animal Testing

There was no pre-clinical in vivo animal testing performed for the Megadyne Mega Power Electrosurgical Generator prior to release. However, there was a pre-clinical ex vivo study performed during the development of the Ethicon Megadyne Electrosurgical Generator comparing the performance of the existing subject device to the new subject device. Further details of the pre-clinical ex vivo study are provided below.

5.2.2.1. Thermal Effects on Tissue

Study: Ex Vivo

Protocol: Ethicon Megadyne ESU, Thermal Effects on Tissue (ENG-PRT-529, **Windchill**)

Report: Ethicon Megadyne ESU, Thermal Effects on Tissue (ENG-RPT-635, **Windchill**)

Purpose:

The purpose of this study is to evaluate the thermal tissue effects of the subject device, Ethicon Megadyne Electrosurgical Generator ESU (Product code: MEGEN1) in comparison to its predicate device, the Mega Power Generator (Product code:1000 and abbreviated as MP).

Methods and Setup:

Each of the nine Ethicon Megadyne ESU modes were evaluated alongside eight predicate Mega Power modes using representative electrodes (SOFT Coag for Monopolar Coag is new to Ethicon Megadyne ESU.

Testing was performed on ex vivo harvested animal tissue—Skeletal muscle (femur), liver (without gall bladder), and kidney (loose).

Design:

To simulate true use while keeping application consistent for accurate comparison, an Instron mechanical tester will be used, applying 0.1 lb. force for one second. This application pressure is representative of typical use. One second is a representative unit of time to compare between modes in a controlled way.

Thermal damage will be measured using gross thermal spread measurements under magnification through image analysis using the open source image processing program ImageJ.

Conclusion:

Each Ethicon Megadyne ESU mode maintained from predicate Mega Power generator (GEM H/ACE, Pure Cut, Blend, Coag 1, Coag 2, Spray, Micro Bipolar, Macro Bipolar) has similar thermal spread for each corresponding mode and tissue type. Soft Coag has less eschar build-up on average than Coag 1 for each tissue type, approximated via gray value measurement. GEM L has less thermal spread on average than GEM H for each tissue type.

Average Gray Value Measurement:

- Graphs of average gray value, a proxy for eschar build-up, in each tissue type at each power setting for new Monopolar SOFT Coag and existing Coag 1
    - The lower the value, the greater the eschar build-up.
    - The higher the value, the whiter the tissue.
    - A value of zero is a result of no spread at that given power setting.

Disclaimers:

- Three activations per combination of power setting, tissue type, and mode (as directed by FDA guidance) are not sufficient to claim statistical significance, which is out of scope for this study. Duration of activation, electrode contact area, tissue type and resistance, application of saline, and presence of blood all impact the tissue effect. Many of these variables are not captured in an ex vivo tissue effect study.
- As tissue effect is modulated by the surgeon via power setting selection and surgical technique, any anomalies may be compensated by the user, which is outside of the Ethicon Megadyne ESU design.

End Pre-Clinical Animal Testing Section.

5.3. Pre-Market Clinical Investigations – N/A

No pre-market clinical trials were conducted for the devices in this CER, which are Class IIb electrosurgical devices. Not conducting pre-market clinical trials was duly justified for the subject devices, which were placed on the market via a rationale for equivalence to existing CE Marked devices, noting that the equivalence rationale presented at time of launch were deemed compliant with the continuously evolving interpretations of the MDD via Notified Body audits and reviews, as well as the various revisions of the guidance provided in MEDDEV 2.7.1. The products continue to meet the requirements of sufficient clinical evidence based on the clinical evidence reported in this CER.

5.4. Review of External Registry Data – N/A

Not applicable. Review of external registry data was not conducted for this CER.

5.5. Review of Internal Registry Data – N/A

Not applicable. Review of internal registry data was not conducted for this CER.

5.6. Post-Market Clinical Follow-Up (PMCF)

As referenced below in Section 6.1 of this Clinical Evaluation Report and in accordance with the requirements of the Medical Device Directive MDD 2007/47/EC, MEDDEV 2.12/2 Rev 2 and MEDDEV 2.7/1 Rev 4, Megadyne Medical Products Inc.'s established Post Market Surveillance Plan continues to provide ongoing data to address long-term risk management of the Megadyne Mega Power electrosurgical Generator. The established Post Market Surveillance system routinely monitors the clinical safety and performance of the existing subject device as part of its quality management system (QMS). Any new, clinically significant data detected from complaints, vigilance reports, safety reports, published literature, device registries, as well as any other source, are monitored, trended, and critically and objectively evaluated with respect to the device's clinical benefit-risk profile to confirm and maintain a high degree of protection of safety for the patient and the users of this device. These PMS data are incorporated in the clinical evaluation report regularly based on the device classification and the level of residual risk present in accordance with the CER Frequency Update Matrix presented in Table 8-2, Section 8 below.

Any new, clinically significant data detected from complaints, vigilance reports, safety reports, published literature, device registries, PMCF studies, as well as any other source, are monitored, trended, and critically and objectively evaluated with respect to the device's clinical benefit-risk profile to confirm and maintain a high degree of protection of safety for the patient and the users of this device. The PMS Plan provides ongoing and long-term risk management of the subject device.

To date, PMCF has not been conducted on the Megadyne Mega Power Electrosurgical Generator given the established safety and performance profile that the generator has demonstrated over the past 15 years since its regulatory approval and CE Mark in 2005. The continued review of the post market

surveillance data also supports the safety and performance of the subject device; however, in general, clinical publications on the use of the Megadyne Mega Power Electrosurgical Generator are limited, given the long term (decades) history of electrosurgery and acceptability as a “standard of care” device in the majority of surgical procedures performed globally.

The review of the post market surveillance (PMS) data also continues to conclude that there are no safety or performance related trends. However, given limitations of the amount of clinical literature, Megadyne Medical Products Inc. has elected to develop a PMCF Plan that will allow for the collection of clinical data on the existing Megadyne Mega Power Generator and will also include data collection on the newly developed Ethicon Megadyne Electrosurgical Generator as well as other devices within the Megadyne Electrosurgical System Portfolio going forward. Post Market Clinical Follow-up (PMCF) is currently planned for the Megadyne Mega Power Electrosurgical Generator and Ethicon Megadyne Electrosurgical Generator. The broad-reaching PMCF Plan will facilitate the collection of post-market clinical data for both existing and newly launched Ethicon Megadyne Electrosurgical Generator. Further details of the PMCF Plan are provided below.

5.6.1. PMCF Clinical Data Methods

Objective:

The objective of this Post Market Clinician Survey (PMCS) is to further confirm the clinical safety and performance of the Megadyne Electrosurgical Generators in US and EU sites.

Sites:

6-10 sites in the US and EU.

Patient Population:

A minimum of 500 uses of both Megadyne Electrosurgical Generators

Performance Confirmation Variables:

- Overall Performance of the Megadyne Mega Power and Ethicon Megadyne Electrosurgical Generators.
- Overall Performance of any other Megadyne products used with the Megadyne Electrosurgical Generators including the ACE Blade 700^{TM} Soft Tissue Dissector where applicable.
- Overall Performance of Universal MegaSoft Patient Return Electrode or disposable electrode(s) – Only the use of the generator is required.

This study is sponsored by Ethicon Endo-Surgery, Inc. (EES, Cincinnati, OH, USA) and will be conducted in up to 6-10 surgical centers in the US and EMEA under a single protocol. IRB/EC approval is not applicable as this is not a study of clinical patient outcomes and there will be no patient identifying information. Data will be collected via a surgeon survey that will capture the physician’s assessment of the safe and effective use of the Megadyne system. An electronic (web-based) survey will be utilized by study site personnel to send data to the Sponsor.

5.6.2. PMCF Data Results

Data is expected to be reviewed and analyzed at 1-year post launch of the new Ethicon Megadyne Electrosurgical Generator.

5.7. Literature Review Methods (Literature Protocol)

The review was conducted in accordance with the prospective Systematic Literature Review Protocol. The protocol documents the explicit plan for the systematic review and details the priori methodological and analytical approaches including the search strategy, selection and eligibility criteria, data collection methods, and analysis plan. Refer to attachment, SCN073157 for a copy of the Literature Protocol. The Literature Search Results can be found in Appendix 9.3.2.

This systematic literature review will evaluate the safety and performance of the subject devices, the new Ethicon Megadyne Electrosurgical Generator, and the Megadyne Mega Power Electrosurgical Generator based on published literature included in the Systematic Literature Review found in Section 6.8 below.

5.8. Literature Review Results (Literature Report)

This review was undertaken to support the clinical evaluation of the Ethicon Megadyne Electrosurgical Generator and the Megadyne Mega Power Electrosurgical Generator. The devices in scope for this review are detailed below, along with the assumptions used throughout the review:

Subject Devices:

1. Ethicon Megadyne Electrosurgical Generator, which is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.
2. Megadyne Mega Power Electrosurgical Generator, which is intended as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation to be delivered to target tissue through an accessory electrode during open and laparoscopic surgical procedures.

The following assumptions were used throughout the systematic literature review:

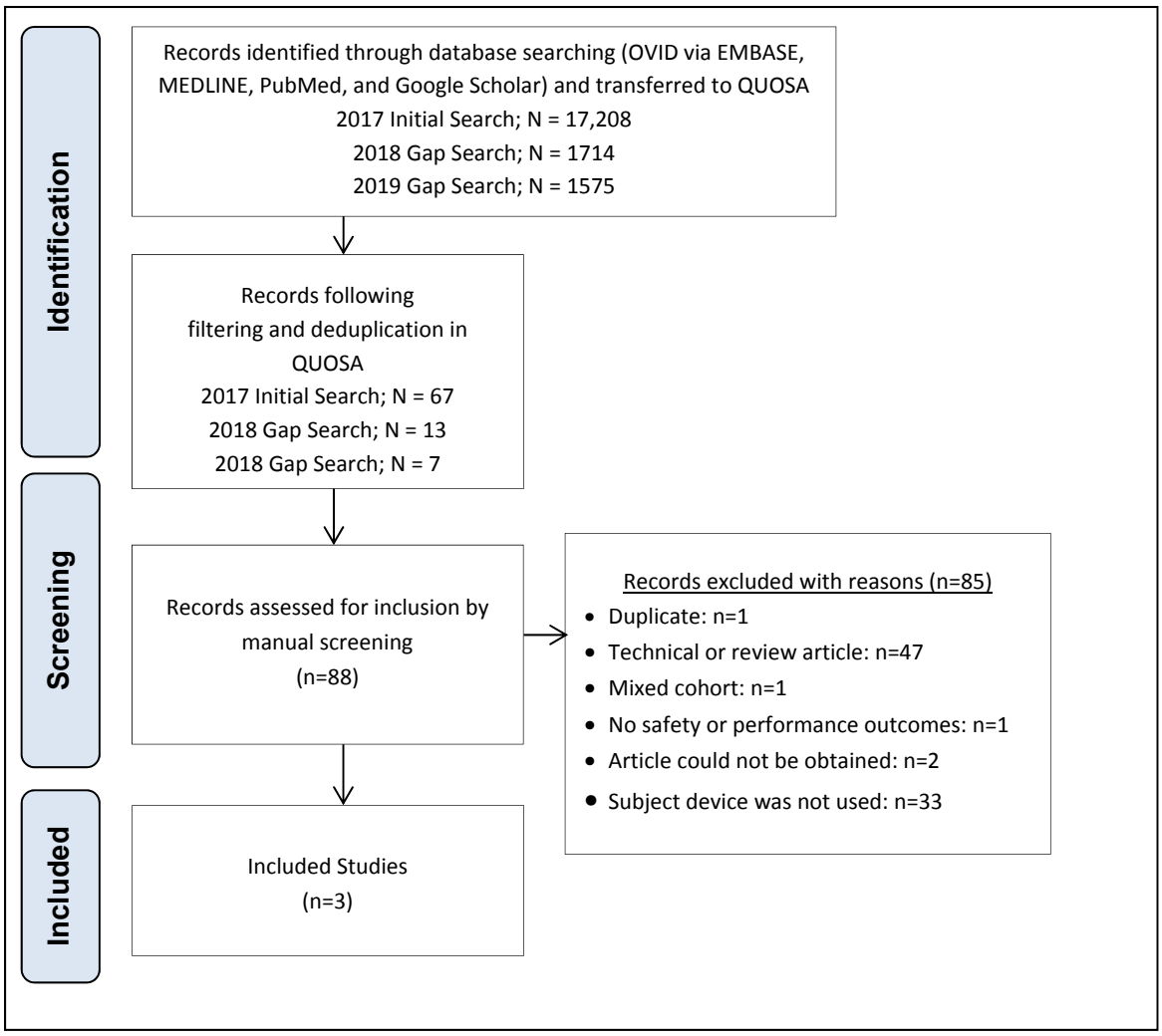
- The Megadyne Mega Power Generator and Ethicon Megadyne Electrosurgical Generator are equivalent to each other and data for Megadyne Mega Power Generator will support the clinical and safety performance of the Ethicon Megadyne Electrosurgical Generator.
- The Mega Power Generator is a unique and trademarked brand name. The brand name was considered sufficient to identify this subject device, regardless of whether the manufacturer, Megadyne, was specified.

5.8.1. Search and Selection Results

Broad literature searches were conducted to identify all published literature on Megadyne devices, including the Mega Power Generator. The search was performed for the period of 01 January 1986 to 03 September 2019 (Refer to attachment, SCN073157 for a copy of the Literature Protocol for details). The core bibliographic databases were Medline and Embase via Ovid, and PubMed. These databases are reliable and cover the vast majority of medical and scientific journals. In addition to the databases, Google Scholar was also searched.

The search results were imported into an internal literature management system (QUOSA). The full text, abstract, key words and title were then searched by the subject device names. The Literature Search Reports, with detailed search queries, are provided in the appendices. Out of the 88 possible results, 3 articles were included while 85 were excluded due to the reasons presented in Figure 5-1 below.

Figure 5-1: Search and Selection Flow Chart



Relevant studies identified in the search and selected by previously defined criteria are summarized by indication in Table 5-6 below. As expected, all studies reported on the Mega Power Electrosurgical Generator. The Ethicon Megadyne Electrosurgical Generator is a new device and therefore no literature-based studies could have been performed to date.

Table 5-6: Mega Power Electrosurgical Generator Clinical Literature Data by Indication

Indication	# Articles	# Patients
Overall	**3**	**69**
Open Procedures	**2**	**67**
Cutting and Coagulation	2	67
Laparoscopic Procedures	**1**	**2**
Cutting and Coagulation	1	2

5.8.2. Study Population Characteristics

5.8.2.1. Study Design, Demographics, Device Type and Surgical Procedure

The three included studies had a total of 69 patients shared among them. All studies reported on-label use of the Mega Power Generator, which was used in open and laparoscopic surgical procedures. All three of the articles reported on plastic surgical procedures (skin incisions and breast augmentation revision). Demographics and device use data related to each study are presented in Table 5-7. Articles were evaluated for study design via the Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 Levels of Evidence.

Two included articles were published by the same team and conducted as a collaboration between Megadyne and clinical consultants for Megadyne (Lee et al., 2014; Lee et al., 2017). Both of these studies were conducted in the United States. The third article was performed in South Korea (Kim et al., 2014).

In the first study, from 2014, Lee et al. used the Mega Power Generator to energize ACE Blade EZ Clean Electrodes in 64 patients (Lee et al., 2014). In the second study from 2017, the authors used the Mega Power Generator with ACE Blade 700 Soft Tissue Dissector instruments in 3 patients (Lee et al., 2017). The third study powered a “#15 Bovie electrocoagulator” with the Mega Power Generator (Kim et al., 2014).

The follow-up time was reported in 2 of the 3 included studies. For both studies the follow-up time was much greater than the exposure time to the subject device, which was only used intraoperatively.

- Lee et al. (2014), included an original population of 81 patients, 6 were excluded due to procedure postponement (1), or patients where only scalpels were used, and the subject device was left out of the procedure (5). Another 9 patients were lost to follow up, and 1 patient withdrew from the study. The remaining 64 patients completed the self-assessment at a minimum follow-up of 30 days, and the reported maximum follow-up was 120 days (4 months) where the photographs of the wounds were sufficient for analysis by the expert observers for 57 patients.
- Kim et al. (2014) followed their patients for 90 days and demonstrated the revision procedures they had undertaken were successful at that time.

Table 5-7: Demographics and Device Use

Reference	Device Used	Study Design	Procedure type	Patients	Demographics	Follow-up	Country
Lee et al. (2014)	Mega Power Generator	Comparative Cohort Study	Plastic surgery (breast, thighs, buttocks, or abdomen)	64	64 females Mean age 41.7y (range 22.3 to 60)	30 to 120 days	United States
Lee et al. (2017)	Mega Power	Comparative Cohort	Abdominoplasty	3	Not reported	Not reported	United States

	Generator	Study					
Kim et al. (2014)	Mega Power Generator	Case Report	Breast augmentation revision	2	2 females Ages 26 and 29 years	90 days	South Korea

5.8.3. Clinical Performance and Safety Results

Due to the small numbers of included studies, discrete data analysis tables were not created, and each article was summarized below with regard to clinical performance and safety outcomes.

Lee et al. (2014)

In this Megadyne sponsored study, Lee and colleagues screened and evaluated 64 patients to compare the scar formation of incisions made with the ACE Blade EZ Clean Electrodes powered by the Mega Power Generator or cold steel scalpels in various plastic surgeries. Surgeons had previously shown preference to cold steel scalpels for initial skin incisions due to perceived thermal damage caused by early generation electrosurgery systems. This study aimed to demonstrate that at 120 days, wound healing in patients treated with the ACE Blade System was noninferior to cold steel scalpels for cutaneous incisions, as measured by the primary outcome of Observer Scar Assessment Scale (OSAS).

Exclusion criteria included smoking, coagulopathy, diabetes, and active infection. Enrollment of plastic surgery patients between 18 and 60 years old occurred across three sites. All included patients were treated with both devices, the ACE Blade System on one side of the body and the scalpel for the same incision on the opposite side of the body. Surgeons for each case performed incisions according to their individual preferences and the same incision pattern was used on each side. No randomization, or allocation of devices to the respective sides of the body was described by the authors, however. The patients and observers were blinded to which comparator was used on each side of the body. The sutures were removed at post-operative day 10 and follow-up continued at 30 and 120 days. All of the patients were female, with a mean age of 41.7 ± 8.9 years. The patients had a mean BMI of 28.7 ± 7.2.

Wound healing was assessed at 120 days by the patients and physicians using the POSAS Patient Observer Scar Assessment Survey (van de Kar et al., 2005), which consisted of two parts. The first part, the Patient Scar Assessment Scale (PSAS), included six individual criteria, each graded on a 10-point scale by the patients, for a maximum possible score of 60 points. Higher scores represent better outcomes. The second part was the Observer Scar Assessment Scale (OSAS), which typically includes five criteria that are also scored on a 10-point scale which leading to a maximum possible score of 50 points. Like the PSAS, higher scores represent better outcomes. The OSAS portion was completed by two physicians based on photographs. Patients in this study were scored using photographs, so one of the criteria, the pliability measure, was omitted. This lowered the maximum possible score to 40 points.

The mean OSAS score assigned to the wounds from the patients treated with the ACE Blade System was 11.1 ± 4.4, and the mean score for the patients treated with the scalpel was 10.8 ± 3.7. The median (min, max) for both treatments was almost identical at 10.0 (3.0, 23.0) for the ACE Blade System, and 10.0

(3.0, 24.0) for the scalpel. The non-inferiority of the ACE Blade System compared to the scalpel was confirmed with a paired test for the noninferiority hypothesis (p<0.0001). The same results were found with the patient assessment, where the mean PSAS score for the wounds created with the ACE Blade System was 9.4 ± 9.2, and the mean score for the scalpel wounds was slightly lower at 9.3 ± 8.5. Noninferiority of the ACE system was met with PSAS as well (p<0.0001).

In terms of adverse events, there was a single case of wound dehiscence and a single unspecified "other" complication (no details provided) in each treatment group. There were also no cases of infection or hypertrophic scars.

- The authors theorized that the ACE Blade System may be better than previous electrosurgery electrodes because the Both advanced bipolar devices and ultrasonic surgical instruments, as the two representatives of advanced energized devices, were generally associated with superior clinical safety and performance outcomes relative to conventional electrosurgical devices.

The authors concluded, "These findings support the use of the ACE electrosurgical system throughout the entire incision process for surgeries involving extensive skin incisions. The ACE system effectively cuts, coagulates, and dissects, without causing dissipated thermal injury and its consequential adverse effects on wound healing."

Lee et al. (2017)

In this Megadyne sponsored study, Lee and colleagues studied the width of thermal injury from incisions made with the Megadyne Ace Blade 700 Soft Tissue Dissector powered by the Mega Power Generator. This treatment group was compared to two different cut settings on the PEAK PlasmaBlade used with the PULSAR II generator (Medtronic). The incisions were done on three patients undergoing abdominoplasties and all were performed by the same surgeon. Three paired, full-thickness incisions were made in the abdominoplasty flap remnants of each patient, prior to excision for a total of 9 incisions per device. The width of the thermal damage was then evaluated by a pathologist. The PEAK PlasmaBlade settings that were chosen for comparison with the Megadyne System were the medium cut mode (PEAK 7) and the high cut/blend 1 lowest setting (PEAK 9), while the Megadyne System was set to "ACE Mode" to accommodate the Ace Blade instrument that it was energizing.

Histopathology revealed no significant differences (p=0.982) in the mean widths of thermal necrosis between the Megadyne System and PEAK 7, values which were measured at 99 ± 26 µm vs. 97 ± 14 µm respectively. At the PEAK 9 setting, however, the mean width of thermal necrosis increased to 136 ± 43 µm, which was a significantly greater than the Megadyne system (p=0.014).

Both Figure 5-2 and Figure 5-3 show the representative width of thermal damage at the same 100x magnification for the Megadyne System (ACE Blade EZ Clean Electrodes powered by the Mega Power Generator) and PEAK 9 incisions respectively.

Figure 5-2: Incision Histopathology of Megadyne System Incision. Mean = 99 µm (Lee et al., 2017)

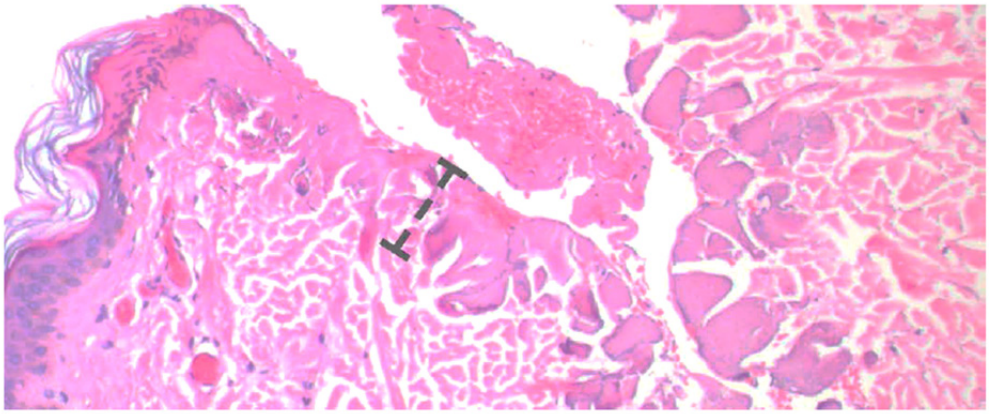


Figure 5-3: Incision Histopathology of a PEAK9 Incision (Medtronic). Mean = 136 µm (Lee et al., 2017)

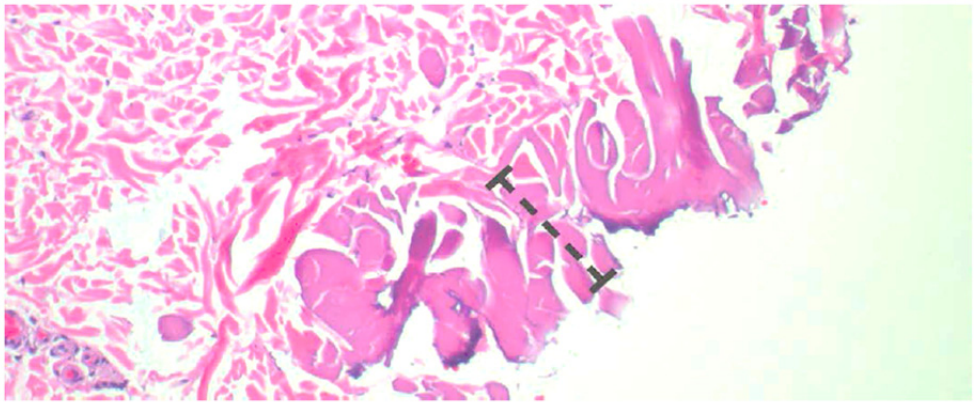
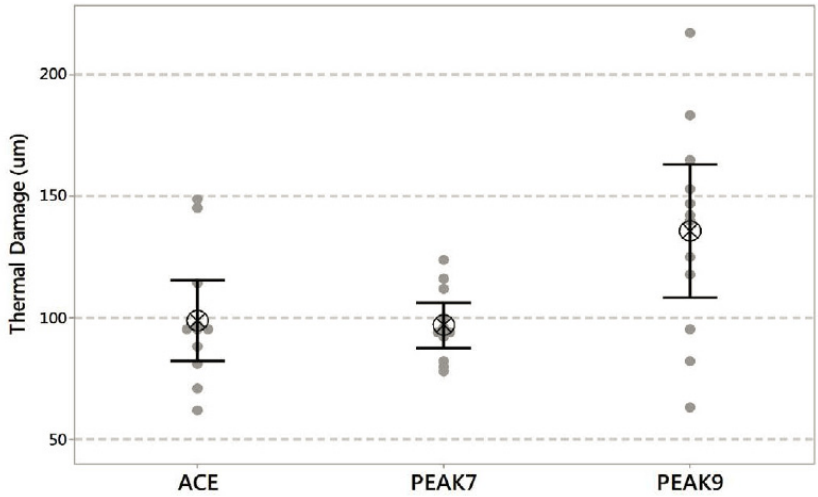


Figure 5-4 shows the analysis of the width of thermal damage. The bars represent the 95% CI and the crossed circles represent the mean width in µm.

Figure 5-4: Width of Thermal Damage Analysis (Lee et al., 2017)



The authors concluded, "…the ACE Blade (Megadyne System) and PEAK systems produced similar levels of thermal necrosis when the Pulsar generator is adjusted to a setting of 7, while a PEAK setting of 9 produces significantly greater thermal damage. The zone of thermal necrosis created during a skin incision is the most likely indicator of wound healing. Both technologies may increase efficiency in the operating room and decrease sharps injuries while providing wound healing equivalent to the gold standard, a cold scalpel."

Kim et al. (2014)

Treatment of "bottoming out", a common complication of breast augmentation procedures, was the focus of this study. Bottoming out occurs when the implant is displaced inferiorly over time, increasing the distance between the nipple areolar complex and the inframammary fold. The authors disclosed a new method for revising implant position in patients suffering from this complication, a method that employed a #15 Bovie electrocoagulator powered by the Mega Power Generator.

Two representative female patients were included, and their ages were 26 and 29 years old respectively. The approach consisted of an axillary incision with a scalpel, an incision that was deepened with the subject device and the Bovie. The upper capsule of the implant was eventually reached and then divided using this same method. Removal of the implant followed and in the bottom of the capsule, a new, more superiorly placed inframammary fold was created with the Bovie-Mega Power Generator system. The generator was set to a power of 45 watts and after coagulating the lower portion of the pocket, new textured implants were inserted. Supportive brassieres were worn during recovery and at three months postoperatively no recurrence was apparent in either patient.

No adverse events were reported in this study, and the utility of electrocoagulation was noted as a primary factor enabling this minimally invasive revision approach. Apparently, the electrocauterization of the lower portion of the implant capsule leads to contraction of the tissues, which in turn heal in the

new, more desirable location. Their closing statement was: “In conclusion, we present a novel technique that is simple and effective for managing inferior implant malposition, ‘bottoming out,’ using endoscopy-assisted electrocauterization. Due to its short surgical time, endoscopy was able to result in a high level of satisfaction among the ‘bottoming out’ patients.”

5.8.4. Literature Review Conclusions

The reviewed literature encompassed all published clinical studies using the Megadyne Mega Power Generator. Because the Ethicon Megadyne Electrosurgical Generator is a new device, there were no expectations to capture studies describing its use. There were three studies with 69 patients and the literature search covered the period between 01 January 1986 and 03 September 2019. All included studies used the subject device as intended.

Two of the included articles were published by the same group (Lee et al., 2014 and 2017 respectively) and were company supported by Megadyne. These studies had the objective of assessing the subject device compared to cold steel or other electrical scalpels in a non-randomized fashion. In the first article from 2014, the authors established the non-inferiority of the ACE Blade EZ Clean Electrodes powered by the Mega Power Generator when compared to standard cold steel scalpels. This result was measured in terms of wound healing and was conducted over the course of 120 days in 64 patients undergoing various plastic surgery procedures. In both groups, there was one case of wound dehiscence and one unspecified adverse event. In the second article from 2017, the authors demonstrated comparable or lower thermal damage at the incision compared to the PEAK Plasma Blade (Medtronic) on the medium or high cut mode. No adverse events were reported. Finally, Kim et al. (2014) discussed a novel approach to breast augmentation revision, for patients presented with bottoming out complications. This study discussed the use of a Bovie electrocoagulator powered by the Mega Power Generator and described an approach for using them to reshape the implant pocket. Application of electrocoagulation in this way forced the pocket to contract, thus raising the apparent inframammary fold and resolving the complication. No adverse events were reported, and no recurrences were seen as late as three months postoperatively.

No deaths were reported, and no new harms were identified.

This analysis supports the safety and performance of the Megadyne Mega Power Generator and the Ethicon Megadyne Electrosurgical Generator when used as intended. It should be noted, however, that the quantity of data identified in this review was very limited.

6. POST-MARKET EXPERIENCE AND SURVEILLANCE (PMS)

The Post Market Surveillance (PMS) process for the Ethicon Megadyne Electrosurgical Generator and the Megadyne Mega Power Electrosurgical Generator is conducted under the Franchise Procedure for Evaluation of Clinical Data for CE-Marking (PR-0000277 **ADAPTIV**). In accordance with this procedure, the methods should obtain relevant and new production and post-production information to evaluate any potential early warning signs of design and quality problems, emerging issues or safety signals, and to assign action items as necessary throughout the lifetime of the medical device.

The PMS data for the Megadyne Mega Power Electrosurgical Generator (equivalent subject device) includes internal, external, and market-based sources of active data analysis as defined in the PMS Plan (Table 6-1). PMS data has been provided from November 2014 through October 2019 as extracted from the PMS Report (Table 6-1).

Table 6-1: Megadyne Mega Power Electrosurgical Generator PMS Plan and Report Overview

PMS Plan and Report	Report Review Period and Conclusions	Supplemental PMS Data Review Period and Conclusions
Mega Power Electrosurgical Generator Plan # RA-REC-012 Rev C Report # RA-REC-013 Rev C	November 2014 to October 2019 (Reactive Monitoring data captured). (Compliant data is updated real-time through 06 January 2019). Report Conclusion: Overall complaints and rates were low in the reporting period. There were no adverse trends or signals that could contribute to the efficacy of the Electrosurgical Generator product families. The periodic data review will continue as per the PMS procedures. The current PMS plan RA-REC-012 is deemed acceptable.	N/A: Supplemental PMA Data not required

6.1. Complaint and Vigilance Data

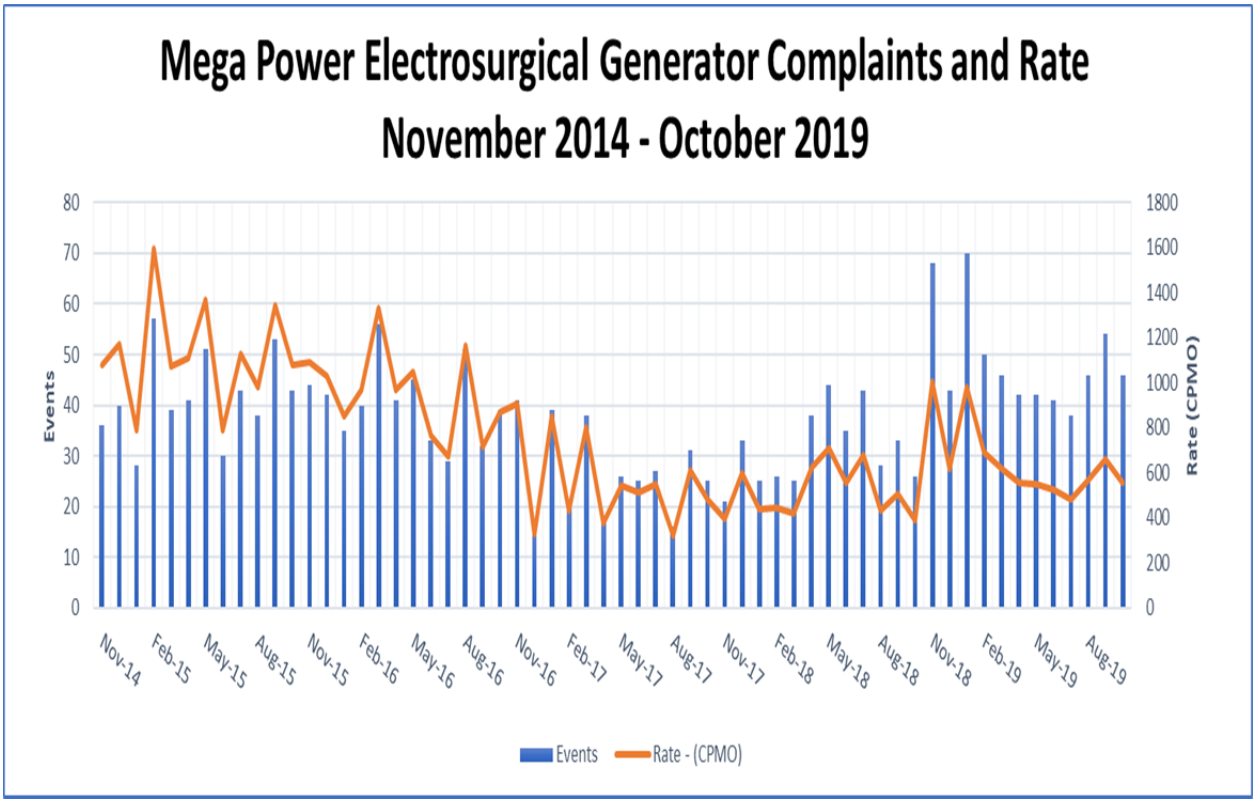
6.1.1. Overall Complaints/ Sales Data for Equivalent Subject Device

This complaint review is for the Mega Power Electrosurgical Generator (equivalent subject device). reflect **the total product quantity involved in the unique reported events. Opportunities used in the complaint rate in this figure represent a 3-month rolling average.**

Figure 6-1 below presents the total number of complaints and the complaint rate for the current PMS Review period. There were 2270 complaint events received from November 2014 through October 2019 reporting 2356 Product Experience Code (PEC) issues with an overall complaint rate of 71.6 CPMO (0.01%). The complaint counts captured in the graph below (Figure 6-1) reflect the total product

quantity involved in the unique reported events. Opportunities used in the complaint rate in this figure represent a 3-month rolling average.

Figure 6-1: Mega Power Electrosurgical Generator Complaints and Rate



Mega Power Electrosurgical Generator - Summary Of Overall Complaints

Five years' worth of data was stratified into multiple time periods to allow for comparison of complaint rates and identification of trends. Per the Global Trending and Signal Detection Procedure (100583575 **Windchill**), Complaint data is normalized by product sales or shipment unless otherwise indicated under 'Other Product for Opportunity Estimation'; as a result, the rates were calculated by dividing the number of events by the Average "Opportunity Period".

Below, Table 6-2 summarizes the total number of events and CMPO event rate of 71.6 for the Mega Power Electrosurgical Generator .

Table 6-2: Summary of Overall Mega Power Electrosurgical Generator Complaints

Complaint Summary	Nov 2014-Oct 2015	Nov 2015-Oct 2016	Nov 2016-Oct 2017	Nov 2017-Oct 2018	Nov 2018-Oct 2019	Total
Complaints (Unique Files)	499	487	321	131	832	2270

Events (Total quantity involved)		499	487	321	131	832	2270
WW Sales		880	641	850	1877	2051	6299
Opportunities		4433131	5106703	5760438	7282661	9110142	31693075
Complaint Rate	**CPMO**	112.6	95.4	55.7	18.0	91.3	71.6

6.1.2. Complaints Data by Category

6.1.2.1. Summary Of Complaints By Product Experience Code

Complaint data compiled by Product Experience Code is presented for the equivalent subject device in Table 6-3 below.

Table 6-3: Mega Power Generator - Summary of Complaints by Product Experience Code

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Error Code 208	61	13.76	75	14.69	69	11.98	17	2.33	132	14.49	354	11.17
Error Code 203	133	30.00	103	20.17	42	7.29	7	0.96	32	3.51	317	10.00
Performance Failure Unknown	95	21.43	66	12.92	58	10.07	32	4.39	0	0.00	251	7.92
Diminished Power or Output	40	9.02	67	13.12	18	3.12	12	1.65	31	3.40	168	5.30
Error Code 221	57	12.86	25	4.90	18	3.12	3	0.41	22	2.41	125	3.94
Not Specified	0	0.00	0	0.00	0	0.00	0	0.00	92	10.10	92	2.90
Bipolar Issue	20	4.51	13	2.55	17	2.95	5	0.69	33	3.62	88	2.78
Error Code Unspecified	13	2.93	10	1.96	8	1.39	2	0.27	50	5.49	83	2.62
Error Code 220	10	2.26	21	4.11	11	1.91	4	0.55	35	3.84	81	2.56
Exterior Damage	0	0.00	0	0.00	0	0.00	0	0.00	68	7.46	68	2.15
Error Code 219	3	0.68	9	1.76	3	0.52	16	2.20	26	2.85	57	1.80
Error Code 231	5	1.13	9	1.76	12	2.08	1	0.14	28	3.07	55	1.74

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Error Code 205	7	1.58	6	1.17	4	0.69	0	0.00	31	3.40	48	1.51
Alarming	8	1.80	19	3.72	15	2.60	5	0.69	0	0.00	47	1.48
Power Up Issue	0	0.00	0	0.00	0	0.00	0	0.00	29	3.18	29	0.92
Alarm Unspecified	0	0.00	0	0.00	0	0.00	1	0.14	28	3.07	29	0.92
Monopolar Issue	0	0.00	0	0.00	0	0.00	0	0.00	27	2.96	27	0.85
Error Code 211	3	0.68	7	1.37	2	0.35	4	0.55	8	0.88	24	0.76
Error Code 206	3	0.68	8	1.57	2	0.35	1	0.14	10	1.10	24	0.76
Error Code 214	0	0.00	6	1.17	4	0.69	2	0.27	12	1.32	24	0.76
Generator Button or Switch Issue	0	0.00	0	0.00	0	0.00	0	0.00	19	2.09	19	0.60
Footswitch Does Not Activate System	0	0.00	0	0.00	0	0.00	0	0.00	19	2.09	19	0.60
Fails to Respond to Hand Switch	0	0.00	0	0.00	0	0.00	0	0.00	18	1.98	18	0.57
Error Code 204	3	0.68	1	0.20	2	0.35	1	0.14	10	1.10	17	0.54
Injury	4	0.90	2	0.39	4	0.69	6	0.82	0	0.00	16	0.50

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Cautery Issue	0	0.00	0	0.00	0	0.00	0	0.00	16	1.76	16	0.50
Self-Activation	2	0.45	0	0.00	0	0.00	0	0.00	13	1.43	15	0.47
Electrical Shock	1	0.23	6	1.17	1	0.17	3	0.41	4	0.44	15	0.47
Damaged Product	3	0.68	4	0.78	6	1.04	1	0.14	0	0.00	14	0.44
Cutting Issue	9	2.03	0	0.00	5	0.87	0	0.00	0	0.00	14	0.44
CQM Alarm	0	0.00	0	0.00	0	0.00	0	0.00	13	1.43	13	0.41
Activation Issue	4	0.90	5	0.98	2	0.35	1	0.14	0	0.00	12	0.38
Coag Issue	2	0.45	3	0.59	7	1.22	0	0.00	0	0.00	12	0.38
Generator Connection Issues	0	0.00	0	0.00	0	0.00	0	0.00	11	1.21	11	0.35
Error Code 207	0	0.00	5	0.98	1	0.17	0	0.00	5	0.55	11	0.35
Tissue Effect Issue	0	0.00	0	0.00	0	0.00	0	0.00	11	1.21	11	0.35
Out of Box Failure	0	0.00	0	0.00	0	0.00	0	0.00	10	1.10	10	0.32
Flame Flash Fire	1	0.23	0	0.00	1	0.17	0	0.00	8	0.88	10	0.32
Electromagnetic	0	0.00	0	0.00	0	0.00	0	0.00	10	1.10	10	0.32

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Interference												
Error Code 215	3	0.68	2	0.39	0	0.00	0	0.00	5	0.55	10	0.32
Audio Issue	0	0.00	0	0.00	1	0.17	0	0.00	8	0.88	9	0.28
Intermittent	4	0.90	2	0.39	1	0.17	2	0.27	0	0.00	9	0.28
Excessive Power or Output	0	0.00	0	0.00	0	0.00	0	0.00	8	0.88	8	0.25
Electrical Safety Issue	0	0.00	0	0.00	0	0.00	0	0.00	8	0.88	8	0.25
Display	1	0.23	4	0.78	3	0.52	0	0.00	0	0.00	8	0.25
Unintended Thermal Injury Less Than 2nd Degree	0	0.00	0	0.00	0	0.00	0	0.00	7	0.77	7	0.22
Arcing/Sparking	1	0.23	2	0.39	3	0.52	1	0.14	0	0.00	7	0.22
Burning Smell or Smoking	0	0.00	0	0.00	0	0.00	0	0.00	6	0.66	6	0.19
Switch Button Issue	0	0.00	3	0.59	0	0.00	1	0.14	0	0.00	4	0.13
Error Code 217	0	0.00	1	0.20	0	0.00	1	0.14	1	0.11	3	0.09

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Unintended Thermal Injury	0	0.00	0	0.00	0	0.00	0	0.00	3	0.33	3	0.09
Error Code 201	0	0.00	0	0.00	0	0.00	0	0.00	3	0.33	3	0.09
Fit/Connection	1	0.23	0	0.00	1	0.17	0	0.00	0	0.00	2	0.06
Error Code 225	2	0.45	0	0.00	0	0.00	0	0.00	0	0.00	2	0.06
Error Code 251	0	0.00	2	0.39	0	0.00	0	0.00	0	0.00	2	0.06
Error Code 216	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Error Code 212	0	0.00	1	0.20	0	0.00	0	0.00	0	0.00	1	0.03
Misassembly	0	0.00	0	0.00	0	0.00	1	0.14	0	0.00	1	0.03
Error Code 249	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Error Code 254	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Error Code 218	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Loaner Return	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Customer Dissatisfaction	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03

Product Experience Code Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
User Related Issue	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Heating	0	0.00	0	0.00	0	0.00	1	0.14	0	0.00	1	0.03
Hemostasis Controllable	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11	1	0.03
Grand Total	499	112.56	487	95.36	321	55.72	131	17.99	918	100.77	2356	74.34

6.1.2.1.1. Critical Analysis of Mega Power Electrosurgical Generator Complaints

Error Code: 208, Error Code: 203 and Performance Failure: Unknown were the top reported Product Experience Code (PEC) for the Mega Power Electrosurgical Generator. The PEC is discussed in further detail below. The remaining PECs were not discussed due to their low volume of complaints. Table 6-3 above captured the exhaustive list of all complaints received during the review period.

PEC1. Error Code: 208: A total of 354 Error Code: 208 events with a rate of 11.17 CPMO were reported during the time periods included in this PMS report. These events were reviewed and evaluated. Error Code: 208 is described as, Active Measurement Diagnostics Error B+, meaning an error was detected in the B+ Voltage sense network during Power on Self-Test (POST). The reporting countries associated with this PEC were US (107), China (34), Indonesia (27), Latin America (27) and no other country greater than 19. None of the 354 events were MDV or MDR reportable. There were no Patient codes associated with the Error Code: 208 PEC. The Analysis Codes associated with the Error Code: 208 events were Random Component Failure (145), Motherboard Replaced Pend Mb Receipt (62), Device/ Records meet specification (47), and no other Analysis Codes reported greater than 34. The PEC, “Error Code 208,” is included in the Risk Analysis ENG-RMF-018 Rev. 012 under the failure mode of Hardware or Software failure” and is below the predicted rate of 5 (≥ 10%)”.

PEC2. Error Code: 203: A total of 317 Error Code: 203 events with a rate of 10.00 CPMO were reported during time period included in this PMS report. These events were reviewed and evaluated. Error Code 203 is described as a “Dosage Error”, meaning the Master microcontroller has detected an excessive amount of power consumption compared with RF output power being delivered. The reporting countries for the 317 events were USA (96), Indonesia (43), Latin America (34), India (20) and no other country greater than 15. None of the events were MDV or MDR reportable. There were also no Patient Codes associated with this PEC. The Analysis Codes associated with the Error Code: 203 events were Random Component Failure (216), Motherboard Replaced Pend Mb Receipt (29), Device/Records Meet Specifications (25) and no other Analysis code greater than 16. The, “Error Code: 203,” PEC is included in the ENG-RMF-018 Rev. 012 under the failure mode of “Incorrect Surgical Effect (too much power),” and is below the predicted Occurrence rate of 3 (> 1% and < 10%).

PEC3. Performance Failure: Unknown A total of 251 Performance Failure: Unknown events with a rate of 7.92 CPMO were reported during time period included in this PMS report. These events were reviewed and evaluated. The reporting countries were USA (132), Latin America (18), Japan (13) and no other country greater than 11. None of the 251 events were MDV or MDR reportable. The Patient Codes associated with this PEC were Injury (2) and Potential Safety Hazard (1). The Analysis Codes associated with the Performance Failure: Unknown event were MPE-Random Component Failure (76), GEN-Performs within Specifications (57), Device/record meet specifications (42), and no other Analysis code greater than 15. The PEC, “Performance Failure: Unknown,” is included in the Risk Analysis ENG-RMF-018 Rev.012. It is below the predicted Occurrence rate of 1 (≤ 0.1%).

6.1.2.2. Summary Of Complaints Patient Code

Complaint data compiled by Patient Code is presented for the Mega Power Electrosurgical Generator in Table 6-4 below.

Table 6-4: Mega Power Electrosurgical Generator – Summary Of Complaints Patient Code

Patient Codes Breakdown	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO
Injury	4	0.90	7	1.37	4	0.69	7	0.96	0	0.00	22	0.69
Potential Safety Hazard	2	0.45	3	0.59	6	1.04	3	0.41	0	0.00	14	0.44
Burn	0	0.00	0	0.00	0	0.00	0	0.00	6	0.66	6	0.19
Hematoma	0	0.00	0	0.00	0	0.00	0	0.00	3	0.33	3	0.09
Grand Total	6	1.35	10	1.96	10	1.74	10	1.37	9	0.99	45	1.42

6.1.2.2.1. Critical Analysis of Electrosurgical Generator Patient Codes

Patient Codes (PC) Potential Safety Hazard" and "Injury were discussed due to their rate and volume reported for the Mega Power Electrosurgical Generator. The PC's are discussed in further detail below. The remaining PCs were not discussed due to their low volume complaints. Table 6-4 captured the exhaustive list of all complaints received during the review period.

PC1. Injury: A total of 22 Injury events was reported during the time period included in this PMS report. This event was reviewed and evaluated. The reporting countries were USA (15), Canada (2) and no other country greater than 1. The PEC reported were Injury (12), Shock (6), and no other PEC's reported greater than 2. Of the 22 events, 8 were MDR reportable (7 Serious Injury and 1 Malfunction). There was 1 MDV reportable event (Malfunction). The patient code is addressed in the Risk Analysis ENG-RMF-018 Rev. 012 under various "Injury" line items.

PC2. Potential Safety Hazard: A total of 22 Injury events was reported during the time period included in this PMS report. This event was reviewed and evaluated. The reporting countries were USA (15), Canada (2) and no other country greater than 1. The PEC reported were Injury (12), Shock (6), and no other PEC's reported greater than 2. Of the 22 events, 8 were MDR reportable (7 Serious Injury and 1 Malfunction). There was 1 MDV reportable event (Malfunction). The patient code is addressed in the Risk Analysis ENG-RMF-018 Rev. 012 under various "Injury" line items.

6.1.2.3. Overall Complaint Analysis Conclusions:

Over a 5-year review period there were 2270 complaints for a rate of 71.6 CPMO. Of the 2270 complaints there were 45 PC's, reported. The product family review identified no new harms or hazards and the product family is preforming as predicted.

6.1.3. FDA: MDR/MDV Data

6.1.3.1. Summary of Reportable Events for Mega Power Generator

6.1.3.1.1. Medical Device Reporting (MDR) Review:

A total of 2270 complaints were reported for the Mega Power Electrosurgical Generator over the period included in this PMS Report. Of the 2270 complaints, 31 were MDR reportable during the time period (22 Malfunctions and 9 Serious Injury). Table 6-5 below summarizes the MDR's by device type. Table 6-6 follows with MDR Breakdown of nine PE Codes, with a total of 28 malfunctions and 10 serious injuries.

Table 6-5: Mega Power Electrosurgical Generator - Summary of MDR Reportable Events by MDR Type

MDR Breakdown by Type	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Malfunction	0	0.00	0	0.00	0	0.00	1	0.14	21	2.31	22	0.69
Serious Injury	3	0.68	0	0.00	2	0.35	2	0.27	2	0.22	9	0.28
Grand Total	3	0.68	0	0.00	2	0.35	3	0.41	23	2.52	31	0.98

Table 6-6: Mega Power Electrosurgical Generator - Summary of the Serious Injury MDRs by PE Code

	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
MDR Breakdown by PE Code	M	SI	M	SI	M	SI	M	SI	M	SI	M	SI
Self-Activation	0	0	0	0	0	0	0	0	13	0	13	0
Flame Flash Fire	0	1	0	0	0	1	0	0	7	1	7	3
Injury	0	2	0	0	0	1	1	2	0	0	1	5
Unintended Thermal Injury	0	0	0	0	0	0	0	0	1	2	1	2
Generator Button or Switch Issue	0	0	0	0	0	0	0	0	2	0	2	0
Alarm Unspecified	0	0	0	0	0	0	0	0	1	0	1	0
CQM Alarm	0	0	0	0	0	0	0	0	1	0	1	0
Error Code 214	0	0	0	0	0	0	0	0	1	0	1	0
Error Code Unspecified	0	0	0	0	0	0	0	0	1	0	1	0
Grand Total	0	3	0	0	0	2	1	2	27	3	28	10

Key: M = Malfunction; SI = Serious Injury

NOTE: Table 6-6 *contains PE codes that are associated with the overall MDR reportable events and may not be the PE code that triggered the file to be reportable and also may contain duplicate complaints overall. Rates not applicable for this chart.*

6.1.3.1.2. Summary of Medical Device Vigilance (MDV) Review:

A total of 2356 complaints (based on unique events) were reported for the Mega Power Electrosurgical Generator over the period included in this PMS Report. Of the 2270 complaints, 1 was MDV reportable.

Table 6-7 below provides the breakdown of the MDV reportable event by type (1-Malfunction) followed by **Table 6-8** which provides the breakdown of the MDV reportable event by PE code.

Table 6-7: Mega Power Electrosurgical Generator - Summary of MDVs by Device Type

MDV Breakdown by Type	Nov 2014-Oct 2015		Nov 2015-Oct 2016		Nov 2016-Oct 2017		Nov 2017-Oct 2018		Nov 2018-Oct 2019		Total	
	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)	N	Rate (CPMO)
Malfunction	0	0.00	0	0.00	0	0.00	1	0.14	0	0.00	1	0.03
Grand Total	0	0.00	0	0.00	0	0.00	1	0.14	0	0.00	1	0.03

Table 6-8: Mega Power Electrosurgical Generator - Summary of MDV Reportable Events by PE Code

MDV Breakdown by PE Code	Nov 2014-Oct 2015	Nov 2015-Oct 2016	Nov 2016-Oct 2017	Nov 2017-Oct 2018	Nov 2018-Oct 2019	Total
	N/A	N/A	N/A	Malfunction	N/A	Malfunction
Injury	0	0	0	1	0	1
Grand Total	0	0	0	1	0	1

6.1.4. Death-Related Events

There were no death events reported during the review period of this report.

6.2. Corrective Actions

6.2.1. Corrective and Preventive Actions (CAPAs)

The Corrective and Preventative Action process for the subject device is conducted under PR575-001. In accordance with the procedure, a risk assessment is conducted to evaluate the significance of the risk of the issue and its associated impact. If the CAPA requires escalation, the appropriate management representatives are required to review and assess the escalation based on their scope of responsibility. For further details pertaining to the CAPAs, refer to applicable CAPA file.

During the 5-year total period covered by this PMS Review, 7 CAPA's were initiated in relation to Mega Power Electrosurgical Generator. The seven CAPA's initiated during this review are provided in Table 6-9 below.

Table 6-9: Megadyne Mega Power Electrosurgical Generator Summary

CAPA #	CAPA Title	Create Date	Closed Date	CAPA Status	CAPA Description

CAPA-009279	Indirect Service and Material Vendor Approval Process	Jul 11, 2019	N/A	Implementation	During review of Megadyne supplier utilization in OBS-026886, AP-050164, it was identified that there were a significant number of legacy indirect suppliers that the Megadyne site actively utilizes. These Megadyne legacy suppliers were not included on Approved Supplier/Vendor List prior to implementation of Megadyne integrated supplier management procedure, OPER-SOP-010 Rev 007, as required.
CAPA-008296	Mega Power Dual Activation Issue	May 25, 2018	N/A	Effectiveness Monitoring	On April 19, 2018, QRB determined field notification (#7282) was required for complaint 2017012570 where sales rep reported burn to patient. Customer reported doing a breast augmentation with cut/coag settings of 40/40. They had a Megadyne pencil in Port A and were using an additional instrument called Endo-Breast that was also plugged into Port A. They had been in serviced about where to plug in instruments and foot control devices. The pencil was placed on the patient and when the second device was activated, it burned the patient on the chest. Burn was reported as 2nd degree. No holster was used. Per PR575-001 Rev 58, CAPA is required for issues escalated to field notification.
CAPA-008050	Mega Power: 219 Error Code	Apr 5, 2018	Oct 15, 2019	Closed	Mega Power Electrosurgical Generator 219 error code exceeded the 3-sigma limit for the complaint trending. It was decided by Megadyne Product Quality Safety Surveillance Data Review Board (PQSS DRB, meeting number DR-006201) in a meeting held on 4/2/2018 to initiate a CAPA. The number of complaints (13) in January and February 2018 exceeded the total number of complaints in 2017 (5).
14031	N/A	Nov 4, 2014	Feb 10, 2015	Closed	Several motherboards had missing components. Some of the missing components were found at station 2 in the ESU room.
14032	N/A	Nov 10, 2014	Mar 10, 2015	Closed	221 Errors caused by errant reading on the monopolar output feedback voltage. This is due to Ohmite Resistor B20J10KE.
15005	N/A	Jul 31, 2015	Feb16, 2016	Closed	The Leakage Current Test conducted on the model was performed at 240 V. The requirement per the Description is to be done at 110% of highest rated which is 264V. The Applied Parts to Mains Dielectric Test was conducted at 3000 Vdc. The requirement per the Description is 4000 Vac.
15011	N/A	Sep 9, 2015	Nov 9, 2019	Closed	ESUs U6/U7 failures during burn-in process in production.

Corrective and Preventive Action Conclusion:

There are no safety signals or trends identified for the 7 CAPA's initiated during this 5-year period review. Five of the 7 CAPA's are closed and two remain under review.

6.2.2. Escalations – Mega Power Electrosurgical Generator

During the 5-year period covered by this PMS Review, 4 Escalations were initiated along with 1 Field Action specifically for Megadyne Mega Power Electrosurgical Generator.

Table 6-10: Mega Power Electrosurgical Generator - Escalations Summary Alerts

Escalation #	Orig. Date	Origination Source	Escalation Descriptions	Field Action: Yes / No	CAPA #
1599739	9/16/2019	Internal Notification	The Mega Power Rear Panel Label (3150452-01 Rev 004) and the IFU/Manual (3000158-01 Rev 005) both list the incorrect EU authorized representative (AR) information. - Rev 004 of the label and Rev 005 of the IFU incorrectly lists Ethicon Endo-Surgery (Europe) GmbH as the authorized rep. - QFI should still be listed as the authorized rep on the label. The Rear Panel Label (3150452-01 Rev 004) and IFU/Manual (3000158-01 Rev 005) were being updated to support IEC 60601-1 3.1. - Rev 004 of the label was released on DCO 2018-MKT-DCO-122 (released Nov. 2019) - The change reviewed at the collaboration phase (April 2019) still had QFI has the AR. When the label was released it had been updated to Ethicon Endo-Surgery (Europe) GmbH IFU/Manual (3000158-01 Rev 005) released on DCO 2017-MKT-DCO-077 (release Nov. 2019) - The change reviewed at the collaboration phase (April 2019) still had QFI has the AR. When the IFU was released it had been updated to Ethicon Endo-Surgery (Europe) GmbH There was a consideration to switch the AR from QFI to Ethicon Endo-Surgery (Europe) GmbH due to Brexit. The steps needed to make this change had not been completed and there was a decision to not pursue.	No	NA
1587012	8/28/2019	Complaint	"On 16 July 2019 Megadyne became aware that a unit (S/N 184928001) associated with Complaint # PC-000384252 had a component failure for P/N 4034003-02, the Monopolar Inductor (Designator L7). This was the second unit returned to S&R for Error 220 which had a faulty L7 component where the failure occurred within six months of delivery. Complaint and S&R records indicated that another L7 failure had occurred in August 2018 on Unit S/N 180521001, associated with Complaint # PC-000180676. Complaint PC-000180676 was thoroughly investigated but no trend in complaints were detected for L7 component failures. The L7 component acts as a filter on the Monopolar output to help form the wave shape. If L7 fails, the generator Power-On-Self-Test (POST Test) fails and the generator will display Error 220. On 16 July 2019, Megadyne became aware of a failed L7 during a S&R evaluation related to Complaint # PC-000384252; Error 220. Note, Error 220 may be caused by other conditions other than a failed L7. Once L7 fails, the generator will continue to function until the generator is powered OFF. Once powered back ON, the generator will display an Error 220 and will not function."	No	NA
10064324	6/20/201	Complaint	Megadyne generator - Continuous activation	No	NA

100612095	2/15/2018	Complaint	Megadyne customer complaint (2017012570) and adverse event-patient burn caused by 2 products plugged into same generator port at the same time.*	Yes	CAPA-008296

*Note: By design, the new Ethicon Megadyne Generator has removed the possibility of the user to plug 2 products into the same generator port at the same time.

Escalation Conclusion:

Of the 4 Escalations initiated over the 5- year time period review, only one resulted in a Field Action. Field Action number 2018-1000390 was open in association to Escalation number 100612095 due to patient injury caused by 2 products plugged into same generator port at the same time*. MHRA reference: 2018/005/030/701/005. This Field Alert became CAPA-008296.

6.2.2.1. Alert Summary – Mega Power Electrosurgical Generator

MHRA Review:

A total of 14 alerts came back in the Medicines and Healthcare Products Regulatory Agency (MHRA) Database maintained by the Department of Health of the United Kingdom. The search conducted on January 13, 2020 returned 1 alert for “Megadyne Generator,” related to the Mega Power Electrosurgical Generator for the period of November 2014 to October 2019. This is referencing the open CAPA-008296. (MHRA reference: 2018/005/030/701/005.)

TGA Recall Review:

A search of the Therapeutic Goods Administration (TGA) Australian Recall Actions maintained by the Australia Health Authority returned no alerts for the period November 2014 to October 2019. The search was conducted on January 13, 2020 for “Megadyne”.

Health Canada Recalls and Safety Alerts Review:

A search of the Recalls and Safety Alerts maintained by Health Canada returned no alerts for the period November 2014 to October 2019 in relation to the Megadyne Mega Power Electrosurgical Generator Product family. The search was conducted on January 13, 2020 for “Megadyne”.

6.2.3. Field Actions and Recalls – Mega Power Electrosurgical Generator

Of the 4 Megadyne Mega Power Generator Escalations described above, only one resulted in a Field Action. The Field Action number, 2018-1000390 was opened in association to Escalation number 100612095 (Table 6-10) due to patient injury caused by two products plugged into same generator port at the same time. Table 6-11 below provides the details for the current Field Action.

Table 6-11: Summary Table of Field Actions for Mega Power Electrosurgical Generator

QRB/FA #	Orig. Date	Origination Source	QRB/FA Description*	Status	Customer Letter #	CAPA #
100612095 (QRB) /1000390 (FA)	4/19/2018	Complaint	Megadyne customer complaint and adverse event-patient burn caused by 2 products plugged into	Open	N/A	CAPA 008296

* By design, the new Ethicon Megadyne Generator has removed the possibility of this specific type of occurrence.

The Field Action remains open due to the desire/necessity to increase the response rate from affected consignees. Currently, the number of consignees that have responded by Business Reply Form to the recall notice is lower than standard metrics. Ongoing work is underway to receive more responses. Once the response rate has reached a metric deemed suitable for closure, then actions will be taken to do so. (MHRA reference: 2018/005/030/701/005.)

There were no recalls during the 5-year review period for the Megadyne Mega Power Electrosurgical Generator.

End Post-Market Experience and Surveillance Section 7.

7. BENEFIT / RISK ANALYSIS

7.1. Clinical Benefits / Performance Analysis

Clinical safety and performance outcomes include the ability of the subject devices to achieve the intended purpose per the indications for use and as claimed. There are several types of clinical benefits, including but not limited to, the impact of the subject device on clinical management, patient health, and patient satisfaction in the target population, such as significantly improving patient management and quality of life, reducing the probability of death, aiding improvement of patient function, reducing the probability of loss of function, and providing relief from symptoms. Therefore, the clinical benefits on the subject devices have been substantiated via evidence from the appraised data (either clinical, non-clinical, or both) in accordance to the Data Appraisal Plan (See Section 5.1) to assess the ability of a medical device to achieve its intended purpose as claimed by the manufacturer including any direct or indirect medical effects on humans as well as the clinical benefit on patients.

Both subject devices in this evaluation are intended to be used as a general-purpose electrosurgical generator designed to produce radio frequency (RF) current for cutting and coagulation of target tissue through an accessory electrode in a broad range of open and laparoscopic surgical procedures. The benefits of the use of radio frequency energy for monopolar and bipolar cutting and coagulation, such as the subject devices, can be defined through State of Art (Section 2), Clinical Literature, Post Market Surveillance, and Clinical data (proactive and post-market). A summary of the Benefits for the subject devices, including comparisons to alternative therapies, is described in Table 7-1 below.

Key Safety and Performance Parameters

Regarding the Key Safety and Performance Parameters found in the previous Section 1.4., the Megadyne Electrosurgical Generators clinical evaluation report analyzed key safety and performance parameters derived from the outcome information based on the following but not limited to; intended use, Instructions for Use (IFU), design requirements (Section 5.2 Non-Clinical Data) and information related to the clinical data (Section 5.8) , State of the Art (Section 2) and Post Market Surveillance reporting (Section 6). The key safety and performance summarizations are provided below:

- The state-of-the-art literature review concludes that use of electrosurgical devices provided the following safety benefits: (Bukhari and Al-Ammar, 2007) (Lin et al., 2006) (Singh et al., 2005) (Srivastava et al., 2016)
  - Decreased Blood Loss
  - Increased Wound Healing
  - No Adverse Events (AE's)
  - Decreased Operative Time
  - Decreased Complications

- The state-of-the-art literature review found that technologies and advanced device designs are further reducing the inherent risks involved in the use of the subject devices thus increasing performance outcomes with:
  - Warning systems: audio signaling, visual display, auto shut off
  - Temperature controls
  - Minimized use of power to minimize patient injury while performing its intended effects
- The Non-clinical Data Section validates design function and performance:
  - The system has audio and visual indicators during activation and displays error codes when the system is not functioning properly.
  - Computer-controlled voltage and power curve are adjusted automatically, regardless of the tissue impedance that allows for acceptable delivery of energy by the generator subject devices to the electrodes without excess energy or energy spikes that would result in thermal burns of patient tissues.
  - Ex vivo study comparing the thermal effects after activation of three power settings on 3 tissue types documenting equivalent performance to the existing subject device for tissue cutting and coagulation performance outcomes.
  - Appropriate generator interface and warning feedback (audio, visual and computer-controlled) design.
- The Post Market Surveillance data reveals:
  - There were 2270 complaint events received from November 2014 through October 2019 reporting 2356 Product Experience Code (PEC) issues with an overall complaint rate of 71.6 CPMO (0.01%).
- Clinical Literature Review Conclusions states the use of electrosurgical devices result in:
  - Less thermal damage
  - Surgical time
  - Less blood loss
  - Decreased majority of complications

The clinical benefits of the Megadyne Electrosurgical Generators are provided below in Table 7-1.

Table 7-1: Clinical Benefits of Megadyne Electrosurgical Generators

Source	Benefit	Reference
State of Art Literature	• Energy-based electrosurgical devices exhibited overall advantages over conventional non-energized techniques of cutting, dissection, and coagulation in terms of surgical time, blood loss, and a majority of complications. • Energy-based electrosurgical devices are especially needed in the laparoscopic, minimally invasive field where non-energy-based surgical instruments alone prove to be difficult to use in dissection and coagulation. • More than 80% of surgical procedures performed in the current clinical environment utilize advanced devices such as electrosurgical instruments.	Section 3
Non-Clinical Data	• Pre-clinical ex vivo study confirmed the new line extension Ethicon	Section 6.2

Source	Benefit	Reference
	Megadyne Electrosurgical Generator was similar to the equivalent Mega Power Generator by comparing thermal effects on tissue. • Both subject devices meet the requirements for European Union Restriction of Hazardous Substances and is RoHS compliant to RoHS ISO 10993-1:2009 Annex A. • The Design Verification and Validation testing documentation shows that the subject devices: Perform as designed, perform as intended and design outputs meet design Inputs.	
	The Clinical Literature search was performed for the existing subject device for the period of 01 January 1986 to 03 September 2019 resulting in 3 articles, 69 patients, 2 open procedures and 1 minimally invasive procedure (axillary access) with all studies reporting use on the Mega Power Electrosurgical Generator. • **Lee et al., 2014** concluded the ACE Blade system effectively cuts, coagulates, and dissects, without causing dissipated thermal injury and its consequential adverse effects on wound healing and may be better than previous electrosurgery electrodes because the computer-controlled (Mega Power generator, equivalent subject device) voltage and power curve are adjusted automatically, regardless of the tissue impedance. • **Lee et al., 2017** concluded comparable or lower thermal damage at the incision compared to blade competitor on the medium or high cut mode. • **Kim et al., 2014** revealed the utility of electrocoagulation as a primary factor enabling minimally invasive revision approach. The low volume of clinical literature is addressed in Section 8.1 PMCF Recommended.	Section 6.2
Post Market Surveillance Data	There were no adverse trends or signals that could contribute to the efficacy of the subject devices during the five year review period included in this evaluation. There were no deaths reported and no new harms were identified for the existing subject device – Megadyne Mega Power Electrosurgical Generator.	Section 7.1

7.2. Clinical Risks / Safety Analysis

Potential harms and hazards have been identified and documented for both Megadyne Electrosurgical Generators in the risk documentation as noted in Table 7-2 below. These documents are created from the Megadyne Medical Products Inc. Risk Management process and plan in compliance with harmonized standard EN ISO 14971 to satisfy the requirements of Medical Device Directive 93/42/EEC and other requirements that use this standard.

Table 7-2: Risk Management Documents for Megadyne Electrosurgical Generators

Risk Management Document	Reference Number*
Risk Management of Medical Devices (Ethicon Megadyne Electrosurgical Generator Risk Management Plan)	QA-SOP-015
Megadyne Mega Power Electrosurgical Generator Risk Management Plan	ENG-RMF-039
Megadyne Mega Power Electrosurgical Generator Risk Management Report	ENG-RMF-042
Ethicon Megadyne Electrosurgical Generator Risk Management Report	ENG-RMF-077

* WindChill document control

All hazards that applied to the Megadyne Electrosurgical Generator devices were assessed by Hazard Categories as listed below:

- Energy (HE)
- Mechanical (ME)
- Biological / Chemical Contamination(s) (BC)
- Human Interface (HI)

The Risk Management Reports summarize the residual risks of the Generators based on the severity of the Harm and the probability of Harm occurrence at that severity. Collectively, this is the Overall Residual Risk for the Megadyne Electrosurgical Generators. The risk assessments document the risk of individual failure modes that are reduced as far as possible in accordance with current state of the art in the design, labeling, and manufacturing methodologies. The risk level by Harm assessment documents the residual risk associated for each Harm/Severity level. In its entirety, it represents the Overall Residual Risk for the product. For each Harm, the maximum expected occurrence rate is presented for each severity category. This occurrence rate is the ongoing, stable frequency for the product.

7.2.1. Harms Mapping - Megadyne Mega Power Electrosurgical Generator

The identified risks associated with the use of the Mega Power Generator include patient harms from the Design Failure Mode Effects Analysis (DFMEA) (ENG-RMF-018), the Mega Power Hazard Assessment Summary (ENG-RMF-019), and the Mega Power Risk Management Report (ENG-RMF-042). The Risk Management Report (RMR) includes all known hazards during use of the subject device and identifies possible patient and user harms resulting from these hazards.

The risk assessment in the RMR found that individual risks identified in the applicable risk assessments were mitigated to levels *as low as possible,* and within the acceptable region of the Risk Rating Table included in the Megadyne Risk Management Plan (ENG-RMF-039). Based on the residual risk profile, the overall residual risk for the CE marked Mega Power Generator is deemed acceptable.

The Megadyne Mega Power Electrosurgical Generator Harms Summary is provided in Table 7-4 below (ENG-RMF-042, **Windchill**). The legend for the abbreviations are provided in Table 7-4 below.

Table 7-3: Legend for Abbreviations in Potential Harms Summary Matrix

Abbreviation:	Applies To:	Definition:
A	Clinical Data / PMS	"Analyzed" data set within CER
NO	Clinical Data / PMS	"No Occurrence" as part of data set within CER
C	RM / IFU	"Captured" in the applicable Risk Document and/or IFU
HNR	RM / C	"Harm Not in Risk" documents – identified new or emerging potential harm that is not currently included in the Risk Assessment Summary (RAS)
NC	IFU	"Not Captured" risk analyzed in the Risk Documents and determined not to be directly declared in the IFU
TBD	RM / IFU	"To Be Determined" Analysis Pending"

Table 7-4: Megadyne Mega Power Electrosurgical Generator Potential Harms Summary

Harm Category	Clinical Data	PMS	RM	IFU*
Alarm causes customer dissatisfaction	NO	NO	C	C
Alternate current path (patient burn)	NO	NO	C	C
Cannot complete procedure, delay of surgery	NO	NO	C	NC
Change in tissue effect	NO	NO	C	C
Change of power	NO	NO	C	C
Change tissue effect (up or down)	NO	NO	C	C
Customer dissatisfaction	NO	NO	C	NC
Delay of surgery	NO	NO	C	NC
Delay of surgery due to loss of device	NO	NO	C	NC
Does not change functionality of product, Customer dissatisfaction	NO	NO	C	NC
Does not perform within specification.	NO	NO	C	NC
Electric shock to user	NO	NO	C	C
Electric shock to user, delay of surgery	NO	NO	C	C
End user burn	NO	NO	C	C
End user injury	NO	NO	C	C
End user shock	NO	NO	C	C
ESU malfunction	NO	NO	C	C

Fire, complete loss of device	NO	NO	C	C
Generator malfunction causing reduced or no surgical effect	NO	NO	C	C
Hazard to service technician	NO	NO	C	NC
Neuro-muscular stimulation	NO	NO	C	C
No output or wrong output	NO	NO	C	C
No power, delay of surgery	NO	NO	C	NC
No protection to user from current leakage	NO	NO	C	NC
Nonfunctional ESU	NO	NO	C	C
Nuisance and has permanent damage to ear	NO	NO	C	NC
Operator and/or patient infection	NO	NO	C	NC
Patient injury	NO	A	C	C
Patient / user burn	NO	A	C	C
Patient / user injury	NO	A	C	C
Patient burn	NO	A	C	C
Patient or User burn due to inadvertent activation to wrong channel.	NO	A	C	C
Potential shock	NO	A	C	C
Reduced surgical effect	NO	NO	C	C
Shock to operator	NO	NO	C	C
Shorted components, ESU malfunction	NO	NO	C	C
Thermal injury to patient.	NO	NO	C	C
User burn	NO	NO	C	C
Wrong tissue effect	NO	NO	C	C

***Note 1:** Harms noted as "C" (captured) in the IFU column of the table above denotes that the harm is listed directly in the IFU. For those harms noted as "BRL" (below risk level), note that many potential harms have an Overall Residual Risk level (ORR) that is below that required to be explicitly included in the IFU. However, even when the specific harm is not captured in the IFU, it is additionally important to note that the harm is often inferred in Contraindications, Warnings, and Precautions and other sections (as applicable) of the IFU as described in the Risk Documentation.

Clinical safety signals reported from all the data sources were compared to potential harms identified in the risk management documents and verified that the IFU sufficiently identifies potential adverse events. There were no new harms found in the clinical or PMS data that are not already addressed in the risk documentation.

7.2.2 Harms Summary - Ethicon Megadyne Electrosurgical Generator

The following summary of potential Harms and hazards was compiled using the AFMEA (ENG-RMF-068), DFMEA (ENG-RMF-063), and SWFMEA (ENG-RMF-072). The frequency of harm and risk level represents

the worst-case for the given harm and severity category, as defined per these FMEAs. There are 10 categories of identified potential harms associated with the new line extension subject device.

The Ethicon Megadyne Electrosurgical Generator Potential Harms Summary is provided in Table 7-5 below (ENG-RMF-077, **Windchill**).

Table 7-5: Harms Summary - Ethicon Megadyne Electrosurgical Generator

Harm	Related Standardized Hazards	Severity Category	Frequency of Harm	Harm Risk Level
Auditory disorder	ME-05 - Acoustic energy	S1 - Brief transient period of temporary decrease, change or disturbance in hearing; Fully resolves on its own, no intervention indicated	**F2**	**Level 1**
Burn	HE-01 - Leakage current HE-11 - Inappropriate Output Power HE-18 - Incorrect Output Mode Characteristics HI-01 - Erroneous data transfer HI-02 - Incorrect clinical measurements or clinical metrology HI-03 - Misinterpretation of results or display due to ambiguous or unclear presentation of data, settings, or other information HI-05 - Ambiguous or unclear device state HI-06 - Complex or confusing control system or incomplete instructions HI-09 - Insufficient visibility, audibility, or tactile feedback HI-16 - Reasonably foreseeable misuse or inadequate specification of intended use or limits HI-18 - Use by unskilled or untrained persons HI-19 - Violation or abbreviation of instructions, procedures, etc. HI-22 - Inadequate specification of accessories, assembly, or pre-use checks ME-09 - Inadequate maintenance ME-16 - Loss of electrical/mechanical integrity ME-17 - Incorrect mechanical force (too high or too low)	S5 - Life threatening burn	**F2**	**Level 2**
		S4 - Irreversible organ damage or significant scar	**F1**	**Level 1**
		S3 - Surgical intervention to prevent further injury or damage	**F4**	**Level 2**
		S2 - First-degree burn	**F2**	**Level 1**
		S1 - Superficial localized redness/irritation without blistering or loss of tissue	**F2**	**Level 1**
Haemorrhage	HI-06 - Complex or confusing control system or incomplete instructions HI-09 - Insufficient visibility, audibility, or tactile feedback HI-22 - Inadequate specification of accessories, assembly, or pre-use checks	S3 - Bleeding for which additional intervention is indicated to prevent further injury	**F2**	**Level 1**
		S2 - Small amount of localized bleeding	**F2**	**Level 1**
		S1 –Minimal bleeding	**F2**	**Level 1**

		identified on clinical exam; intervention not indicated		
Infarction	HE-04 - Electro-magnetic emissions	S5 - Death of vital organ/structure due to loss of blood flow to area which is life threatening requiring urgent intervention	**F1**	**Level 1**
Infection	BC-06 - Re- and/or cross-infection (re-use) HI-09 - Insufficient visibility, audibility, or tactile feedback	S3 - Systemic antibiotic treatment or surgical intervention is required	**F1**	**Level 1**
		S2 - Localized infection (topical or oral antibiotics indicated).	**F2**	**Level 1**
Nerve injury	HE-17 - Excessive Muscle Stimulation HI-20 - Inadequate specification of performance characteristics or limitations HI-22 - Inadequate specification of accessories, assembly, or pre-use checks ME-07 - Accidental mechanical damage to the device ME-16 - Loss of electrical/mechanical integrity	S3 - Sensory or motor disturbance which might become permanent without appropriate intervention	**F2**	**Level 1**
		S2 - Sensory or motor disturbance which is reversible	**F2**	**Level 1**
Pain	HI-22 - Inadequate specification of accessories, assembly, or pre-use checks	S2 - symptomatic treatment	**F2**	**Level 1**
Soft tissue injury	HE-10 - Inadequate supply of power HI-17 - Slips and blunders (mental or physical) ME-07 - Accidental mechanical damage to the device ME-01 - Suspended masses ME-19 - Sharp edges or points	S3 - Requires treatment to prevent significant impairment .	**F2**	**Level 1**

		S2 - Compromised tissue or location temporarily limits patient activities.	**F3**	**Level 1**
		S1 - Small superficial wound or bruise,	**F3**	**Level 1**
Surgery	HE-01 - Leakage current HE-04 - Electro-magnetic emissions HE-11 - Inappropriate Output Power HE-14 - Incorrect Output Waveform HE-18 - Incorrect Output Mode Characteristics HI-01 - Erroneous data transfer HI-05 - Ambiguous or unclear device state HI-06 - Complex or confusing control system or incomplete instructions HI-09 - Insufficient visibility, audibility, or tactile feedback HI-14 - Mistakes or errors in judgment HI-16 - Reasonably foreseeable misuse HI-17 - Slips and blunders (mental or physical). HI-22 - Inadequate specification of accessories, assembly, or pre-use checks ME-07 - Accidental mechanical damage to the device ME-08 - Degradation or deterioration in function from repeated use (within surgery and over the life of reusable devices) ME-10 - Inadequate cooling ME-11 - Incompatibility with consumables, accessories, or other devices intended for joint or concurrent use ME-16 - Loss of electrical/mechanical integrity ME-20 - Storage or operation outside prescribed environmental conditions	S2 - Delay does not result in any impact to the expected surgical outcome	**F4**	**Level 1**
		S1 - Procedure completed within expected time	**F5**	**Level 1**
Vascular injury	HI-09 - Insufficient visibility, audibility, or tactile feedback	S3 - will likely require intervention or repair to prevent further injury to the tissue	**F2**	**Level 1**

7.2.1.1. Risk Reduction – Ethicon Megadyne Electrosurgical Generator

There were 10 potential Harm classifications listed in Table 7-5 above resulting in 21 Levels of potential harms. There were no Level 3 Harms associated with the 10 Harm classifications and there were only

two Level 2 Harms and nineteen Level 1 Harms. Actions taken to reduce the Level 2 and Level 1 risks described above have been determined to be 'as far as possible' and are described below:

Level 2 - Burns:

- **Primary Hazards Contributing to this Harm:**
  - The DFMEA identified the largest contributor to this harm as the loss of electrical/mechanical integrity. This is due to components failing and causing premature reliability failures, resulting in the system over heating, intermittent or inaccurate operation, or not working.
  - The AFMEA identified a contributor to this harm as complex or confusing control system or incomplete instructions. This is due to controls, display, or labeling not clear or intuitive or the system is operated by someone untrained in the use of electrosurgery.
  - The SWFMEA identified multiple contributors to this harm as inappropriate output power, insufficient visibility, audibility, or tactile feedback, and incorrect output mode characteristics. This is due to corrupted, inaccurate, or ineffective software or the software incorrectly configures or fails to initiate an event.
- **Actions Taken to Reduce Risk As Far as Possible:**
  - The DFMEA identified contributor is mitigated by using redundant components, component selection, proper design analysis, current limiting circuits, feedback loops, POST tests, active tests, standards testing, and reliability testing.
  - The AFMEA identified contributor is mitigated by ensuring the IFU addresses proper set-up and the system is used by users trained in electrosurgery and usability testing.
  - The SWFMEA identified contributors are mitigated by visual and audible indicators to indicate functionality, alarms, and error codes, POST tests (error checking), active tests, standards testing, white and black box testing, and reliability testing.
- **Methods for Notifying the User of this Residual Risk:**
  - The IFU contains the following cautions: Failure of the electrosurgical generator could result in an unintended increase of output power. Apparent low power output or failure of the electrosurgical equipment to function correctly at normal settings may indicate faulty application of the dispersive electrode or failure of an electrical lead. Do not increase power output before checking for obvious defects or misapplication. For monopolar surgery, effective coupling between the patient and the dispersive electrode must be verified whenever the patient is repositioned. Regularly inspect electrosurgical accessories for damage. In particular, electrode cables and endoscopic accessories should be checked for damaged insulation. The IFU also recommends annual calibration and preventive maintenance. The system has audio and visual indicators during activation and displays error codes when the system is not functioning properly.

Level 1 - Auditory Disorder:

- **Primary Hazards Contributing to this Harm**:
  - The DFMEA identified a contributor to this harm as acoustic energy output is too great. This is due to component failing and causing the system audio volume to be excessively loud.
- **Actions Taken to Reduce Risk As Far as Possible:**

- The DFMEA identified contributor is mitigated by component selection of the speaker with an output that does not exceed 80dBA and performing standards testing. The residual risk is considered to be reduced to level 1 (lowest level possible).

- **Methods for Notifying the User of this Residual Risk:** The IFU contains the audio levels for active signals and alarms in the Technical Specifications section.

Level 1 - Haemorrhage

- **Primary Hazards Contributing to this Harm:**
  - The AFMEA identified the contributors to this harm as complex or confusing control system or incomplete instructions, insufficient visibility, audibility, or tactile feedback, or inadequate specification of accessories, assembly, or pre-use checks. This is due to controls, display, or labeling not clear or intuitive or the system is operated by someone untrained in the use of electrosurgery.
- **Actions Taken to Reduce Risk As Far as Possible:**
  - The AFMEA identified contributors are mitigated by ensuring the IFU addresses proper set-up and the system is used by users trained in electrosurgery and usability testing. The residual risk is considered to be reduced to level 1 (lowest level possible).
- **Methods for Notifying the User of this Residual Risk:** The system has audio and visual indicators during activation and displays error codes when the system is not functioning properly. The IFU states in the introduction section, For additional information on Electrosurgery please see Megadyne's continuing education programs, "The Basics of Electrosurgery" and "Principles of Electrosurgery."

Level 1 - Infarction

- **Primary Hazards Contributing to this Harm:**
  - The AFMEA identified a contributor to this harm as electro-magnetic emissions. This is due to the user activates energy device near patient's implant (Inadequate filtering/ shielding) causing interference with the patient's implanted device (e.g.: pace-maker) during activation.
- **Actions Taken to Reduce Risk As Far as Possible:**
  - The AFMEA identified contributor is mitigated by the IFU warning of a possible hazard when using HF current near active implants, per the electrical safety standard. The residual risk is considered to be reduced to level 1 (lowest level possible).
- **Methods for Notifying the User of this Residual Risk:** The IFU contains the following caution: For patients with cardiac pacemakers, electrically conductive or other active implants, a possible hazard exists due to the concentration or re-direction of HF currents. The pacemaker or other active implant may be damaged due to the interference of HF currents. In case of doubt, approved qualified advice should be obtained from the device manufacturer.

Level 1 - Infection

- **Primary Hazards Contributing to this Harm:**

- The AFMEA identified a contributor to this harm as Re- and/or cross-infection (re-use) and insufficient visibility, audibility, or tactile feedback. This is due to the capital equipment is not disinfected or is hard to clean or the user unintentionally activates a used device.

- **Actions Taken to Reduce Risk As Far as Possible:**
  - The AFMEA identified contributors are mitigated by ensuring the IFU addresses proper set-up and cleaning. The system also has visual and audible indicators to indicate activation and the system is used by users trained in electrosurgery and usability testing. The residual risk is considered to be reduced to level 1 (lowest level possible).
- **Methods for Notifying the User of this Residual Risk:** Instructions for Use detail cleaning and disinfection process for generator and accessories.

Level 1 - Nerve Injury

- **Primary Hazards Contributing to this Harm:**
  - The DFMEA identified contributors to this harm as the loss of electrical/mechanical integrity and accidental mechanical damage to the device. This is due to components failing and causing premature reliability failures, resulting in the system being powered with the wrong frequency or the loss of mains/patient isolation. Also, this is due to the enclosure not having sufficient strength for anticipated usage and forces, resulting in the enclosure breaking or cracking, allowing user access.
  - The AFMEA identified a contributor to this harm as inadequate specification of accessories, assembly, or pre-use checks. This is due to improper AC power cord is used or grounded outlet is not available.
- **Actions Taken to Reduce Risk As Far as Possible:**
  - The DFMEA identified contributors are mitigated by using neuro-stimulation caps, proper mechanical design, system layout, and component mounting, and standards testing. The residual risk is considered to be reduced to level 1 (lowest level possible).
  - The AFMEA identified contributor is mitigated by the proper cord is provided with the unit and the system is standards tested for two MOOP. The residual risk is considered to be reduced to level 1 (lowest level possible).
- **Methods for Notifying the User of this Residual Risk:** The IFU states to use the provided power cord and addresses proper set-up.

Level 1 - Pain

- **Primary Hazards Contributing to this Harm:**
  - The AFMEA identified a contributor to this harm as inadequate specification of accessories, assembly, or pre-use checks. This is due to the user trips over power cord and is injured.
- **Actions Taken to Reduce Risk As Far as Possible:**
  - The AFMEA identified contributor is mitigated by the IFU addresses proper set-up. The residual risk is considered to be reduced to level 1 (lowest level possible).

- **Methods for Notifying the User of this Residual Risk:** The IFU addresses proper set-up and contains the following caution: The maximum permissible length of any accessory connected to the generator, including its cord shall not exceed 15 feet (4.57 meters).

Level 1 - Soft Tissue Injury

- **Primary Hazards Contributing to this Harm:**
    - The DFMEA identified contributor to this harm is sharp edges or points. This is due to incorrect specification of surface finish and treatments.
    - The AFMEA identified a contributor to this harm as accidental mechanical damage to the device. This is due to misuse by applying too much force to the system or moving the cart across an uneven surface.
- **Actions Taken to Reduce Risk As Far as Possible:**
    - The DFMEA identified contributor is mitigated by rounded external design, enclosure inspected against Material Specification, and standards testing. The residual risk is considered to be reduced to level 1 (lowest level possible).
    - The AFMEA identified contributor is mitigated by electrical safety standards testing. The **residual risk is considered to be reduced to level 1 (lowest level possible).**
- **Methods for Notifying the User of this Residual Risk:** The IFU addresses proper set-up.

Level 1 - Extended Surgery

- **Primary Hazards Contributing to this Harm:**
    - The DFMEA identified the largest contributor to this harm as the loss of electrical/mechanical integrity. This is due to components failing and causing premature reliability failures, resulting in the system over heating, intermittent or inaccurate operation, or not working.
    - The AFMEA identified a contributor to this harm as inadequate specification of accessories, assembly, or pre-use checks. This is due to incompatibility issues, use errors, or user not following instructions.
    - The SWFMEA identified multiple contributors to this harm as inappropriate output power, insufficient visibility, audibility, or tactile feedback, and incorrect output mode characteristics. This is due to corrupted, inaccurate, or ineffective software or the software incorrectly configures or fails to initiate an event.
- **Actions Taken to Reduce Risk As Far as Possible:**
    - The DFMEA identified contributor is mitigated by using redundant components, component selection, proper design analysis, current limiting circuits, POST tests, active tests, standards testing, and reliability testing. The residual risk is considered to be reduced to level 1 (lowest level possible).
    - The AFMEA identified contributor is mitigated by ensuring the IFU addresses proper set-up of the system and Megadyne compatible accessories are listed in the IFU.
    - The SWFMEA identified contributors are mitigated by visual, tactile, and audible indicators to indicate functionality, alarms, and error codes, POST tests (error checking), active tests, standards testing, white and black box testing, tissue testing, and reliability testing.

- **Methods for Notifying the User of this Residual Risk**: The IFU contains the following cautions: Failure of the electrosurgical generator could result in an unintended increase of output power. Apparent low power output or failure of the electrosurgical equipment to function correctly at normal settings may indicate faulty application of the dispersive electrode or failure of an electrical lead. Do not increase power output before checking for obvious defects or misapplication. For monopolar surgery, effective coupling between the patient and the dispersive electrode must be verified whenever the patient is repositioned. Regularly inspect electrosurgical accessories for damage. In particular, electrode cables and endoscopic accessories should be checked for damaged insulation. The IFU also recommends annual calibration and preventive maintenance. The system has audio and visual indicators during activation and displays error codes when the system is not functioning properly.

Level 1 - Vascular Injury

- **Primary Hazards Contributing to this Harm:**
    - The DFMEA identified a contributor to this harm as insufficient visibility, audibility, or tactile feedback. This is due to alarm can be manually adjusted and does not have sufficient volume for clear communication.
- **Actions Taken to Reduce Risk As Far as Possible:**
    - The DFMEA identified contributor is mitigated by POST test checks for activation and alarm audio. Alarms are preset and cannot be adjusted externally, below 65dBA. The residual risk is considered to be reduced to level 1 (lowest level possible).
- **Methods for Notifying the User of this Residual Risk:** The POST test displays an error code if alarm is functioning improperly. The IFU contains the audio levels for active signals and alarms in the Technical Specifications section.

7.2.1.2. Harms Mapping – Ethicon Megadyne Electrosurgical Generator

Clinical safety signals reported from all the data sources were compared to potential harms identified in the new line extension subject device risk management documents and verified that the IFU sufficiently identifies potential adverse events. As per CP0212 (Device Risk Analysis And Management Procedure), harms with a residual risk of Level 2 or 3 must be communicated to the user via labeling (such as the IFU) accompanying the product.

It should be noted that not all potential harms identified in the Risk documentation are represented in the clinical or PMS data. The table below groups together adverse event reports from both on-label and off-label sources found in their respective clinical data sections (Literature and Post-Marketing Surveillance), neither of which was shown to note any adverse event signals or trends in safety or performance of the subject devices.

The potential harms noted in the Risk Management Report have been mapped against the IFUs, clinical literature data (Section 5.7and 5.8), and PMS data (Section 6). Table 7-6 summarizes the harms mapping for the new line extension Ethicon Megadyne Electrosurgical Generator. The legend for the abbreviations is included in the Harms Mapping table below.

No new harms were identified in the data analysis. The two Level 2 Harms identified are represented in the Ethicon Megadyne Electrosurgical Generator IFU/Operator's Manual.

Table 7-6: Harms Mapping - Ethicon Megadyne Electrosurgical Generator

Harm Category*	Clinical Data	PMS	Risk Management	IFU/Owner's Manual**
Level 2 Burn - Life threatening burn	A	A	C	C
Level 2 Burn - Surgical intervention to prevent further injury or damage	A	A	C	C

*Global Harms terms (Per ADAPTIV PR-95959) are typically utilized in this section of the CER. However, alternate terminology or wording that means the same as the Global Harms term are often utilized in the internal and external clinical data, risk management, and post-market surveillance data.

**Harms designated as "C" (captured) in the IFU column in the table above, denote that the Harm is listed directly in the IFU using either the Risk Management nomenclature terminology or appropriate alternate terminology. Those Harms designated as "NC" (not capture) in the IFU column, denotes that the risk is analyzed within the appropriate Risk documents and is determined not to be directly declared in the IFU. However, even when the specific Harm is not captured directly in the IFU, it is additionally important to note that the Harm is often inferred in Contraindications, Warnings, Precautions or other applicable sections of the IFU as described in the Risk documentation. Additionally, as per the Procedure for Product Risk Management Plan (ADAPTIV PR-602-003), any Harms, adverse events, or new risk identified in the CER will trigger updates to the corresponding risk documentation and be reflected as applicable in updates to appropriate documentation, including IFUs.

Abbreviation:	Applies To:	Definition:
A	Clinical Data / PMS	"Analyzed" data set within CER
NO	Clinical Data / PMS	"No Occurrence" as part of data set within CER
C	RM / IFU	"Captured" in the applicable Risk Document and/or IFU
HNR	RM / C	"Harm Not in Risk" documents – identified new or emerging potential harm that is not currently included in the Risk Assessment Summary
NC	IFU	"Not Captured" risk analyzed in the Risk Documents and determined not to be directly declared in the IFU
TBD	RM / IFU	"To Be Determined" Analysis Pending"

Clinical safety signals reported from all the data sources were compared to potential harms identified in the risk management documents and verified that the IFU sufficiently identifies potential adverse events.

7.3. Side Effects Acceptability

Acceptability of the subject devices side-effects needs to be interpreted considering currently available alternative treatments and acceptability of side-effects from those treatments. As discussed in Section

2.2.1, there are numerous energy based and non-energy based options available to the surgeon for dissection and coagulation of tissues, each with their own risk and benefit profiles. The specific clinical benefits for monopolar and bipolar surgical systems are discussed in Section 7.1. The specific clinical risks and associated potential patient/user harms for the Megadyne Electrosurgical Generators are discussed in the risk documentation. A summary of potential patient/user harms crossed-referenced to their occurrence in the clinical literature and their discussion in the subject device IFU is provided in Section 0.

A review of the individual clinical data sources available for this CER on the existing Megadyne Mega Power Generator shows that there are no new or emerging risks that are a cause for concern, and no new potential patient harms or emerging risks have been identified through this clinical evaluation. The reviewed clinical data verifies that all adverse events reported in the clinical data specific to the existing Megadyne Mega Power Generator and new Ethicon Megadyne Electrosurgical Generator subject device were appropriately addressed in the IFU's/Owner's Manuals and Risk documentation and does not suggest any further risk mitigation or required amendments to the product information, IFU, or warnings. To mitigate the risks known to exist for energy-based surgery (e.g., thermal injury), both IFUs/Operator's Manuals (3000158-01, 3000315-01, **Windchill**) specifies the following:

> *The equipment described herein is for use by qualified medical personnel skilled in the particular techniques and procedures to be performed.*

Analysis of the PMS patient codes reported for the existing Megadyne Mega Power Electrosurgical Generator demonstrated harms rates below predicted rates, with no new harms identified (Section 7.2.1)**Error! Reference source not found.**. No new unanticipated, emerging, or unacceptable risks were identified in the existing subject device or new subject device's clinical data review. The reviewed clinical data does not suggest any further risk mitigation or required amendments to the product information, IFU, or warnings for the equivalent subject devices.

7.4. Benefit-Risk Profile Acceptability

There are no non-surgical or pharmaceutical options for dissection and coagulation of tissue, since these tasks by definition require physical manipulation of tissues with sharp instruments and/or heat. With more than 80% of surgical procedures performed in the current clinical environment, energy applying devices (Meeuwsen et al., 2017), generators, like the Megadyne Electrosurgical Generators, provide a clinical benefit of powering these electrosurgical instruments.

As with all surgical procedures, side effects and adverse events can occur that are not directly related to the device, but rather to the surgical procedure or general anesthesia. While many possible reactions may occur, some of the most common observed as a result of surgical procedures include infection, hematoma, seroma, and problems resulting from anesthesia. In considering the overall benefit risk analysis for the Megadyne Electrosurgical Generators, it is important to consider the risk of these events to the patient as part of the residual risks of using the devices. Other factors to consider include, but are

not limited to, concomitant diseases, concomitant medications, and other confounding factors affecting patient health.

Both Megadyne Electrosurgical Generator's Operator's Manuals note that the Generators are for use only by qualified medical personnel skilled in the particular techniques and procedures to be performed (3000158-01, 3000315-01, **Windchill**). Inappropriate use of the equipment by untrained medical personnel may result in hazardous electrical output.

The key safety and performance measures for the Generators, when used as a system in conjunction with electrosurgical devices (electrodes), included the following:

- Safety: no unanticipated adverse events and no discernable trends in the clinical safety data compared to State of the Art for tissue cutting/dissection and control of bleeding
- Performance: successful tissue coagulation (hemostasis)

Considering the well-established risk profile and well-accepted technological and clinical history of ES/RFDS devices, including the subject Megadyne devices, PMS data contribute significantly to the acceptability of the safety and performance of such devices. As such, PMS (Section 7) data, are provided to support safety and performance of the Megadyne Electrosurgical Generator's with the use of the existing, equivalent device data, provided on the Mega Power Electrosurgical Generator. The PMS data analysis of the existing Mega Power Generator covers data for the period from November 2014 through October 2019. There were 2270 complaint events received from November 2014 through October 2019 reporting 2356 Product Experience Code (PEC) issues with an overall complaint rate of 71.6 CPMO (0.01%). Furthermore, no adverse trends were observed for CAPA, NCR, or Escalations/Field Action during the current reporting period. This extremely low complaints rate establishes acceptable safety and performance for this, as stated, well-accepted and well-established technology, along with the additional clinical data analyzed within this CER and the planned PMCF.

To continue, additional objective performance and safety data on the subject Megadyne Electrosurgical Generator devices has come from non-clinical testing documentation including benchtop hardware and software validation and pre-clinical, thermal effects study comparing the function and performance of the existing Megadyne Mega Power Electrosurgical Generator to the new line extension Megadyne Electrosurgical Generator (Section 6.2).

The systematic literature review (Section 5.7) covers published clinical data on the existing (equivalent subject device) the Mega Power Generator, between 01 January 1986 to 03 September 2019. The review include three articles that met the predefined selection criteria on 69 patients. All studies reported on-label use of the equivalent subject device, the Mega Power Generator, which was used in both open and minimally invasive surgical procedures. The indications of open and laparoscopic (minimally invasive) procedures and soft tissue incisions (breast, thigh, buttock and abdomen) were covered by the included studies however the numbers were low and the patient population in the reviewed literature and clinical studies was not representative of the target patient population with respect to demographics (gender and age) since the limited number of studies (3) yielded an all-female

demographic. This total number of included clinical studies will be supplemented with the participation of both subject devices in the planed Real-World Experience PMCF study. Refer to Sections 5.6 (PMCF) and 8.1 (PMCF Recommended).

Furthermore, since the Megadyne Electrosurgical Generators are used to power the electrodes used for tissue cutting and coagulation, the safety and performance outcomes specific to the existing subject device was limited in number. This is expected since generators are part of a system and the focus of clinical publications is typically on the actual handpiece/end-effector and/or the overall surgical outcomes for the subject procedure(s). Since generators are part of a system, proper safety and performance are also measured in the devices that are utilized as part of that system, i.e. handpieces / end-effectors and patient return electrodes. Therefore, the data contained in the CERs that cover the devices utilized with the Megadyne Generators also contributes direct evidence of the safety and performance profile of the generators (Reference Megadyne ACE Blade CER RA-RPT-007, Megadyne Electrodes Electrosurgical Pencils and Suction Coagulators SCN070741, Megadyne Lietz Loop Electrodes CER RA-RPT-009, Megadyne Patient Return Electrodes Disposable SCN070739, and Megadyne MegaSoft Reusable Patient Return Electrodes and Accessories). The volume of clinical literature included for this evaluation is limited but sufficient to demonstrate acceptable safety and performance for the Megadyne generators, in line with the use of generators, which is to provide controllable, uninterrupted power, via surgeon command, to the respective handpieces/end-effectors that can be used with the generator. To supplement the existing clinical evidence analyzed within this clinical evaluation and to provide assurance of additional proactive monitoring of the existing generator and the new line-extension generator, post-market clinical follow-up (PMCF) studies will be initiated to collect additional proactive clinical data on both subject devices. The PMCF data will contribute further toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device.

Regarding establishing state of the art for the subject devices, the State of the Art (Section 3) analysed direct and therapeutic alternatives. This information further supports the subject devices as being state of the art with acceptable safety and performance profiles. In particular, the analysis of “Conventional (Mono- or Bipolar) Electrosurgical Devices (ES/RFDS) vs Advanced Bipolar (Electrosurgical Bipolar Vessel Sealer) (EBVS) or Ultrasonic Surgical (UES) Devices” stated that there were no direct head-to-head comparisons of outcomes between a standard bipolar electrosurgical device and either an advanced bipolar electrosurgical vessel sealer or an ultrasonic energy device in the included SOA literature. However, as shown in Table 2-13 and Table 2-14, Allaix et al.’s systematic review of laparoscopic colorectal resection compared outcomes of unspecified conventional electrosurgical devices (either monopolar or bipolar) with advanced bipolar electrosurgical devices (such as Ligasure or Enseal vessel sealing systems) as well as a multifunctional ultrasonic surgical dissector-sealer, the Cavitron Ultrasonic Surgical Aspirator (CUSA) (Allaix et al., 2016). Since no meta-analysis was performed, the findings were summarized for individual studies (Allaix et al., 2016). Both types of advanced vessel sealing systems

were found to be advantageous in terms of less blood loss compared with conventional electrosurgical devices. The operative time for the vessel sealing systems was significantly shorter in one study (Hubner et al., 2007), but not in the other. There were no statistically significant differences between the conventional electrosurgical devices and Cavitron Ultrasonic Surgical Aspirator (CUSA) in operative time and intraoperative blood loss in three studies. The authors concluded that ultrasonic surgical devices and advanced bipolar vessel systems are advantageous in terms of less blood loss and/or a shorter operative time compared with conventional electrosurgical devices. However, they noted that the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection (Allaix et al., 2016). Given this information, ES/RFDS devices still remain state of the art depending on surgical circumstances, surgeon training / surgeon choice, healthcare reimbursement and several other factors, as demonstrated by the clinical evaluation contained herein.

Further to establishing the subject devices as state of the art with acceptable safety and performance profiles, none of the included studies or clinical data described any AEs that could be directly associated with the existing Mega Power Electrosurgical Generator and there were no patient deaths associated with or attributed to the equivalent subject device from any clinical data source. Overall, no new unanticipated, emerging, or unacceptable risks were identified for the equivalent subject device and these three included studies do support the performance and safety of the Megadyne Mega Power Electrosurgical Generator when used as intended - to power the electrodes for tissue cutting and coagulation.

All risks associated with the Generator subject devices have been assessed individually in the risk management documents along with the severity of harms. The risk management documents have been reviewed by a cross-functional team to ensure labelling and warnings are appropriate for the associated risks, and the overall residual risk of the Megadyne Electrosurgical Generators has been deemed acceptable. Design Verification and Validation activities have been used to ensure the effectiveness of the risk control measures identified during the risk mitigation process. The residual risk for both generators is as low as possible based on the current technology and State of the Art for electrosurgery. The existing subject device has been utilized clinically for 15 years and has an acceptable risk benefit profile.

Based on the overall medical benefits and the possible harms identified through complaint clinical literature review, it is determined that if the Megadyne Electrosurgical Generators are utilized according to the intended use, the occurrence of the risks identified for the system have been reduced as far as possible and the benefits outweigh the possible risks over the lifetime of the device.

8. CONCLUSION

The class IIb Megadyne Electrosurgical Generators subject devices supply energy to electrosurgical (electrode) instruments and have been CE-Mark certified for 15 years. The use of the existing equivalent subject device, the Mega Power Generator during open and laparoscopic minimally invasive surgical procedures is a well-established technology that remains state of the art. With the majority of surgical procedures performed in the current clinical environment utilizing energy applying surgical instruments (Meeuwsen et al., 2017), the generators, such as the Megadyne Electrosurgical Generators, provide a clinical benefit of powering electrosurgical instruments for cutting and coagulation of tissues.

As detailed in the State of the Art Section (Section 2), electrosurgical devices, consisting of monopolar and bipolar electrosurgical instruments (electrodes), are utilized in contemporary surgery and are associated with a significantly shorter operating time, lesser perioperative bleeding, and lesser postoperative pain. It bears repeating that the findings reported across studies do not consistently demonstrate the superiority of one form of energized surgery tool over the other. As in the utilization of monopolar and standard bipolar electrosurgical devices, the selection of a particular energized surgical devices may ultimately depend on surgeon preference, based on factors such as cost, skill in using the instrument, type of surgical operation, and patient characteristics.

The PMS data (Section 6) showed there were 2270 complaint events received from November 2014 through October 2019 reporting 2356 Product Experience Code (PEC) issues with an overall complaint rate of 71.6 CPMO (0.01%). No new harms or hazards were identified.

Overall, of the adverse events reported in the clinical data, none were unexpected. These risks were assessed individually within the appropriate risk management reports, along with their potential contributing causes of failure and related mitigation activities (Section 0).

Since the Megadyne Electrosurgical Generators are used to power the electrodes used for tissue cutting and coagulation, the safety and performance outcomes specific to the existing subject device was limited in number. This is expected since generators are part of a system and the focus of clinical publications is typically on the actual handpiece/end-effector and/or the overall surgical outcomes for the subject procedure(s). Since generators are part of a system, proper safety and performance are also evaluated in the devices that are utilized as part of that system, i.e. handpieces / end-effectors and patient return electrodes. Therefore, the data contained in the CERs that cover the devices utilized with the Megadyne Generators also contributes direct evidence of the safety and performance profile of the generators (Reference Megadyne ACE Blade CER RA-RPT-007, Megadyne Electrodes Electrosurgical Pencils and Suction Coagulators SCN070741, Megadyne Lietz Loop Electrodes CER RA-RPT-009, Megadyne Patient Return Electrodes Disposable SCN070739, and Megadyne MegaSoft Reusable Patient Return Electrodes and Accessories). The volume of clinical literature included for this evaluation is limited but sufficient to demonstrate acceptable safety and performance for the Megadyne generators, in line with the use of generators, which is to provide controllable, uninterrupted power, via surgeon command, to the respective handpieces/end-effectors that can be used with the generator. To

supplement the existing clinical evidence analyzed within this clinical evaluation and to provide assurance of additional proactive monitoring of the existing generator and the new line-extension generator, post-market clinical follow-up (PMCF) studies will be initiated to collect additional proactive clinical data on both subject devices. The PMCF data will contribute further toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device.

In conclusion, it has been shown that there is sufficient evidence that supports the safety and performance of the Megadyne Electrosurgical Generators when used in accordance with the Operator's manual. The data is also sufficient to assess the benefits and risks associated with the use of these devices and to conclude that the risk benefit profile is acceptable. Megadyne Medical Products Inc. has undertaken all necessary steps to ensure that the risk factors associated with the use of the Megadyne Electrosurgical Generators are minimized by applying the available state of the art techniques in design, manufacture, and testing of the medical devices and ensure safe usage and that the device will perform as intended. Additional post-market clinical follow-up (PMCF) studies will be initiated to collect proactive clinical data on both subject devices. The PMCF data will contribute further toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device.

Therefore, this clinical evaluation has established that the available clinical data are sufficient to support the demonstration of conformity with the relevant ERs of the Medical Device Directive (MDD), Section 5.1 and supports the safety and performance for the use of the Megadyne Electrosurgical Generators.

Table 8-1: Megadyne Electrosurgical Generators Post Market Clinical Follow-up Studies Guide

Circumstances that may justify PMCF studies include, for example:	Yes/No
• Innovation, e.g., where the design of the device, the materials, substances, the principles of operation, the technology or the medical indications are novel	No
• Significant changes to the products or to its intended use for which premarket clinical evaluation and re-certification has been completed	No
• High product related risk e.g. based on design, materials, components, invasiveness, clinical procedures	No
• High risk anatomical locations	No
• High risk target populations e.g. pediatrics, elderly	Yes*
• Severity of disease/treatment challenges	No
• Questions of ability to generalize clinical investigation results	No
• Unanswered questions of long-term safety and performance	No

Circumstances that may justify PMCF studies include, for example:	Yes/No
• Results from any previous clinical investigation, including adverse events or from post-market surveillance activities	No
• Identification of previously unstudied subpopulations which may show different benefit/risk-ratio e.g. hip implants in different ethnic populations	No
• Continued validation in cases of discrepancy between reasonable premarket follow-up time scales and the expected life of the product	No
• Risks identified from the literature or other data sources for similar marketed devices	No
• Interaction with other medical products or treatments	No
• Verification of safety and performance of device when exposed to a larger and more varied population of clinical users	Yes**
• Emergence of new information on safety or performance	No
• Where CE marking was based on equivalence	Yes**
PMCF Recommended (based on factors above indicating residual risk):	**Yes**

*Device is used on all demographic ranges of patients; however, there is a well-established history of device use.
** PMCF study will contribute further proactive data toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device..

8.1. PMCF Recommended

The Safety & Performance (S&P) of the existing Megadyne Mega Power Electrosurgical Generator is confirmed for all existing data sources discussed in this clinical evaluation and indicates no adverse safety or performance trends in the overall use of the subject device. However, the PMCF data will contribute further proactive data toward the continued safety and performance profile of the existing generator and will confirm the acceptability of the safety and performance profile, established herein via equivalence, with data directly on the new line-extension device.

Table 8-2: Megadyne Electrosurgical Generators CER Frequency Matrix

	CER Update Frequency - Risk Determination Matrix						
What attribute is addressing	**Attribute**	**Very Low**	**Low**	**Med**	**High**		
- characterizes patient health consequences associated with device failure	**Highest potential risk to patient as a result of device failure***	Limited (transient, minor impairment, or complaints) **OR** No adverse health consequences	Failure unlikely to cause or contribute to serious injury, or death under circumstances of normal use with results being temporary or reversible without medical intervention	Failure likely to cause or contribute to serious injury, or death under circumstances of normal use that is likely reversible with medical / surgical intervention	Results in permanent impairment of body function or permanent damage to a body structure **OR** Life-threatening (death has or could occur) regardless of medical / surgical intervention	**Device Risk Category**	***High rating in any of these attribute categories mandates highest update frequency within risk band**
- characterizes # of complaint events per determined volume associated with device to provide evidence if device is not safe or is not performing	**Complaint Rate***	Negligible rate per time or volume	Low rate per time or volume	Medium rate per time or volume	High/Very High rate per time or volume		
- characterizes how long (theoretically, how often) subject device used for the intended use	**Subject Device Product Maturity**					**Well-established Device Category**	
- lower risk the longer the device is on market / more devices used	**# Units of worst case variant(s) sold / shipped since launch**	x > 10,000	1000 < x < 10,000	100 < x < 1000	x < 100		
- worst case = devices with highest potential risk to patient as a result of device failure	**Time on Market: Implantable Device:**	> 10 years	5 - 10 years	3 - 5 years	< 3 years		
	Time on Market: Non-Implantable Device:	> 5 years	3 - 5 years	1 -3 years	< 1 year		
- characterizes how long the equivalent device technology (design, mfg, materials) has been on the	**Technological Maturity of Equivalent Device (if applicable)**						

	CER Update Frequency - Risk Determination Matrix					
market - lower risk the longer the device is on market / more devices used	**Time on Market: Implantable Device:**	> 10 years	5 - 10 years	3 - 5 years	< 3 years	
	Time on Market: Non-Implantable Device:	> 5 years	3 - 5 years	1 -3 years	< 1 year	
- characterizes how well established the clinical science is (i.e. how long clinicians have been using similar devices for the intended use / technique)	**Maturity of Clinical Science**					
	Time of Clinical Use:	> 10 years	5 - 10 years	3 - 5 years	< 3 years	
- characterizes general risk of device	**MDD Device Classification**	I	IIa	IIb	III	**Device Risk Category**
- characterizes degree of device contact	**Degree and Duration of Device Invasiveness**	Non-Invasive Device No patient contact or exposure to device	Invasive Device (non-implantable, body orifice) Transient / Short-Term patient contact or exposure (seconds / minutes / Hours)	Surgically Invasive Device (non-implantable) Transient / Short-Term patient contact or exposure (seconds / minutes / Hours)	Surgical Implant Extended time frame of contact or exposure to the device (partially implantable devices that are implanted >30 days and/or fully implantable devices)	
- characterizes state of health (i.e. patient motivation/risk), not about the device	**Natural course and consequences of medical conditions if left untreated**	Limited (transient, minor impairment or pain) **OR** No adverse health consequences	Natural course unlikely to cause or contribute to serious injury, pain, or death	Natural course could possibly cause or contribute to serious injury, pain, or death	Natural course likely causes or contributes to serious injury, pain, or death	
- characterizes risk by anatomic area / physiological functions	**Anatomical location where device used**	No body contact	Body orifice, intact skin	All other anatomical locations	CNS, CCS	

	CER Update Frequency - Risk Determination Matrix					
- characterizes the Safety / Performance evidence for intended use / technique across lifetime - nominal (subject or equivalent) = low amount of data but sufficient to launch / update - ample (subject) = does not require equivalent device	**Clinical Data (quantity / quality)**	Ample level I - III data on subject device across all indications / lifetime OR Clinical data was deemed not necessary (e.g. MDD - Annex X, 1.1d; AIMD - Annex 7, 1.5)	Nominal level I - III data on subject device and ample data on equivalent device across all indications / lifetime	No level I - III data on subject device and ample data on equivalent device across all indications / lifetime	No level I - III data on subject device and nominal data on equivalent device across all indications / lifetime	**Well-established Device Category**
		CER Update Frequency - Risk Determination Matrix				
	Attribute	**Very Low**	**Low**	**Med**	**High**	
	Highest potential risk to patient as a result of device failure*	Limited (transient, minor impairment, or complaints) **OR** No adverse health consequences	Failure unlikely to cause or contribute to serious injury, or death under circumstances of normal use with results being temporary or reversible without medical intervention	Failure likely to cause or contribute to serious injury, or death under circumstances of normal use that is likely reversible with medical / surgical intervention	Results in permanent impairment of body function or permanent damage to a body structure **OR** Life-threatening (death has or could occur) regardless of medical / surgical intervention	***High rating mandates highest update frequency**
	CER Update Frequency Guide:	**5 years**	**3 years**	**2 years**	**1 year**	
	Justification for selection: • The CER frequency for the Megadyne Electrosurgical Generators is every 2 years. This class IIb device carries known risks. Clinical and PMS data supports the use of the devices in a wide variety of open and laparoscopic minimally invasive surgical procedures with no unanticipated harms identified in the current clinical evaluation.					
	Background: • The existing equivalent subject device (Megadyne Mega Power Electrosurgical Generator), used for the establishment of the new line extension subject device (Ethicon Megadyne Electrosurgical Device) is a well-established device with 15 years in the current market. The Equivalence comparison and documentation in this CER established the devices to be 83% identical and 17% sufficiently the same to be considered equivalentor equivalent.					

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CER Update Frequency - Risk Determination Matrix
• There are no uncertainties or unanswered questions regarding the safety and performance of the use of the Megadyne Electrosurgical Generators.

9. APPENDICES

9.1. Supporting Documents Reference

Document Name	Document Number	Revision
Design Control Megadyne Mega Power Electrosurgical Generator	ENG-SOP-005	013
Device Risk Analysis And Management Procedure	CP0212	BD
Electrosurgical Generator CMR Faceplate	MKT-CMR-009	001
ESU Product Specification	ENG-PS-001	003
Ethicon Megadyne Electrosurgical Generator CMR	MKT-CMR-030	005
Ethicon Megadyne Electrosurgical Generator Risk Management Report	ENG-RMF-077	001
Ethicon Megadyne Electrosurgical Generator Software Requirements	ENG-SWS-009	001
Ethicon Megadyne Electrosurgical Generator Technical File	500441224	A
Ethicon Megadyne ESU Application Failure Mode Effects Analysis (AFMEA)	ENG-RMF-068	A
Ethicon Megadyne ESU Design Failure Mode Effects Analysis (DFMEA)	ENG-RMF-063	A
Ethicon Megadyne ESU Software Failure Mode Effects Analysis (SWFMEA)	ENG-RMF-072	A
Ethicon Megadyne Generator the Input and Output Conformance Matrix	ENG-IOM-020	A
Franchise Procedure for Corrective and Preventive Action (CAPA)	PR575-001	65
Franchise Procedure for Evaluation of Clinical Data for CE-Marking	PR-0000277	21
Global Trending and Signal Detection Procedure, Complaint data	100583575	
IFU 1000 Mega Power Operator's Manual	3000158-01	006
IFU Ethicon Megadyne ESU Operator's Manual	3000315-01	B
Mega Power ESU Design Failure Mode Effects Analysis (DFMEA)	ENG-RMF-018	009
Mega Power Generator Input and Output Conformance Matrix	ENG-IOM-010	001
Mega Power Hazard Assessment Summary	ENG-RMF-019	001
Mega Power Risk Management Report	ENG-RMF-042	002
Mega Power Upgrade	ENG-DMR-008	009

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Document Name	Document Number	Revision
Megadyne Mega Power Electrosurgical Generator Risk Management Plan	ENG-RMF-039	004
Megadyne Mega Power Electrosurgical Generator Risk Management Report	ENG-RMF-042	002
Megadyne Mega Power Electrosurgical Generator Software Requirements	ENG-WI-005	002
MEGEN1 RoHS Compliance Memorandum	500430815	A
PMS Report Mega Power Electrosurgical Generator	RA-REC-013	002
PMSP for Mega Power Electrosurgical Generator	RA-REC-012	C
PMSR for Mega Power Electrosurgical Generator	RA-REC-013	C
Protocol: Ethicon Megadyne ESU, Thermal Effects on Tissue	ENG-PRT-529	001
Report: Ethicon Megadyne ESU, Thermal Effects on Tissue	ENG-RPT-635	002
Risk Management of Medical Devices (Ethicon Megadyne Electrosurgical Generator Risk Management Plan)	QA-SOP-015	006
Test Protocol, Mega Power Electrosurgical Generator, RoHS Compliance	1150744-10	002
Test Report, Mega Power Electrosurgical Generator, RoHS Compliance	ENG-RPT-338	001
Usability Specification – Mega Power	MKT-US-001	002

9.2. Product Codes

Table 9-1 Megadyne Electrosurgical Generator Product Codes

Product Code	Description	Device Class MDD	GMDN Number	Original CE-Mark Date	Technical Documentation #
MEGEN1	Ethicon Megadyne Electrosurgical Generator	IIb	11490	Pending	ENG-DMR-015
1459J	Bipolar Footswitch	I	N/A	N/A	ENG-DMR-015
1000	Megadyne Mega Power Electrosurgical Generator	IIb	11490	12 May 2005	ENG-DMR-008

9.3. Literature Search Results

9.3.1. Systematic SOA Search

9.3.2. Systematic Literature Review Search

9.1. Literature Search Results

9.1.1. Search 1

Megadyne CER – Literature Search Results
Product: Megadyne Products and Accessories
Ref: Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1.
Dates Searches run: December 28, 2017 and January 4, 2018
Contains: 67 documents
Databases: Embase/Medline in OVID, PubMed, Google Scholar
Search Date Limitation: January 1, 1986 to the present.
Search Strategies:
EMBASE/MEDLINE in OVID:

Embase 1988 to 2018 Week 01
Ovid MEDLINE(R) 1946 to December Week 4 2017
Ovid MEDLINE(R) Epub Ahead of Print January 03, 2018
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 03, 2018
Ovid MEDLINE(R) Daily Update January 03, 2018
NOTE: MEDLINE Daily and Ovid MEDLINE were frozen on November 22, 2017 due to the annual MEDLINE reload.

	Search Statement	Results
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	44616
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	46875
3	1 or 2	59332
4	Surgical Instruments/ or surgical equipment/	43713
5	exp Electrodes/	232835
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	263
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	1971089
8	4 or 5 or 6 or 7	2051481

9	3 and 8	11791
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	7661
11	electrosurgical knife/	222
12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1122
14	((smoke or fluid?) adj3 (evacuat* or remov*)).mp.	6533
15	or/10-14	15482
16	megadyne*.mp.	16
17	("EZ clean" or "E-Z clean" or "E Z clean").mp.	4
18	("stainless steel" adj5 (ball? or electrode*)).mp.	1505
19	("reusable stainless steel" and "indicator shaft").mp.	0
20	((ssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	0
21	"ace blade?".mp.	2
22	LERIS.mp.	39
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	25
25	(("ez clean" or "e-z clean" or "e z clean") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	69
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*)).mp.	3
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	65
30	(LLETZ and LEEP).mp.	65
31	(large adj loop adj excision?).mp.	865
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*)).mp.	10
33	("mega power*" or mega-power* or Mega Power*).mp.	3
34	((Megasoft or megasoftTM or mega-soft or mega-softTM or "mega soft" or "mega softTM") and electode*).mp.	0
35	("Mega 2000" or "Mega 2000TM" or Mega-2000 or Mega-2000TM or Mega2000 or Mega2000TM).mp.	7
36	"disposable patient return electrode*".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac or Mega-Vac or "Mega Vac" or UltraVac or Ultra-Vac or "Ultra Vac" or AttachaVac or	8

	Attacha-Vac or "Attacha Vac").mp.	
39	("ZIP Pen" or ZIP-pen).mp.	0
40	or/16-39	2596
41	9 or 15 or 40	27180
42	conference abstract.pt.	2834045
43	41 and 42	2423
44	limit 43 to yr="1986 -Current"	2418
45	41 not 42	24757
46	limit 45 to yr="1986 - 2002"	8678
47	remove duplicates from 46	5757
48	limit 45 to yr="2003 - 2010"	6549
49	remove duplicates from 48	4295
50	limit 45 to yr="2011 -Current"	6802
51	remove duplicates from 50	4291
52	44 or 47 or 49 or 51	16761

Within the above search sets, results from set 52 were exported to QUOSA.

PUBMED

Search completed: 12/28/17

#	Searches	Results
1	(electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])	15315
2	(electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]	294
3	1 or 2 Executed by PubMed: (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]))) OR ((((((electro surg*[Title/Abstract]) OR electro cauter*[Title/Abstract]) OR electro dessicat*[Title/Abstract]) OR electro diatherm*[Title/Abstract]) OR electro dissect*[Title/Abstract]) OR electro coagulat*[Title/Abstract])	15501
4	(surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])	4066

5	(electrode[Title/Abstract] OR electrodes[Title/Abstract])	128172
6	(((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract]))	80
7	(((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	499505
8	4 or 5 or 6 or 7 Executed by PubMed: ((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]))))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract]))))) OR ((((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))	503173
9	3 and 8 Executed by PubMed: (((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]))))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))))) AND (((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]))))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract]))))) OR ((((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))))	2050
10	((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])))) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract]))	393
11	("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])	230
12	smoke evacuat*[Title/Abstract]	99

13	("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract]	827
14	10 or 11 or 12 or 13 Executed by PubMed: (((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])))) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))))) OR (("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR ((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract]))	1546
15	megadyne*[Title/Abstract]	5
16	((EZ clean[Title/Abstract]) OR E-Z clean[Title/Abstract]) OR "E Z clean"[Title/Abstract]	10
17	((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract]))) OR (("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract]))	367
18	("reusable stainless steel"[Title/Abstract]) AND indicator shaft[Title/Abstract]	0
19	((((((("ssteel"[Title/Abstract]) OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract]) OR "button"[Title/Abstract]) OR "stainless"[Title/Abstract]) OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])	23
20	("ace"[Title/Abstract]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])	8
21	"leris"[Title/Abstract]	2
22	laparoscopic electrode reusable indicator[Title/Abstract]	0
23	("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])	10
24	("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract]	17
25	((megatip*[Title/Abstract]) OR "mega tip"[Title/Abstract]) OR mega-tip*[Title/Abstract]	1
26	("indicator"[Title/Abstract]) AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])	78
27	("lletz"[Title/Abstract]) AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	252
28	("lletz"[Title/Abstract]) AND "leep"[Title/Abstract]	24
29	(("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract]))	341
30	(("all in one"[Title/Abstract] OR "aio"[Title/Abstract])) AND (("hand piece"[Title/Abstract] OR "hand	29

	pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	
31	(mega-power*[Title/Abstract]) OR Mega Power*[Title/Abstract]	0
32	(("megasoft"[Title/Abstract]) OR mega soft*[Title/Abstract]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	0
33	("mega 2000"[Title/Abstract]) OR mega2000[Title/Abstract]	3
34	((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]))) AND "patient return"[Title/Abstract]	0
35	((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]))) AND "disposable"[Title/Abstract]	0
36	(re cordable[Title/Abstract]) OR re-cordable[Title/Abstract]	0
37	("megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract) OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract]	7
38	("zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract]	0
39	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 Executed by PubMed: ((((((((((((((((((((((((((EZ clean[Title/Abstract]) OR E-Z clean[Title/Abstract]) OR "E Z clean"[Title/Abstract]))) OR (((((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract])))) OR (("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])))))) OR ((("reusable stainless steel"[Title/Abstract]) AND indicator shaft[Title/Abstract]))) OR (((((((("ssteel"[Title/Abstract]) OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract]) OR "button"[Title/Abstract]) OR "stainless"[Title/Abstract]) OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])))) OR ((("ace"[Title/Abstract]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])))) OR "leris"[Title/Abstract]) OR laparoscopic electrode reusable indicator[Title/Abstract]) OR ((("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])))) OR ((("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])))) OR ((((megatip*[Title/Abstract]) OR "mega tip"[Title/Abstract]) OR mega-tip*[Title/Abstract]))) OR ((("indicator"[Title/Abstract]) AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])))) OR ((("lletz"[Title/Abstract]) AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR ((("lletz"[Title/Abstract]) AND "leep"[Title/Abstract]))) OR ((((("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])))))) OR ((((("all in one"[Title/Abstract] OR "aio"[Title/Abstract])) AND (("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR (((mega-power*[Title/Abstract]) OR Mega Power*[Title/Abstract]))) OR ((((("megasoft"[Title/Abstract]) OR mega soft*[Title/Abstract]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR ((("mega 2000"[Title/Abstract]) OR mega2000[Title/Abstract]))) OR (((((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]))) AND "patient return"[Title/Abstract]))) OR ((((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]))) AND	929

	"disposable"[Title/Abstract])))) OR (((re cordable[Title/Abstract]) OR re-cordable[Title/Abstract]))) OR ((("megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract) OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract]))) OR ((("zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract]))	
40	9 or 14 or 39 Executed by PubMed: ((((((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND ((((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))))))) OR (((((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract]))) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))) OR ((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR ((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract])))) OR ((((((((((((((((((((((((((EZ clean[Title/Abstract]) OR E-Z clean[Title/Abstract]) OR "E Z clean"[Title/Abstract]))) OR (((((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract])))) OR (("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])))))) OR ((("reusable stainless steel"[Title/Abstract]) AND indicator shaft[Title/Abstract])))) OR (((((((("ssteel"[Title/Abstract]) OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract]) OR "button"[Title/Abstract]) OR "stainless"[Title/Abstract]) OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])))) OR ((("ace"[Title/Abstract]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])))) OR "leris"[Title/Abstract]) OR laparoscopic electrode reusable indicator[Title/Abstract]) OR ((("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])))) OR ((("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])))) OR ((((megatip*[Title/Abstract]) OR "mega tip"[Title/Abstract]) OR mega-tip*[Title/Abstract])))) OR ((("indicator"[Title/Abstract]) AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])))) OR ((("lletz"[Title/Abstract]) AND ("loop"[Title/Abstract] OR	4343

	"loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))))) OR ((("lletz"[Title/Abstract]) AND "leep"[Title/Abstract])))) OR ((((("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])))))) OR ((((("all in one"[Title/Abstract] OR "aio"[Title/Abstract])) AND (("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))))) OR (((mega-power*[Title/Abstract]) OR Mega Power*[Title/Abstract])))) OR ((((("megasoft"[Title/Abstract]) OR mega soft*[Title/Abstract]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))))) OR ((("mega 2000"[Title/Abstract]) OR mega2000[Title/Abstract])))) OR (((((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract])))) AND "patient return"[Title/Abstract])))) OR (((((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract])))) AND "disposable"[Title/Abstract])))) OR (((re cordable[Title/Abstract]) OR re-cordable[Title/Abstract])))) OR ((("megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract) OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract])))) OR ((("zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract]))))	
41	#40 and ("1986/01/01"[Date - Publication] : "3000"[Date - Publication])) NOT MEDLINE [sb]	447

***Within the above search sets, results from set 41 were exported to QUOSA*.**

GOOGLE SCHOLAR

#	SEARCH STATEMENTS	RESULTS
1	With **all** of the word(s): megadyne With **at least one** of the words: diathermy or electrosurgery or electrosurgical or electrocautery or electrocauterization or electrocauterisation or medical or electrode or electrodes or cauterization or cauterisation or cautery or monopolar Return articles **dated** between: 1986-2017	**162**

Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts where the only mention of Megadyne is as a sponsor were removed. The remaining 44 results were compared to the results from the Ovid and PubMed searches and 11 duplicates were removed. The 33 items that remained were added to the final search results.

QUOSA

17,208 documents from the Ovid and PubMed search results were exported to QUOSA. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results

1	Megadyne*	**17**
2	"EZ clean" OR "EZ cleanTM"	**1**
3	"E-Z clean" OR "E-Z cleanTM" OR "E Z clean" OR "E Z cleanTM"	**4**
4	"ssteel pencil"~3 OR "ssteel pencils"~3 OR "ssteel pencilTM"~3	**0**
5	"s steel pencil" OR "s steel pencils" OR "s steel pencilTM"	**0**
6	"ace blade"~3 OR "ace blades"~3 OR "acetm blade"~2	**4**
7	Leris OR lerisTM	**2**
8	"laparoscopic indicator"~3	**1**
9	megatip* OR "mega tip" OR "mega tipTM" OR mega-tip OR mega-tipTM	**2**
10	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	**0**
11	mega-power* OR Mega Power* OR "mega power"	**4**
12	(megasoft* OR "mega soft" OR "mega softTM") AND electrode*	**1**
13	"mega 2000" OR "mega 2000tm" OR mega2000*	**4**
14	"re cordable" OR re-cordable* OR "re cordableTM"	**0**
15	megavac* OR "mega vac" OR "mega vacTM" OR mega-vac*	**4**
16	ultravac* OR "ultra vac" OR "ultra vacTM" OR ultra-vac*	**4**
17	attachavac* OR "attacha vac" OR "attacha vacTM" OR attacha-vac*	**0**
18	"zip pen" OR "zip pens" OR "zip penTM" OR zip-pen*	**1**

After deduplication, there were 34 results from sets 1-18 above. These items were combined with the 33 Google Scholar results as noted above, resulting in 67 final items. These are listed below for your review.

9.1.2. Search 2

Megadyne CER – Literature Search Results

Product: Megadyne Products and Accessories

Ref: Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1., Megadyne CER December 2017

Dates Searches run: October 12, 2018

Contains: 13 documents

Databases: Embase/Medline in OVID, PubMed, Google Scholar

Search Date Limitation: November 1, 2017- Present (October 2018)

Search Strategies:

EMBASE/MEDLINE in OVID:

Embase 1988 to 2018 October 11
Ovid MEDLINE(R) 1946 to October Week 1 2018
Ovid MEDLINE(R) Epub Ahead of Print October 11, 2018
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations October 11, 2018
Ovid MEDLINE(R) Daily Update October 11, 2018

Embase, Ovid MEDLINE(R)		
#	**Search Statement**	**Results**
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	41053
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	43540
3	1 or 2	54625
4	Surgical Instruments/ or surgical equipment/	40159
5	exp Electrodes/	222016
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	246
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	2332388
8	4 or 5 or 6 or 7	2400137
9	3 and 8	13403
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	6963
11	electrosurgical knife/	310
12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1046
14	((smoke or fluid?) adj3 (evacuat* or remov*)).mp.	6126
15	or/10-14	14388
16	megadyne*.mp.	15
17	("EZ clean" or "E-Z clean" or "E Z clean").mp.	4
18	("stainless steel" adj5 (ball? or electrode*)).mp.	1394

19	("reusable stainless steel" and "indicator shaft").mp.	0
20	((ssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	0
21	"ace blade?".mp.	2
22	LERIS.mp.	40
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	27
25	(("ez clean" or "e-z clean" or "e z clean") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	74
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*)).mp.	3
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	60
30	(LLETZ and LEEP).mp.	64
31	(large adj loop adj excision?).mp.	818
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*)).mp.	11
33	("mega power*" or mega-power* or Mega Power*).mp.	4
34	((Megasoft or megasoftTM or mega-soft or mega-softTM or "mega soft" or "mega softTM") and electode*).mp.	0
35	("Mega 2000" or "Mega 2000TM" or Mega-2000 or Mega-2000TM or Mega2000 or Mega2000TM).mp.	7
36	"disposable patient return electrode*".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac or Mega-Vac or "Mega Vac" or UltraVac or Ultra-Vac or "Ultra Vac" or AttachaVac or Attacha-Vac or "Attacha Vac").mp.	8
39	("ZIP Pen" or ZIP-pen).mp.	0
40	or/16-39	2443
41	9 or 15 or 40	25857
42	limit 41 to yr="2016-Current"	3424
43	limit 42 to ed=20171101-20181012 use ppez [Limit not valid in Embase; records were retained]	421
44	limit 42 to dc=20171101-20181012 use emefd	899
45	limit 42 to dd=20171101-20181012 use emefd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	439
46	limit 42 to rd=20171101-20181012 use emefd	560
47	limit 42 to up=20171101-20181012 use medp	48
48	42 and 2017-11-01:2018-10-12.(dt). use prem	174
49	43 or 44 or 45 or 46 or 47 or 48	1631
50	remove duplicates from 49	**1338**

Within the above search sets, results from set 50 were exported to QUOSA.

PUBMED - *Search completed on October 12th, 2018*

#	*Searches*	*Results*
1	(electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])	15,771
2	(electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]	310
3	**#1 or #2** **Executed as:** (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR ((((((electro surg*[Title/Abstract]) OR electro cauter*[Title/Abstract]) OR electro dessicat*[Title/Abstract]) OR electro diatherm*[Title/Abstract]) OR electro dissect*[Title/Abstract]) OR electro coagulat*[Title/Abstract])	15,967
4	(surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])	4,270
5	(electrode[Title/Abstract] OR electrodes[Title/Abstract])	135,491
6	(((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract]))	80
7	(((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	521,910
8	**#4 or #5 or #6 or #7** **Executed as:**	525,761

	((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]))))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract]))))) OR (((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))	
9	**#3 and #8** **Executed as:** (((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]))))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))))) AND ((((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]))))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract]))))) OR (((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))))	2,128
10	((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract]))	415

11	("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])	235
12	smoke evacuat*[Title/Abstract]	104
13	("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract]	851
14	**#10 or #11 or #12 or #13** **Executed as:** (((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])))) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))))) OR ((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR ((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract]))	1,601
15	megadyne*[Text Word]	5
16	((EZ clean[Text Word]) OR E-Z clean[Text Word]) OR "E Z clean"[Text Word]	12
17	((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word]))) OR (("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word]))	376
18	("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word]	0

19	((((((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR "stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word])	24
20	("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word])	8
21	"leris"[Text Word]	2
22	laparoscopic electrode reusable indicator[Text Word]	0
23	("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word])	11
24	("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word]	19
25	((megatip*[Text Word]) OR "mega tip"[Text Word]) OR mega-tip*[Text Word]	1
26	("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word])	79
27	("lletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])	265
28	("lletz"[Text Word]) AND "leep"[Text Word]	26
29	(("large loop excision"[Text Word] OR "large loop excisions"[Text Word]))	356
30	(("all in one"[Text Word] OR "aio"[Text Word])) AND (("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])	37
31	(mega-power*[Text Word]) OR Mega Power*[Text Word]	0
32	(("megasoft"[Text Word]) OR mega soft*[Text Word]) AND ("electrode"[Text Word] OR "electrodes"[Text Word])	0
33	("mega 2000"[Text Word]) OR mega2000[Text Word]	3

34	((("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word])) AND "patient return"[Text Word]	0
35	((("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word])) AND "disposable"[Text Word]	0
36	(re cordable[Text Word]) OR re-cordable[Text Word]	0
37	("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Text Word) OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word]	8
38	("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word]	0
39	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 Executed as: ((((((((((((((((((((((((EZ clean[Text Word]) OR E-Z clean[Text Word]) OR "E Z clean"[Text Word])))) OR (((((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word])))) OR (("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word])))))) OR ((("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word])))) OR (((((((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR "stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word]))))) OR ((("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word]))))) OR "leris"[Text Word]) OR laparoscopic electrode reusable indicator[Text Word]) OR ((("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word]))))) OR ((("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word])))) OR ((((megatip*[Text Word]) OR "mega tip"[Text Word]) OR mega-tip*[Text Word])))) OR ((("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word]))))) OR ((("lletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word]))))) OR ((("lletz"[Text Word]) AND "leep"[Text Word])))) OR ((((("large loop excision"[Text Word] OR "large loop excisions"[Text Word])))))) OR ((((("all in one"[Text Word] OR "aio"[Text Word])) AND (("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word]))))) OR (((mega-power*[Text Word])	969

	OR Mega Power*[Text Word])))) OR ((((("megasoft"[Text Word]) OR mega soft*[Text Word]) AND ("electrode"[Text Word] OR "electrodes"[Text Word])))) OR ((("mega 2000"[Text Word]) OR mega2000[Text Word]))) OR (((((("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word])))) AND "patient return"[Text Word]))) OR (((((("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word])))) AND "disposable"[Text Word]))) OR (((re cordable[Text Word]) OR re-cordable[Text Word]))) OR ((("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Title/Abstract) OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word]))) OR ((("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word]))	
40	**#9 or #14 or #39** **Executed as:** ((((((((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND ((((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR ((((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))))))) OR ((((((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract]))) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))))) OR ((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR ((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract])))) OR ((((((((((((((((((((((((((((((EZ clean[Text Word]) OR E-Z clean[Text Word]) OR "E Z clean"[Text Word]))) OR (((((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word])))) OR (("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word])))))) OR ((("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word]))) OR (((((((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR	4,505

	"stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word]))) OR (("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word]))) OR "leris"[Text Word]) OR laparoscopic electrode reusable indicator[Text Word]) OR (("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word]))) OR (("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word])) OR ((megatip*[Text Word]) OR "mega tip"[Text Word]) OR mega-tip*[Text Word])) OR (("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word]))) OR (("lletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word]))) OR (("lletz"[Text Word]) AND "leep"[Text Word])) OR (("large loop excision"[Text Word] OR "large loop excisions"[Text Word]))) OR (("all in one"[Text Word] OR "aio"[Text Word])) AND (("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word]))) OR ((mega-power*[Text Word]) OR Mega Power*[Text Word])) OR (("megasoft"[Text Word]) OR mega soft*[Text Word]) AND ("electrode"[Text Word] OR "electrodes"[Text Word]))) OR (("mega 2000"[Text Word]) OR mega2000[Text Word])) OR (("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word])) AND "patient return"[Text Word])) OR (("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word])) AND "disposable"[Text Word])) OR ((re cordable[Text Word]) OR re-cordable[Text Word])) OR (("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Title/Abstract) OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word])) OR (("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word]))) and ("2017/11/01"[Date - Publication] : "3000"[Date - Publication]) NOT medline[sb]	
41	#40 and ("2017/11/01"[Date - Publication] : "3000"[Date - Publication]) NOT medline[sb]	**376**

Within the above search sets, results from set 41 were exported to QUOSA.

GOOGLE SCHOLAR- This search was run on October 12th, 2018.

#	SEARCH STATEMENT	RESULTS
1	With **all** of the word(s): megadyne With **at least one** of the words: diathermy or electrosurgery or electrosurgical or electrocautery or electrocauterization or electrocauterisation or medical or electrode or electrodes or cauterization or cauterisation or cautery or monopolar Return articles **dated** between: 2017-2019	**29**

Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts were removed. The remaining 15 results were added to the final search results.

QUOSA- 1,714 documents from the Ovid and PubMed search results were exported to QUOSA, which automatically de-duplicated resulting in 1,312 documents. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results
1	Megadyne*	**2**
2	"EZ clean" OR "EZ cleanTM"	**0**
3	"E-Z clean" OR "E-Z cleanTM" OR "E Z clean" OR "E Z cleanTM"	**0**
4	"ssteel pencil"~3 OR "ssteel pencils"~3 OR "ssteel pencilTM"~3	**0**
5	"s steel pencil" OR "s steel pencils" OR "s steel pencilTM"	**0**
6	"ace blade"~3 OR "ace blades"~3 OR "acetm blade"~2	**0**
7	Leris OR lerisTM	**0**
8	"laparoscopic indicator"~3	**0**
9	megatip* OR "mega tip" OR "mega tipTM" OR mega-tip OR mega-tipTM	**0**
10	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	**0**
11	mega-power* OR Mega Power* OR "mega power"	**1**
12	(megasoft* OR "mega soft" OR "mega softTM") AND electrode*	**1**
13	"mega 2000" OR "mega 2000tm" OR mega2000*	**0**
14	"re cordable" OR re-cordable* OR "re cordableTM"	**0**
15	megavac* OR "mega vac" OR "mega vacTM" OR mega-vac*	**0**
16	ultravac* OR "ultra vac" OR "ultra vacTM" OR ultra-vac*	**0**
17	attachavac* OR "attacha vac" OR "attacha vacTM" OR attacha-vac*	**0**
18	"zip pen" OR "zip pens" OR "zip penTM" OR zip-pen*	**1**

After deduplication, there were 3 results from sets 1-18 above. These items were combined with the 15 Google Scholar results as noted above, resulting in 16 results. These were de-duplicated against the previous search (CER December 2017), resulting in 13 results for review.

9.1.3. Search 3

Megadyne CER – Literature Search Results

Product: Megadyne Products and Accessories
Ref: Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1.
Date Search run: September 3, 2019
Contains: 7 documents,
Databases: Embase/Medline in OVID, PubMed, Google Scholar
Search Date Limitation: October 1, 2018 to present (August 30, 2019)

Search Strategy:
EMBASE/MEDLINE in OVID:
Embase 1980 to 2018 August 30
Ovid MEDLINE(R) 1946 to August Week 5 2018
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 30, 2018
Ovid MEDLINE(R) Daily Update August 30, 2018
Ovid MEDLINE(R) Epub Ahead of Print August 30, 2018

Embase, Ovid MEDLINE(R)		
#	**Search Statement**	**Results**
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	43066
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	46241
3	1 or 2	57645
4	Surgical Instruments/ or surgical equipment/	41430
5	exp Electrodes/	240203
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	259
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	2472733
8	4 or 5 or 6 or 7	2543230
9	3 and 8	14029
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	7122
11	electrosurgical knife/	436

12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1102
14	((smoke or fluid?) adj3 (evacuat* or remov*)).mp.	6521
15	or/10-14	15122
16	megadyne*.mp.	16
17	("EZ clean*" or "E-Z clean*" or "E Z clean*").mp.	4
18	("stainless steel" adj5 (ball? or electrode*)).mp.	1496
19	("reusable stainless steel" and "indicator shaft").mp.	0
20	((ssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	1
21	"ace blade?".mp.	2
22	LERIS.mp.	43
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	30
25	(("ez clean*" or "e-z clean*" or "e z clean*") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	77
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*)).mp.	4
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	60
30	(LLETZ and LEEP).mp.	70
31	(large adj loop adj excision?).mp.	863
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*)).mp.	21
33	("mega power*" or mega-power* or Mega Power*).mp.	4
34	((megasoft* or mega-soft* or "mega soft*") and electrode*).mp.	1
35	("Mega 2000*" or Mega-2000* or Mega2000*).mp.	7
36	"disposable patient return electrode*".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac* or Mega-Vac* or "Mega Vac*" or UltraVac* or Ultra-Vac* or "Ultra Vac*" or AttachaVac* or Attacha-Vac* or "Attacha Vac*").mp.	16
39	(ZIP-pen* or "ZIP Pen*").mp.	0

40	or/16-39	2624
41	9 or 15 or 40	27272
42	limit 41 to yr="2017 -Current"	3498
43	limit 42 to ed=20181001-20190830 use medall [Limit not valid in Embase; records were retained]	396
44	limit 42 to dc=20181001-20190830 use emefd	885
45	limit 42 to dd=20181001-20190830 use emefd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	344
46	limit 42 to rd=20181001-20190830 use emefd	784
47	limit 42 to up=20181001-20190830 use medp	53
48	limit 42 to dt=20181001-20190830 use prem [Limit not valid in Embase; records were retained]	160
49	limit 42 to dt=20181001-20190830 use prem1 [Limit not valid in Embase; records were retained]	0
50	limit 42 to dt=20181001-20190830 use prem2 [Limit not valid in Embase; records were retained]	12
51	43 or 44 or 45 or 46 or 47 or 48 or 49 or 50	1745
52	remove duplicates from 51	**1379**

***Within the above search sets, results from set 52 were exported to QUOSA*.**

PUBMED *Search performed September 3, 2019*

#	Searches	Results
1	electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]	16271
2	electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]	317
3	**1 or 2**	16468

	Executed as: (electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]) OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])	
4	surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]	4550
5	electrode[Title/Abstract] OR electrodes[Title/Abstract]	144832
6	(adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])	84
7	scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]	549378
8	**4 or 5 or 6 or 7** **Executed as:** (surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract]) OR ((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])	553481
9	**3 and 8** **Executed as:** (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]) OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]))) AND ((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract]) OR	2216

	((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	
10	"electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract]	442
11	"suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract]	238
12	smoke evacuat*[Title/Abstract]	112
13	"fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract]	901
14	**10 or 11 or 12 or 13** **Executed as:** ((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])) OR ("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])) OR smoke evacuat*[Title/Abstract]) OR ("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract])	1687

15	megadyne*[Text Word]	5
16	EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word]	26
17	"stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract]	393
18	"reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract])	0
19	("ssteel"[Title/Abstract] OR s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])	25
20	(ace{Title/Abstract] OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])	14
21	leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]	2
22	laparoscopic electrode reusable indicator[Title/Abstract]	0
23	"electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract]	12
24	"button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract]	20
25	megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega tipR"[Text Word] OR "mega tipTRADE"[Text Word]	1
26	"indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])	83
27	"lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	271
28	"lletz"[Title/Abstract] AND "leep"[Title/Abstract]	27
29	"large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract]	363
30	("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	50
31	mega-power*[Text Word] OR Mega Power*[Text Word]	0
32	(megasoft*[Text Word] OR "mega soft"[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	0
33	"mega 2000"[Text Word] OR mega2000*[Text Word]	3
34	("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract]	0

35	("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract]	0
36	re cordable*[Title/Abstract] OR re-cordable*[Title/Abstract]	0
37	megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word)	360
38	zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word]	0
39	**15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38** **Executed as:** ((((((((((((((((((((((megadyne*[Text Word]) OR (EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word])) OR ("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])) OR ("reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract]))) OR (("ssteel"[Title/Abstract] OR s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract]))) OR (ace{Title/Abstract] OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract]))) OR leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]) OR ("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])) OR ("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])) OR (megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega tipR"[Text Word] OR "mega tipTRADE"[Text Word])) OR ("indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract]))) OR ("lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR ("lletz"[Title/Abstract] AND "leep"[Title/Abstract])) OR ("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])) OR (("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (mega-power*[Text Word] OR Mega Power*[Text Word])) OR (megasoft*[Text Word] OR mega soft*[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR ("mega 2000"[Text Word] OR mega2000*[Text Word])) OR (("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract])) OR (("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract])) OR (re cordable*[Title/Abstract] OR re-	779

	cordable*[Title/Abstract])) OR (megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word])) OR (zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word])	
40	**9 or 14 or 39** **Executed as:** ((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]) OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]))) AND ((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract]) OR ((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))) OR (((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])) OR ("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])) OR smoke evacuat*[Title/Abstract]) OR ("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract]))) OR ((((((((((((((((((((((megadyne*[Text Word]) OR (EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word])) OR ("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])) OR ("reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract]))) OR (("ssteel"[Title/Abstract] OR	4496

	s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract]))) OR (ace{Title/Abstract] OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract]))) OR leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]) OR ("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])) OR ("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])) OR (megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega tipR"[Text Word] OR "mega tipTRADE"[Text Word])) OR ("indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract]))) OR ("lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR ("lletz"[Title/Abstract] AND "leep"[Title/Abstract])) OR ("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])) OR (("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (mega-power*[Text Word] OR Mega Power*[Text Word])) OR (megasoft*[Text Word] OR mega soft*[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR ("mega 2000"[Text Word] OR mega2000*[Text Word])) OR (("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract])) OR (("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract])) OR (re cordable*[Title/Abstract] OR re-cordable*[Title/Abstract])) OR (megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word])) OR (zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word]))	
41	**#40 AND ("2018/10/01"[Date - Publication] : "2019/08/30"[Date - Publication])**	272
42	**#41 NOT medline (sb)**	**196**

***Within the above search sets, results from set 42 were exported to QUOSA*.**

GOOGLE SCHOLAR: *Search performed on September 4, 2019*

#	SEARCH STATEMENTS	RESULTS
1	With **all** of the word(s): megadyne With **at least one** of the words: diathermy electrosurgery electrosurgical electrocautery electrocauterization electrocauterisation medical electrode cauterization cauterisation cautery monopolar Return articles **dated** between: 2018 - 2020	**24**

Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts were removed. The remaining 8 results were added to the final search results.

QUOSA: 1575 documents from the Ovid and PubMed search results were exported to QUOSA, which automatically de-duplicated resulting in 1433 documents. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results
1	Megadyne*	**3**
2	"EZ clean" OR "E-Z clean" OR "E Z clean"	**0**
3	"EZ cleanTM" OR "E-Z cleanTM" OR "E Z cleanTM"	**0**
4	"EZ cleanR" OR "E-Z cleanR" OR "E Z cleanR"	**0**
5	"ssteel pencil"~3 OR "ssteel pencils"~3	**0**
6	"ssteel pencilTM"~3 OR "ssteel pencilR"~3	**0**
7	"s steel pencil" OR "s steel pencils"	**0**
8	"s steel pencilTM" OR "s steel pencilR"	**0**
9	"ace blade"~3 OR "ace blades"~3	**0**
10	"aceTM blade"~2 OR "aceR blade"~2	**0**
11	"aceTM blades"~2 OR "aceR blades"~2	**0**
12	Leris*	**0**
13	"laparoscopic indicator"~3 OR "laparoscopic indicators"~3	**0**
14	megatip* OR mega-tip* OR "mega tip"	**1**
15	"mega tipTM" OR "mega tipR"	**0**
16	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	**0**
17	mega-power* OR Mega Power* OR "mega power"	**0**
18	"mega powerTM" OR "mega powerR"	**0**
19	(megasoft* OR "mega soft") AND electrode*	**1**
20	("mega softR" OR "mega softTM") AND electrode*	**0**
21	mega2000* OR "mega 2000"	**0**
22	"mega 2000TM" OR "mega 2000R"	**0**
23	re-cordable* OR "re cordable"	**0**
24	"re cordableTM" OR "re cordableR"	**0**
25	megavac* OR mega-vac* OR "mega vac"	**0**
26	"mega vacTM" OR "mega vacR"	**0**
27	ultravac* OR ultra-vac* OR "ultra vac"	**3**
28	"ultra vacTM" OR "ultra vacR"	**0**
29	attachavac* OR attacha-vac* OR "attacha vac"	**0**

30	"attacha vacTM" OR "attacha vacR"	**0**
31	zip-pen* OR "zip pen" OR "zip pens"	**0**
32	"zip penTM" OR "zip penR"	**0**

After deduplication, there were 7 results from sets 1-32 above. These items were combined with the 8 Google Scholar results as noted above, resulting in 13 unique results. These were de-duplicated against the previous search (October 2018), resulting in 7 results for review.

9.2. Bibliography

9.2.1. SOA & General Articles

9.2.2. SOA Included Articles

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9.3. Abbreviations

Abbreviation	Definition
BSE	Biological Safety Evaluation
CAPA	Corrective and Preventative Action
CER	Clinical Evaluation Report
CMR	Customer Marketing Requirements
CV	Curriculum Vitae
DOI	Declaration of Interest
DCRM	Design & Clinical Risk Management
dFMEA	Design Failure Modes and Effects Analysis
ESU	Electrosurgical Unit
PMCF	Post-Market Clinical Follow-up
PMS	Post-Market Experience and Surveillance
RBA	Risk Benefit Analysis
RMR	Risk Management Report
SOA	State of the art

9.4. CER Team

Role	Name
Medical Affairs Evaluator	Giovanni A. Tommaselli
Regulatory Affairs Evaluator	Emily Nesbitt
Medical Operations Evaluator	Karl Reese
Post Market Surveillance	Katie Seppa / Shenelle Johnson
Clinical Research	Jason Waggoner / Jamie Connelly
Risk Management / Quality	Tom Bosticco / Scot Harris
R&D / Product Development	Brian Bertke / Tyler Brehm / Mark Glassett
Other	N/A

9.5. CV Of Medical Affairs (MA) Evaluator

CURRICULUM VITAE

Dr. Giovanni A. Tommaselli

General Information

Last name:	TOMMASELLI
First name:	GIOVANNI ANTONIO
Place and date of birth:	Naples, December 29th, 1966
Citizenship:	Italian
Work address:	Johnson & Johnson s.p.a. Via del Mare, 56 00071 Pratica di Mare (RM), Italy Phone: +39 06 9114322 Fax: +39 6 91194290 Email: gtommase@its.jnj.com

Current Position (May 2017-Present)

Medical Director, Lifecycle Management – Ethicon, a Johnson & Johnson Medical Devices Company

- Provide medical leadership to cross functional CER teams and help with CER strategy development
- Responsible for medical input to transition of CER to MEDDEV rev. 4 and MDR
- Participate in the evaluation of PMS data and PMCF studies needs

- Provide consultation to Shared Services in support of literature review, analysis and conclusions for Clinical Evaluation Reports (CER).
- Reviews identified harms from literature in comparison to harms identified in Risk Management documents to ensure they are adequately captured.
- Provide medical input during the writing, review and approval of CERs
- Assists in preparation of periodic safety reports for assigned products.
- Assist in the creation and approval of SSCPs (Summary of Safety and Clinical Performance)
- Additional responsibilities, dependent upon need in the franchise and current workload:
    - May provide medical oversight of publication strategy for selected marketed products in close collaboration with the Franchise Medical Affairs team
    - May contribute to value dossiers for marketed products
    - May provide strategic Medical support for operating companies with no dedicated medical affairs personnel (and as requested for those companies with franchise medical teams)
    - May provide medical insight and overview in writing responses to Medical Information Requests from HCPs and non-HCPs as well as manage responses to Patients' requests.
    - May provide support to Business Leaders by providing medical and scientific expertise to help drive optimal business strategic direction, including product launches, key scientific meetings, relationship management with leading research physicians a, critical evaluation of current literature and competitive activity, and in other domains where medical and scientific expertise is required
    - May assist medical evidence generation leaders in Preclinical Research, Clinical Development, Regulatory, Quality, and Health Economics and Reimbursement to develop and execute global strategies for evidence generation for new and existing products in order to support regulatory approval/clearance, health technology assessment, customer access, medical safety and post-marketing support
    - Medical Leader participating in Governance Forums, e.g. Portfolio Management Teams
    - Internal medical consultant providing expert medical support to Professional Education, Communications, Legal/HCC, HR Communications
    - Function as Medical Affairs member in the team for new product development in the space of Wound Closure

Previous Positions

<u>Country Medical Director, Italy – Johnson & Johnson Medical Devices (2016-2017)</u>

- Member of the Country Board of Directors for Johnson & Johnson Medical Devices and advise on issues of medical, scientific and ethical nature to the Board.
- Manage and provide strategic direction as the MA function in the country. I create and implement Medical functional strategies integral to an aligned corporate vision and company strategic

framework, creating maximum opportunity in local markets, ensuring synergies with the JnJ corporate entity and adherence to global, regional and local operating instructions.

- Support Country/Regional Business Leaders by providing medical and scientific expertise to drive business strategic direction (product launches, scientific meetings, relationship management with research physicians and medical delivery system or government decision makers, critical evaluation of current literature and competitive activity).
- Senior Medical Leader, building relationships externally with key customers and stakeholders to anticipate industry trends, understand clinical/medical insights, unmet medical needs and global standards of care.
- Ensure that scientific data provided locally to HCPs/Authorities/Regulators is fair, balanced and compliant.
- Contributor and reviewer/approver of medical, promotional, market access and other informational material for country/region consumption.
- Internal medical consultant for medical support to Professional Education, Communications, Legal/HCC, Finance, and HR Communications & Investor Relations.
- Country/regional partner with medical evidence generation leaders in R&D, Clinical Development, Regulatory, Quality, and Health Economics and Reimbursement to develop and execute strategies for evidence generation to support regulatory approval/clearance, health technology assessment, customer access, medical safety and post-marketing support.
- At a country and local level, responsible for supporting the entire portfolio. Regionally I can give Medical support of areas of surgical expertise if appropriate.
- Responsible to answer to Medical Information Requests and Patients' questions on all Johnson and Johnson Medical Devices portfolio (surgery, general orthopaedics and other specialized surgery) based upon Franchise input.

<u>Consultant in Obstetrics and Gynecology – Department of Obstetrics, Gynecology and Urology - University Hospital "Federico II", Naples – Italy (2007-2016)</u>

- Main field of interest: pathophysiology of reproduction and contraception, postmenopausal osteoporosis, management of female pelvic floor disorders, and correlations between body weight and reproduction.
- In November 2013, National Scientific Qualification as University Associate Professor.
- Planning, conduction and analysis, in collaboration with peers and trainees, of clinical research studies in the fields of pathophysiology of reproduction, contraception, gynaecological endocrinology and urogynecology.
    - I have gained in-depth experience in designing, executing and reporting randomized control trials, prospective and retrospective cohort studies, systematic reviews and meta-analysis.

  - As a study coordinator of a number of multicenter studies, I gained knowledge in the preparation and submission of protocols to Regulatory Bodies, and relationship with Sponsors, CROs, and cooperating centers.
  - Knowledgeable in the execution of statistical analysis (sample-size and power calculation, distribution analysis, use of parametric and non-parametric tests, univariate and multivariate analysis and survival analysis).
- Responsible for the urogynecology service at the Department of Obstetrics and Gynaecology, University Hospital of Naples “Federico II”.
  - I introduced a dedicated urogynaecology outpatient clinic with a dedicated patient questionnaire/history sheet and diagnostics (urodynamics, perineal ultrasonography). I also introduced a "Combined Urology/Urogynaecology/Proctologic Clinic", in cooperation with peers from Urology and General Surgery.
  - I assess and manage primary and complicated cases of urinary incontinence and pelvic organ prolapse. I am able to perform urodynamic investigations, perineal ultrasonography, and cystoscopy.
- Clinical management of the inpatient care of obstetrics and gynaecological patients and of critical care of obstetric E.R. patients.
  - As the senior on-call doctor of the staff on shift, I coordinate the activities of the obstetric E.R. of our Institution, which is a tertiary referral center for obstetric conditions, and directly manage the most critical cases. This activity allowed me to develop skills in coordinating and conducting a team and a strong sense of priorities.
- Reference surgeon for pelvic floor defects at my Institution.
  - I am in charge of executing the majority of urogynecological procedures at my Institution. I am proficient in performing procedures for the treatment of stress urinary incontinence and pelvic organ prolapse, with or without the use of synthetic material.
- Tutor for resident trainees in gynaecologic and obstetric ultrasonography, obstetrics, and urogynecology (both diagnostic and surgery).
- Tutor for peers in learning or improving new surgical urogynecological procedures.
  - I have experience as a demonstrating surgeon for Ethicon, both at my Institution and as a traveling doctor.
- Trainer for the sale forces of Ethicon Women’s Health and Urology – EMEA.
  - I have worked with Ethicon’s sale force training (lectures, on-line seminars, development of multimedia applications). This activity gave me the opportunity to gain an in-depth knowledge of the needs of a device company in combining medical information and marketing.
- Consultant for Ethicon in the fields of Urogynecology and Obstetrics – EMEA
  - I have acted as consultant for Ethicon since 2013, performing a number of activities such as lectures, webinars, literature searches, expert meetings, advisory boards, and technical advice. My role as a physician consultant to a large healthcare company as Johnson and Johnson has

allowed me to build corporate relationships at multiple levels in the organization as well as establishing strong relationship with key opinion leader treating women's health conditions throughout Europe.

- Consultant for Solace Therapeutics, Inc. in the field of Urogynecology.
  - I have acted as consultant for Solace since 2012 as a study coordinator, supervisor of the development of the protocol, its submission and approval by the Ethical Committees and its application in the Italian Centers, translator (protocols, device instruction for use, informed consents and patient materials), and trainer. Being in close contact with the managers of the company, I was able to come in contact with business and scientific strategies of device-developing companies.
- Co-creator of a web-based nationwide urogynecological database for the Italian Association for Urogynecology (AIUG).
- Freelance translator from English to Italian (medical textbooks, device instruction for use, protocols, physician contracts).

Clinical Fellow in the area of Pathophysiology of Reproduction and Contraception at the Department of Obstetrics and Gynaecology, University Hospital of Naples "Federico II", Italy (2001-2007)

Professional Experience

Clinical Experience: My main research interests have been gynaecological endocrinology and urogynecology. In particular I earned notable experience in the management of postmenopausal issues, including hormonal replacement therapy strategies and the prevention of postmenopausal osteoporosis. I have been mainly involved in the field of urogynecologic complaints, particularly prevalent in postmenopausal women. I possess specific surgical skills in urogynecological procedures, in particular surgical treatment of urinary incontinence and pelvic organ prolapse using prosthetic implants (vaginal meshes, sacrocolpopexy and sacrohysteropexy with mesh using tackers/straps for fixation, sacro-spinous ligament fixation using sutures and automated stich passers).

I have acted as a tutor during ProfEd activities of Ethicon Women's Health and Urology helping peers to learn or improve new surgical procedures, and as a trainer for various international sales forces. In the past several years, I have developed in depth knowledge in other aspects of gynaecological endocrinology, such physiopathology of reproduction, contraception and, to certain extent, infertility. This experience contributed to my skills in conducting endoscopic surgical procedures.

Another aspect of my clinical experience has been the development of diagnostic skills in obstetrics and gynecology, mainly using ultrasonography. In 2013 I participated as a member of an advisory board to determine the best evidence-based practices in abdominal closure during caesarean section as a consultant for Ethicon.

Research Experience: I began my research studying the endocrinology of reproduction, specifically the role of peptides (such as CRF, GnRH, inhibins and activin) in pregnancy and delivery. As part of my PhD research program, I investigated the relationship between body weight homeostasis and reproductive function, stressing the role of leptin, ghrelin and NPY and NPY receptors on reproduction in rodent models (mice and rats) and the actions of these cytokines on reproductive function in humans. Paralleling my clinical interests on postmenopausal issues, I have participated in research focused on the endocrinology of the menopause, contraception and bone metabolism.

During the course of this research, I participated in several national research projects on: gestational potentiality, physiopathology of reproduction, the role of chemical brain mediator on the control of somatic and visceral response during development, functions of leptin and its modulation on hormonal control mechanisms, endometriosis and cytokines, new molecules involved in the physiopathology of gestation, evaluation of cytokine production from eutopic and eterotopic endometrium in patients affected by endometriosis.

As a consequence of my interest in the different aspects of menopause, I got involved in the urogynecological field. I am now researching the efficacy and safety of new devices for the surgical treatment of female urinary incontinence and pelvic organ prolapse and perineal ultrasonographic evaluation of pelvic prostheses. I also promoted, coordinated and acted as the main researcher of international and national multicenter studies (in the field of surgical management of stress urinary incontinence and surgical wound closure).

I have experience in conceiving, planning, implementation and data evaluation of both experimental studies and clinical trial with different designs (observational, cross-sectional, controlled randomized, longitudinal, case-control, retrospective, systematic review).

Through my various research and consulting roles with numerous pharmaceutical and device manufacturers I have developed a strong understanding of the need for technology in medicine and the role of research to support technological advances to improve patient care. I believe strongly in the collaboration of industry and medicine and have developed unique skills at bridging the gap between industry, researchers and physician caregivers.

Industry Experience: In the position of Country Medical Director, I acquired direct experience in working in a matrix environment, providing Medical Affairs strategic support both internally and externally. In particular, I earned experience in managing KOLs, engaging them in clinical studies, evaluating centers and involving them in multiple projects. I presented at different national congresses, in particular on infection prevention, evidence on the effectiveness of antimicrobial suture and the role of advanced energy in surgery. I moderated a number of advisory boards on liver surgery, blood loss management strategies and evidence on topical anti-hemorragic agents. Also, I acted as point of first contact for external stakeholders for proposal for Investigator Initiated Studies and Medical Information Requests.

Internally, my role allowed me to interact with most of the local functions of the industry, such as marketing, regulatory, quality, legal, finance and the commercial organization. I organized and released training to marketing and salesforces, in particular on clinical studies design and interpretation. Acting as the medical function in a multidisciplinary team, I provided evidence strategy appraisal for tenders and evidence strategy needs for the Country, as well as evaluating and approving external-facing materials through the local copy review and approval process.

In my present position of Medical Director for Life Cycle Management for Ethicon, I have the opportunity to closely work with other global function such as Regulatory, Global Strategic Marketing, Quality, R&D and others. I was involved in a number of projects, including labelling, risk management, production of position papers and many others. In particular, my main task is to provide medical leadership to cross functional CER teams and help with CER strategy development, provide consultation in support of literature review, analysis and conclusions for Clinical Evaluation Reports (CER). Finally, I provide medical input during the writing, review and approval of CERs and Medical Information Requests by HCPs and non-HCPs. I also have acquired experience in New Product Development involving different projects associated with wound closure and biosurgery.

Translation Experience

Translation from English of the Italian versions of:

- PA Potter, AG Perry: Fundamentals of Nursing – 6th edition for Idelson Gnocchi, Italy
- L White: Foundations of Nursing for Edises, Italy
- Various authors: Tecniche e procedure infermieristiche: Procedure ginecologiche e materno-infantili for Edises, Italy

Languages

Italian (native speaker), English (fluent and written), French (good)

PC Skills

Windows OSs, Windows Office, SPSS, Statistica for Windows, mobile OSs Symbian and Windows Mobile.

Education and Qualifications

2017-present	Medical Director Life Cycle Management – Ethicon
2016-2017	County Medical Director, Italy – Johnson & Johnson Medical Devices Italy
2013	National Scientific Qualification as University Associate Professor in Obstetrics and Gynecology by the National Ministry of University and Research.

2007-2016	Clinical Specialist in the areas of Pathophysiology of Reproduction and Contraception, Postmenopausal Osteoporosis, Management of Female Urinary Disturbances and Correlations between Body Weight and Reproduction, University Hospital of Naples "Federico II".
2006	Post-doctoral master in Statistics and Informatics in Health Sciences, University of Naples "Federico II"
2001-2007	Clinical fellowship in the area of Pathophysiology of Reproduction and Contraception, Department of Obstetrics and Gynecology, University Hospital of Naples "Federico II".
2001	PhD in Gynecological Endocrinology at the University of Naples "Federico II". Thesis: "Correlation between reproductive function and body weight regulation: leptin and its central mediators".
2000	PhD training in Gynecological Endocrinology at the Division of Growth and Reproduction Biology, Department of Pediatrics, School of Medicine, University of Geneva, Switzerland.
1997-2000	PhD training in Gynecological Endocrinology at the Department of Obstetrics and Gynecology, School of Medicine, University of Naples "Federico II".
1995	Certification in Obstetrics and Gynecology: final exam 70/70 *cum laude*. Thesis: "Treatment of luteal phase defect with purified FSH".
1991	Medical Degree "summa cum laude", School of Medicine "Federico II" of Naples. Thesis: "CRF mRNA expression in the placenta and gravidic decidua".

Scientific Publications

Total Impact Factor: 207,108; h-index: 29 (source: Google Scholar)

1) AFFINITO P., TOMMASELLI G.A., MORGERA R., RINALDI M., DI MAURO P., NAPPI C. [Continuous postmenopausal estrogen-progesterone therapy]. Minerva Ginecol. 1993 Mar;45(3):77-85. Italian.

2) AFFINITO P., TOMMASELLI G.A., DI CARLO C., GUIDA F., NAPPI C. Changes in bone mineral density and calcium metabolism in breast feeding women: a one year follow-up study J. Clin Endocrinol. Metab., 81, 2314-2318, 1996. **(5.605)**

3) GUIDA M., MORGERA R., TOMMASELLI G.A., DI DONATO S., NAPPI C. Underestimation of ovarian pathology: a review. J. Chemother. 9, 135-137, 1997. **(1.599)**

4) GUIDA M., TOMMASELLI G.A., PELLICANO M., PALOMBA S., NAPPI C. An overview of the effectiveness of natural family planning. Gynecol. Endocrinol. 11, 203-219, 1997. **(1.406)**

5) GUIDA M., PELLICANO M., MORGERA R., TOMMASELLI G.A., SAVARESE F., MELE A., NAPPI C. [Underestimation of ovarian pathology. Clinical aspects and medico-legal considerations]. Minerva Ginecol. 1998 Jan-Feb;50(1-2):43-9. Italian.

6) PALOMBA S., AFFINITO P., TOMMASELLI G.A., NAPPI C. A clinical trial of the effects of tibolone administered with gonadotropin-releasing hormone analogues for the treatment of uterine leiomyomata. Fertil. Steril., 70, 111-118, 1998.
(5.411)

7) PELLICANO M., ZULLO F., CIRILLO D., MERCORIO F., GUIDA M., SORRENTINO C., TOMMASELLI G.A., NAPPI C. Salpingectomy for ectopic pregnancy: a comparison between two endoscopic techniques. J Gynecol Surg. 14, 181-184, 1998.

8) GUIDA M., TOMMASELLI G.A., PALOMBA S., PELLICANO M., MOCCIA G.F., DI CARLO C., NAPPI C. Efficacy of methods for determining ovulation in a natural family planning program. Fertil. Steril. 72: 900-904, 1999.
(5.411)

9) DI CARLO C., TOMMASELLI G.A., PISANO G., NASTI A., ROSSI V., PALOMBA S., NAPPI C. Serum leptin levels in postmenopausal women: effects of transdermal hormone replacement therapy. Menopause 7: 36-41, 2000. **(2.942)**

10) TOMMASELLI G.A., GUIDA M., PALOMBA S., NAPPI C. Using complete breastfeeding and lactational amenorrhoea as birth spacing methods. Contraception, 61, 253-7, 2000. **(2.928)**

11) TOMMASELLI G.A., GUIDA M., PALOMBA S., PELLICANO M., NAPPI C. The importance of user-compliance on the effectiveness of natural family planning programmes. Gynecol. Endocrinol., 14, 81-9, 2000. **(1.406)**

12) PELLICANO M, ZULLO F, TOMMASELLI GA, NOLA B, CAPPIELLO F, CRISCUOLO A, NAPPI C. [Ovarian drilling in minilaroscopy and local anesthesia in the therapy of polycystic ovarian syndrome]. MINERVA GINECOL. 2000 JUL-AUG;52(7-8):275-81. Italian.

13) DI CARLO C., PALOMBA S., TOMMASELLI G.A., GUIDA M., DI SPIEZIO SARDO A., NAPPI C. Use of leuprolide acetate plus tibolone in the treatment of severe premestrual syndrome. Fertil. Steril. 75: 380-384,2001. **(5.411)**

14) TOMMASELLI G.A., PELLICANO M., ACUNZO G., FERRARA C., FELE A., DI SPIEZIO SARDO A, NAPPI C. [Effects of gonadotropins on oocyte maturation]. Minerva Ginecol. 2001 Oct;53(5):357-62. Italian.

15) TOMMASELLI G.A., DI CARLO C., PELLICANO M., NASTI A., FERRARA C., DI SPIEZIO SARDO A., NOLA B., NAPPI C. [Changes of leptin levels in menopause]. Minerva Ginecol. 2001 Jun;53(3):193-8. Italian.

16) PELLICANO M., ZULLO F., FIORENTINO A., TOMMASELLI G.A., PALOMBA S., NAPPI C. Consious sedation versus general anaesthesia for minilaparoscopic gamete intra-Fallopian transfer: a prospective randomized study. Human Reprod. 16, 2295-7, 2001. **(5.506)**

17) DI CARLO C., TOMMASELLI G.A., DE FILIPPO E., PISANO G., NASTI A., BIFULCO G., CONTALDO F., NAPPI C. Menstrual status and serum leptin levels in anorectic and menstruating women with very low body mass index. Fertil Steril, 78, 376-82, 2002. **(5.411)**

18) DI CARLO C., TOMMASELLI G.A., NAPPI C. Effects of sex steriods hormones and menopause on serum leptin levels. Gynecol Endocrinol, 16: 479-492, 2003. **(1.406)**

19) TOMMASELLI G.A., DI CARLO C., NASTI A., GIORDANO E., PISANO G., PELLICANO M., BIFULCO G., NAPPI C. Effects of bilateral ovariectomy and postoperative hormonal replacement therapy with 17β-estradiol or raloxifene on serum leptin levels. Menopause, 10, 160-4, 2003.
(2.942)

20) BIFULCO G., TRENCIA A., CARUSO M., TOMMASELLI G.A., MIELE C., DI CARLO C., BEGUINOT F., NAPPI C. Leptin induces mitogenic effects of human choriocarcinoma cell line (JAr) via MAP-kinase activation in a glucose dependent fashion. Placenta, 24, 385-91, 2003. **(2.773)**

21) NAPPI C, DI SPIEZIO SARDO A, ACUNZO G, BIFULCO G, TOMMASELLI GA, GUIDA M, DI CARLO C. Effects of a low-dose and ultra-low-dose combined oral contraceptive use on bone turnover and bone mineral density in young fertile women. A prospective controlled randomized study. Contraception, 67, 355-359, 2003.
(2.928)

22) ACUNZO G, GUIDA M, PELLICANO M, TOMMASELLI GA, DI SPIEZIO SARDO A, BIFULCO G, CIRILLO D, TAYLOR A NAPPI C. Effectiveness of auto-cross-linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic adhesiolysis: a prospective, randomized, controlled study. Hum Reprod, 18: 1-4, 2003.
(5.506)

23) PIGHETTI M., TOMMASELLI G.A., D'ELIA A., DI CARLO C., MARIANO A., DI CARLO A., NAPPI C. Maternal serum and cord blood leptin concentrations in intrauterine growth restricted pregnancies. Obstet Gynecol 102: 535-43, 2003.
(4.965)

24) AFFINITO P, DI SPIEZIO SARDO A, DI CARLO C, SAMMARTINO A, TOMMASELLI GA, BIFULCO G, LOFFREDO A, LOFFREDO M, NAPPI. Effects of hormone replacement therapy on ocular function in postmenopause. Menopause. 10: 482-487, 2003. **(2.942)**

25) TOMMASELLI G.A., DI CARLO C., BIFULCO G., DI SPIEZIO SARDO A., PELLICANO M., NAPPI C. Serum leptin levels in patients with premenstrual syndrome treated with GnRH analogs alone and in

association with tibolone. Clin Endocrinol 59: 716-722, 2003.
(2.897)

26) BIFULCO G, MIELE C, PELLICANO M, TRENCIA A, FERRAIOLI M, PATURZO F, TOMMASELLI GA, BEGUINOT F, NAPPI C. Molecular Mechanisms Involved In Gnrh Analogue-Related Apoptosis For Uterine Leiomyomas. Mol Hum Reprod 10: 43-8, 2004. **(3.396)**

27) DI CARLO C, TOMMASELLI GA, SAMMARTINO A, BIFULCO G, NASTI A, NAPPI C. Serum Leptin Levels And Body Composition In Postmenopausal Women: Effects Of Hormonal Replacement Therapy. Menopause. 11: 466-473, 2004. **(2.942)**

28) TOMMASELLI GA, PIGHETTI M, NASTI A, D'ELIA A, GUIDA M, DI CARLO C, BIFULCO G, NAPPI C. Serum Leptin Levels And Uterine Doppler Flow Velocimetry At 20 Weeks' Gestation As Markers For The Development Of Pre-Eclampsia. Gynecol Endocrinol 2004; 19: 160-165. **(1.406)**

29) NAPPI C, DI SPIEZIO SARDO A, GRECO E, TOMMASELLI GA, BIFULCO G, ACUNZO G, GUIDA M, GIORDANO E. Effects Of An Oral Contraceptive Containing Drospirenone On Bone Turnover And Bone Mineral Density. Obstet Gynecol 2005; 105: 53-60. **(4.965)**

30) PELLICANO, GUIDA M, BRAMANTE S, ACUNZO G, DI SPIEZIO SARDO A, TOMMASELLI GA, NAPPI C. Reproductive outcome after autocrosslinked hyaluronic acid gel application in infertile patients who underwent laparoscopic myomectomy. Fertil Steril 2005; 83: 498-500. **(5.411)**

31) GUIDA M, DI SPIEZIO SARDO A, BRAMANTE S, SPARICE S, ACUNZO G, TOMMASELLI GA, DI CARLO C, PELLICANO M, GRECO E, NAPPI C. Effects of two types of hormonal contraception--oral versus intravaginal—on the sexual life of women and their partners. Hum Reprod. 2005; 20: 1100-6. **(5.506)**

32) DI CARLO C, SAMMARTINO A, DI SPIEZIO SARDO A, TOMMASELLI GA, GUIDA M, MANDATO VD, D'ELIA A, NAPPI C. Bleeding patterns during continuous estradiol with different sequential progestogens therapy. Menopause. 2005; 12: 520-525.
(2.942)

33) MANDATO VD, SAMMARTINO A, DI CARLO C, TOMMASELLI GA, TAUCHMANOVA L, D'ELIA A, NAPPI C. Evaluation of skeletal status by quantitative ultrasonometry in postmenopausal women without known risk factors for osteoporosis. Gynecol Endocrinol. 2005; 21: 149-153.
(1.406)

34) TOMMASELLI GA, DI CARLO C, DI SPIEZIO SARDO A, BIFULCO G, CIRILLO D, GUIDA M, CAPASSO R, NAPPI C. Serum leptin levels and body composition in postmenopausal women treated with tibolone and raloxifene. Menopause, 2006, 13: 660-668. **(2.942)**

35) TOMMASELLI GA, DI SPIEZIO SARDO A, DI CARLO C, BIFULCO G, CERROTA G, GRECO E, CIRILLO D, NAPPI C. Do serum leptin levels have a role in the prediction of pregnancy outcome in the case of threatened miscarriage? Clin Endocrinol, 65, 772-775, 2006. **(2.897)**

36) SAMMARTINO A, TOMMASELLI GA, GARGANO V, DI CARLO C, ATTIANESE W, NAPPI C. Short-term effects of a combination of isoflavones, lignans and Cimicifuga racemosa on climacteric-related symptoms in postmenopausal women: A double-blind, randomized, placebo-controlled trial. Gynecol Endocrinol. 22, 646-650, 2006.
(1.406)

37) DI CARLO C, TOMMASELLI GA, GARGANO V, SAMMARTINO A, BIFULCO G, TAUCHMANOVA L, COLAO A, NAPPI C. Effects of estrogen plus progestin therapy on serum levels of RANKL, osteoprotegerin, osteocalcin, leptin and ghrelin in postmenopausal women. Menopause, 14: 38-44, 2007. **(2.942)**

38) DI CARLO C, TOMMASELLI GA, DI SPIEZIO SARDO A, SAMMARTINO A, ATTIANESE W, GARGANO V, BIFULCO G, NAPPI C. Longitudinal evaluation of serum leptin and bone mineral density in early postmenopausal women. Menopause, 14: 450-454, 2007. **(2.942)**

39) DI CARLO C, DI SPIEZIO SARDO A, BIFULCO G, TOMMASELLI GA, GUERRA G, RIPPA E, MANDATO VD, NAPPI C. Postmenopausal hypoestrogenism increases vasoconstrictor neuropeptides and decreases vasodilator neuropeptides content in arterial-wall autonomic terminations. Fertil Steril, 88: 95-99, 2007. **(5.411)**

40) PICCOLI R, MANDATO VD, LAVITOLA G, ACUNZO G, BIFULCO G, TOMMASELLI GA, ATTIANESE W, NAPPI C. Atypical squamous cells and low squamous intraepithelial lesions in postmenopausal women: Implications for management. Eur J Obstet Gynecol Reprod Biol. 140: 269-274, 2008. **(2.024)**

41) DI CARLO C, BONIFACIO M, TOMMASELLI GA, BIFULCO G, GUERRA G, NAPPI C. Metalloproteinases, vascular endothelial growth factor, and angiopoietin 1 and 2 in eutopic and ectopic endometrium. Fertil Steril. 91: 2315-23, 2009. **(5.411)**

42) NAPPI C, TOMMASELLI GA, MORRA I, MASSARO M, FORMISANO C, DI CARLO C. Efficacy and tolerability of oral bovine lactoferrin compared to ferrous sulphate in pregnant women with iron deficiency anemia: a prospective controlled randomized study. Acta Obstet Gynecol 88: 1031-5, 2009. **(2.741)**

43) DI CARLO C, TOMMASELLI GA, GARGANO V, SAVOIA F, BIFULCO G, NAPPI C. Transdermal estradiol and oral or vaginal natural progesterone: bleeding patterns. Climacteric 13: 442-446, 2010. **(2.533)**

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65) TOMMASELLI GA, DI CARLO C, FORMISANO C, FABOZZI A, NAPPI C. Effectiveness and safety of re-adjustable mid-urethral slings for the surgical treatment of female stress urinary incontinence: a systematic review and meta-analysis. 45th Annual Meeting of ICS, Montreal, October 6-9, 2015.

66) COSIMATO C, CIPULLO LM, TROISI J, TOMMASELLI GA, ORO RR, ZULLO F, ALTIERI V, GUIDA M. Ultrasonographic evaluation of urethrovesical junction mobility: correlation with type of delivery and stress urinary incontinence. 45th Annual Meeting of ICS, Montreal, October 6-9, 2015.

67) DE WACHTER S, WYNDAELE J, TOMMASELLI GA, ANGIOLI R, DE WILDT M, EVERAERT K, MICHIELSEN D, VAN KOEVERINGE G. A randomized, controlled clinical trial of an intravesical pressure-attenuation balloon system for the treatment of stress urinary incontinence in females. 45th Annual Meeting of ICS, Montreal, October 6-9, 2015.

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73) FORTIN SP, CHEN BP, PRACYK J, TOMMASELLI GA, ELANGOVANRAAJ N, JOHNSTON SS. Economic and clinical outcomes of spinal fusion surgeries with skin closure through skin staples plus waterproof wound dressing versus 2-octyl cyanoacrylate plus polymer tape. ISPOR 2020 May 16-20, 2020, Orlando, Florida

Books

1) NAPPI C., TOMMASELLI G.A. [Obstetrics and Gynecology]. Idelson Gnocchi, Naples, 2014. In Italian.

Book Chapters

1) GUIDA M., PELLICANO M., TOMMASELLI G.A., DIDONATO S., ACUNZO G., NAPPI C. [Parental function quality in families created by new reproductive techniques.]. In: [The shattered family.] Gindro S., ed. CIC Edizioni Internazionali, Roma, 1999. pp. 85-95. In Italian.

2) DI CARLO C., TOMMASELLI G.A., NAPPI C. Leptin levels in the menopause. In: Management of the menopause in the millenium. Studd J (ed.). Parthenon Publishing Group, Carnforth, UK. p. 277-286, 1999.

3) NAPPI C., PALOMBA S., TOMMASELLI G.A., AFFINITO P., SAMMARTINO A., ARIENZO M.P. [Menopause, hormonal replacement therapy adn leiomyomatosis.]. In: Perez-Lopez FM: [The climacteric and aging]. SEISGE, Zaragoza, 1999. pp. 143-158. In Spanish.

4) NAPPI C., TOLINO A., DI CARLO C., TOMMASELLI G.A. [Regulation of menstrual cycle]. In: [Obstetrics and Gynecology]. Nappi C. (ed.). Idelson Gnocchi, Naples, 2005. pp. 849-864. In Italian.

5) NAPPI C., PELLICANO M., TOMMASELLI G.A. [Female infertility]. In: [Ostetrics and Gynecology]. Nappi C. (ed.). Idelson Gnocchi, Naples, 2005. pp. 1099-1128. In Italian

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Editorial Experience

Reviewer of the peer-reviewed international journals Clinical Endocrinology, Journal of Postgraduate Medicine, Archives of Medical Research and Psychoneuroendocrinology, International Urogynecological Journal, European Journal of Obstetrics Gynecology and Reproductive Biology, Journal of Endocrinological Investigation, Journal of Urology.

Member of the scientific committee of the Italian version of the British Journal of Obstetrics and Gynecology (1995-2000).

Surgical Activity

Surgical procedures as first operator or assistant:

Obstetric Procedures:

Cesarean section 338

Episiorraphy 150

D & C 137

Suture of vaginal tear 47

Salpingectomy (ectopic pregnancy) 9

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Trachelorraphy 2

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Gynecological Procedures:

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- TVT-Secur 38
- Retropubic TVT 12
- Bulking agents' infiltration 5
- TVT-Abbrevo 6
- Sovrapubic TVT 2
- Burch's colposuspension 2

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Vaginal hysterectomy	55
Sacro-spinous ligament fixation	22
Vaginal mesh/sling removal	8
Cervical biopsy	4
Vaginal annessiectomy	3
Cervical polypectomy	3
Vaginal granulation tissue ablation	1
Posterior fornix suture (traumatic tear)	1
Endocervical curettage	1
Ovarian cyst vaginal ablation	1
Vaginal myomectomy	1
Drainage of ischio-rectal fossa abscess	1
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Drainage of Bartholini's gland abscess	1
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Abdominal oophorectomy 9

Tubal sterilization 3

Adhesiolysis 2

Subtotal hysterectomy 1

Myomectomy 1

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Omentectomy 1

[Laparoscopic Procedures]

Hysteroscopy 19

Sacrocolpopexy 10

Ovarian cyst ablation 2

Myomectomy 1

Adhesiolysis 1

References

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9.6. CV Of Regulatory Affairs (RA) Evaluator

Emily Nesbitt

Cincinnati, Ohio 45242

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Experience:

Ethicon, Johnson & Johnson. – Cincinnati, OH
Manager, Regulatory Affairs, 2014 to present
Regulatory Affairs Associate Senior, 2013 to 2014
Regulatory Affairs Associate II, 2010 to 2013
Regulatory Affairs Associate I, 2008 to 2010

- International registrations, medical device 510(k), IDE (Investigational Device Exemption), & all related supplements, amendments & submissions to gain & maintain global regulatory approval & clearance of new & modified products
- Assuring that product labels & labeling comply with U.S. & foreign government regulations
- Exhibiting a comprehensive expertise in U.S. & foreign government regulations regarding manufacture & distribution of medical devices & pharmaceutical products as an integral part of product development teams
- Developing regulatory strategies
- Interact directly and indirectly with US and Global regulatory authorities. Maintain compliance with future and existing regulation.
- Support New Product Development with regulatory determinations and strategy. Register new products to drive innovation, including: 510ks, Technical Files, and Design Dossiers. (device expertise in: energy-based surgical devices including monopolar and bipolar, software, mechanical surgical devices, minimally invasive procedures, gastrointestinal procedures and thoracic procedures)
- Interpret new government policies, regulations, and guidance's. Create and implement new procedures to address new policies, and train associates on new procedures.
- Develop business strategies in anticipation of new policies. Track trends of new regulations.
- Coordinate and provide strategy to regulatory affairs associates. Assist with regulatory activities that accelerate delivery of product to market. Gain and maintain global regulatory approval and clearance of new products. Prioritize regulatory submissions based on business needs and marketing priority.
- Maintain expertise in US & foreign government regulations regarding the manufacture and pre-market distribution of investigational devices.

- Support Product Life cycle efforts.
- Active participation in internal and external audits, including Notified Body Audits Quality System Audits. Active participation in audits with Notified Bodies for registrations and on-site Quality System Audits

Medpace, Inc. – Cincinnati, OH
Regulatory Submission Coordinator, December 2005 to 2008

- Prepared, filed and maintained components of US and international regulatory submissions in electronic format, including New Drug Applications (NDAs), Common Technical Documents (CTDs), and Investigational New Drug Applications (INDs), Annual Updates to FDA
- Wrote Investigator's Brochures, drug labels, and international Clinical Trial Applications for combination Drug/Device Products
- Reviewed documents to ensure they are compliant and adequate for regulatory filing purposes
- Collected and tracked documentation in accordance with country-specific requirements for Clinical Trial Applications
- Led and coordinated sponsor-initiated audits
- Used Microsoft Project for Project Management of regulatory submissions
- Wrote and reviewed Standard Operating Procedures (SOPs), developed Internal Review procedures and schedule

Medpace, Inc. – Cincinnati, OH

Project Management, Clinical Trials, Coordinator, April 2002 to December 2005

- Compiled and maintained project specific status reports
- Utilized and maintained project management databases
- Maintained site payment schedule
- Created and maintained project timelines
- Developed and implemented Recruitment Development Plans
- Independently interacted with the Sponsor study centers, other contractors, and internal team
- Ascertained required documents in compliance with Code of Federal Regulations and FDA Guidelines
- Composed and provided input on project related documents (data analysis plan, communication plan, final clinical study report, etc.)

BioReliance – Rockville, MD
Research Associate, Quality, September 2000 to April 2002

- Biologic manufacturing under cGMP for phase I/II clinical trials to support Biologics License Application (BLA). Manufactured investigational vaccines and gene therapies. Used tissue culture, virus seed stock production, viral purifications, aseptic final fill, and final product labeling in clean room suites, established Master Cell Banks and Working Cell Banks
- Maintained cGMP Certification and Aseptic Final Fill Certification
- Prepared for FDA audits by creating and updating company SOPs, ensuring work area was compliant, and worked with the QA department on batch records
- Served as a project team leader in virus purification and trained new associates
- Worked with Process Development on transfer of technology for virus purification

Procter & Gamble, Aerotek – Mason, OH
Clinical Laboratory Technician, April 1999 to January 2000, seasonal 1996 to 1999

Worked in microbiology and physical chemistry Research and Development laboratories to investigate efficacy using pre-clinical and bench studies

Sara Lee Corporation, Lab Support – Cincinnati, OH

Research Associate, January 1999 to March 1999

Worked with plant crews and Quality Assurance to assess potential sources of contamination on the manufacturing line

Education:

Ohio University
Bachelor of Science in Microbiology, Minor in Chemistry, 1998

Additional Information:

Regulatory Authority Professional Society Member (RAPS)

- Regulatory Affairs Certification RAC, RAPS RAC Committee Member

Operation Smile

- Team Leader, 2013

United Way Department Team Leader, 2010

- Led department to achieve the highest number of Community Care Hours within the company 100% Department participation.
- Led company-wide bone marrow screening event, The Gift of Life, which identified 2 matches for bone marrow transplant patients.

Parseghian Medical Research Foundation

- Committee Member, July 2005 to 2008

9.7. CV Of Medical Operations (MO) Evaluator

Title, First Name, Surname:	**Karl Reese**
Contact Information:	Karl S Reese 11 Peter Parley Rd, Unit C Boston, MA 02130 U.S.A. karl.s.reese@gmail.com +1-617-953-4644

Relevant work experience

From – To	Employer	Department/ Position	Responsibilities with respect to Products/ Technologies/Quality Management
Nov 2018 - Present	DePuy Orthopaedics Ethicon MA 325 Paramount Dr. Raynham, MA 02767 U.S.A.	Ethicon Medical Affairs / Medical Operations Shared Services / Director of Global Surgery & Robotics	**Director, Medical Operations (Global Surgery & Robotics)** ▪ Provide strategic oversight and governance ensuring high standards of compliance in Medical Operations functions charged with delivery of key regulatory and medical documents ▪ Lead a diverse Medical Operations team based in multiple geographies and ensure the identification and retention of high potential individuals through active engagement, motivation, development, and promotion ▪ Provide leadership and manage relationships through extensive interdependent partnering, benchmarking, leveraging of best practices, and forming strategic alliances with cross functional business partners to drive key business goals and objective ▪ Lead the strategic development of CER requirements/activities (appropriate routes of conformity, data requirements, etc.) in support of devices within the Global Surgery portfolio, including active devices and those devices containing software for OneMD ▪ Support and assist, as needed, across Medical Operations (MO) OneMD businesses regarding New Product Development (NPD) strategies ▪ Establish processes and procedures for CERs related to active devices for OneMD ▪ Provide training and support to the Medical Operations team and business partners across OneMD regarding CER requirements
Jul 2018 – Nov 2018	DePuy Orthopaedics Ethicon MA	Ethicon Medical Affairs / Medical	**Director of Robotics, Medical Operations** ▪ Central lead for Clinical Evaluation Reports (CERs) and related

	325 Paramount Dr. Raynham, MA 02767 U.S.A.	Operations Shared Services / Director of Robotics	activities for both Ethicon Endo-Surgery and Verb Surgical, including developing and co-developing strategies with Medical Affairs, Regulatory, R&D, Clinical Affairs and other cross-functional departments ▪ Responsibilities also include leading and developing CER strategies in support of active devices and those devices containing software for OneMD ▪ Additional responsibilities include supporting and assisting New Product Development (NPD) strategies for Active Devices and related training for Clinical Evaluation Reports, as needed, across OneMD businesses
May 2017 – Jul 2018	DePuy Orthopaedics Ethicon MA 325 Paramount Dr. Raynham, MA 02767 U.S.A.	Ethicon Medical Affairs / Medical Operations Shared Services / Senior Technical Manager	**Senior Technical Manager** ▪ Lead for Robotics Program Verb / Ethicon Endosurgery for Medical Operations activities including: ▪ Lead efforts to develop "Pre-CE Mark Submission Clinical Review" to be reviewed by TÜV ▪ Work directly with R&D to author R&D related portions of Pre-CE Mark Submission Clinical Review ▪ Support development of PMCF Plan for robotics system, components and devices ▪ Support and lead recurring meetings with Notified Bodies; meetings to provide opportunities for discussions and feedback around various robotic program topics with the goal of addressing concerns to increase likelihood of timely and successful CE Mark ▪ Support R&D test and report strategy and design as it relates to data required for CERs and Regulatory Submissions ▪ Execute Clinical Evaluation Report (CER) activities, planning and strategies related to the Robotics Program for Ethicon ▪ Central, OneMD contact for Clinical Evaluation Report (CER) technical reviews and audit strategy & support ▪ Supports implementation of regulatory policy including MDR and Rest of World (ROW) CER & clinical data requirements ▪ Supports R&D / New Product Development (NPD) strategy for EU and ROW CERs ▪ Central integration lead for acquisitions including CER strategy and integration ▪ Responsible for optimization & harmonization of CER processes to meet regulatory requirements ▪ Manage relationships & contracts for external vendors in support of execution strategies

			▪ Supports management of budget and key metrics ▪ Partners for strategy and policies with cross-functional Subject Matter Experts (SME) such as Medical Directors, Quality Engineering, R&D, Regulatory Affairs, Post Market Surveillance and Clinical Affairs
Dec 2014 – May 2017	Ethicon, Inc Route 22 West PO Box 151, Somerville, NJ 08876-0151 U.S.A.	Medical Affairs/Medical Operations / Senior Manager Medical Operations Shared Services, CERs	**Senior Manager, CERs** ▪ Central process owner for the Clinical Evaluation Report process across Global Surgery ▪ Responsible for the effective optimization and harmonization of CER processes within GS ▪ Manages CER processes and linkages within the Quality Systems and Regulatory Processes (e.g. Risk Management, PMS, etc.) ▪ Manages New Product Development, CFDA and RoW CER requirements and documents ▪ Acts as the CER liaison with respective Notified Bodies and regulatory agencies ▪ Develops strategies, policies and efficiencies within procedures and processes for current and future regulatory requirements ▪ Partners with cross-functional business SMEs such as Medical Directors, Post Market Surveillance, Design Quality Engineers, R&D, and Regulatory Affairs relating to CER processes and activities ▪ Manages timelines and project deliverables ▪ Manages the CER staff including project managers, technical and medical writers ▪ Manages the budget and schedule related to current and projected future CER activities
Jan 2011 - Dec 2014	Ethicon, Inc Route 22 West PO Box 151, Somerville, NJ 08876-0151 U.S.A.	Various Departments (Regulatory, R&D, Medical Affairs, Quality Engineering, Post Market Surveillance) / Medical Device Consultant (HR services provided by Kelly Temporary	**Regulatory Consultant** ▪ Consulting on various MDD related policies and procedures within RA ▪ Provided consulting & preparation for Rapid Transfer Initiative (RTI) to develop cross-functional processes & risk-based plan to bring all 119 Ethicon Dossiers / Technical Files (DD/TF) into compliance with applicable directives, standards & guidance ▪ Co-authored revision of Change Reporting Procedure for MDD and FDA ▪ Co-authored revision of Technical File / Design Dossier Procedure and Template for compliance to MDD and guidance. ▪ Assisted in conversion to fully electronic documentation and revision control, eliminating paper-based TF/DD

		Services) / Freelance Regulatory Affairs Manager	▪ Co-lead development of updated process for Class III Design Dossier renewals ▪ Provided regulatory expertise on 2003/32/EC (Animal Tissues Directive) and related standards for a bovine derived manufacturing processing aid to achieve Notified Body approval of a related Class III supplement ▪ Provided detailed review and edits for product CER prior to submission to Dutch Competent Authority
Jan 2011 – Present	Ethicon, Inc Route 22 West PO Box 151, Somerville, NJ 08876-0151 U.S.A.	(Continued from above)	**Regulatory Lead / Manager** ▪ Regulatory Team Lead and Co-Lead for remediation of 15 Tech Files and Dossiers ▪ Participated in teams as RA contact for remediation of multiple additional Tech Files and Dossiers (TF/DD) ▪ Lead or participated in training of new Regulatory Affairs hires and contract workers for TF/DD remediation project ▪ Conducted group training for various topics related to remediation of TF/DD, MDD & other guidance or standards **R&D/Product Development Consultant** ▪ Consulting on various R&D processes and procedures ▪ Consulted on development of requirements for Product Lifetime within Design Control Procedure ▪ Provided guidance on linking Design Control/New Product Development process and procedures to procedures within Clinical Affairs & Medical Affairs ▪ Consulted on Design Requirement Matrices for remediation of pre-design control, legacy products ▪ Consulted on electro-medical standards & testing for Cardiac Pacing Wires **Medical Affairs Consultant** ▪ Consulting on various clinical policies and procedures ▪ Providing detailed commentary & edits for each new product CER or CER revision for existing products ▪ Authored new Clinical Evaluation & Literature Search Procedures for compliance to 93/42/EEC (MDD) and guidance ▪ Consulted on establishing equivalence between devices for MDD certification
Jan 2011 – Present (Continued	Ethicon, Inc Route 22 West PO Box 151,	(Continued from above)	**Quality Engineering / Quality Systems Consultant** ▪ Consulting on various QE / QMS processes and procedures ▪ Provided support for revision of Risk Management Procedure,

from above)	Somerville, NJ 08876-0151 U.S.A.		including process flow and linkages to CER, PMS, TF/DD, and related during Rapid Transfer Initiative (RTI). ▪ Providing review and team support for Risk Management Reports and related subdocuments **Post Market Surveillance Consultant** ▪ Consulting on various PMS processes and procedures ▪ Provided support for development of new PMS Plans and Reports for compliance to MDD ▪ Provided guidance for development of surgeon and V.O.C. surveys as additional proactive PMS ▪ Consulted on PMCF requirements and procedure, including decision process and justifications for not conducting PMCF
Jan 2011 – Present	Mentor Worldwide LLC 201 Mentor Drive Santa Barbara, CA 93111 U.S.A.	Various Departments (Regulatory, R&D, Medical Affairs) / Medical Device Consultant (HR services provided by Kelly Temporary Services)	**Regulatory Consultant** ▪ Consulting support for Mentor during MHRA audit and resulting questions regarding breast implants (stemming from PIP recall) ▪ Consulting on requirements for Clinical Trials, Post Market Clinical Follow-up and analysis of clinical data per MDD, EN ISO 14155, MEDDEV 2.12/2 and MHRA Guidance Note 1. ▪ Support for revising Clinical Evaluation Procedure for compliance to MDD and MEDDEV 2.7.1 ▪ Support for determination of EU change reporting requirements ▪ General consulting support for regulatory team activities
Jan 2011 – Present	Johnson & Johnson Medical GmbH Robert-Koch-Strasse 1 Norderstedt, 22851, Germany	Various Departments (Regulatory, R&D, Quality Engineering) / Medical Device Consultant (HR services provided by Kelly Temporary Services)	**Regulatory Consultant** ▪ Consulting on various MDD related policies and procedures within RA, including compliance to animal tissue directive and standards ▪ Provided support for training of new RA hires ▪ Provided support for implementation of DD/TF Remediation activities to be led out of Norderstedt ▪ Developed process and outline for CAPA related to IFU deficiencies and Notified Body issued nonconformities
Jul 2011 – Sep 2011	Acclarent, Inc. 1525-B O'Brien Dr Menlo Park,	Regulatory Affairs / Medical Device Consultant (HR services	**Regulatory Consultant** ▪ Consulting in consideration of transferring Notified Bodies and support for Notified Body audits ▪ Provided training and support for specific topics, as needed and

	CA 94025 U.S.A.	provided by Kelly Temporary Services)	related to MDD & other guidance or standards
Dec 2010 – Jul 2011	K2M, Inc. 751 Miller Drive SE Leesburg, VA 20175 U.S.A.	Regulatory Affairs and General Compliance Consultant / Medical Device Consultant	**Regulatory Consultant** ▪ Consulting on various MDD related policies and procedures within RA ▪ Provided general consulting support on various activities related to compliance and preparation for government and external audits
Jun 2006 – Jan 2011	BSI Product Services	Technical Specialist and Scheme Manager / Orthopaedic Team and General Devices & New Technologies Team	(Additional Details to be Provided Upon Request) **Technical Specialist** ▪ Desk-top and on-site reviews of existing product Technical Audits and Dossier in support of continuation of CE Mark ▪ Desk-top and on-site review of new product Dossiers and Technical Files ▪ Review of significant change supplements ▪ New client orientation and transfer audits ▪ Assistant Orthopaedic Team Lead, including training of new hires and management support of existing team members ▪ Participation in and preparation of presentations on various topics for internal training ▪ Orthopaedic technical reviews of partial and total joints; absorbable, metallic and ceramic sports medicine implants; spinal implants; antilogous articular cartilage repair; Hyaluronic Acid based dermal fillers and joint lubricants; bone void fillers; etc. ▪ General Devices and New Technologies technical reviews of topical and antibacterial wound care; sutures; absorbable scaffolds for biologics; hernia and gynaecological mesh; non-electromedical aspects of thermal ablation, tissue morcellation and other devices; technical support for combination and animal tissue devices; etc.
Jun 2006 – Jan 2011 (Continued from above)	BSI Product Services	(Continued from above)	**Scheme Manager** ▪ Design Exam Certificate and Full Quality Assurance Certificate renewals ▪ Scheduling of audits and related activities ▪ Tracking of fees, payments, annual contracts and related ▪ Various other related activities

Apr 2004 – Jun 2006	Scandius Biomedical, Inc.	R&D Engineer with support for Quality Assurance and Regulatory Affairs	**R&D Functions** ▪ Designed Class III orthopedic implants and associated instrumentation; collaborating to successfully launch Scandius' first product line and all additional support instrumentation ▪ Generated design control documentation per FDA and ISO requirements including; product specifications, risk analysis, verification and validation protocols and reports, project schedule, 510(k) submission documents, and other documents necessary to complete the Device History File, as well as the Design Dossier ▪ Coordinated product testing internally and with contract facilities ▪ Worked with orthopedic surgeons to conduct cadaveric & market preference testing, and to attend surgeries **QA / RA Functions** ▪ Worked directly with Quality Assurance and Regulatory in small start-up environment to complete related activities including FDA and other agency submissions; led product complaint investigations, conducted and participated in internal audits, acted as design control liaison during external audits, ensured conformance to Product Development Protocol and all applicable internal and external standards
May 2003 - Apr 2004	BioValve Technologies, Inc.	R&D Engineer	• Developed novel single-use, disposable drug delivery devices for start-up company of approximately 25 employees • Conceived and developed technology for drug transfer device that was a key component in securing external partnership agreement • Wrote and maintained all phases of Device History File documentation • Machined prototypes using standard shop equipment: lathe, mill, band saw, grinding wheel, etc. • Collaborated with outside design firm & suppliers to procure machined and molded components for clinical studies
Mar 1999- May 2003	Mitek Products, Inc., a Johnson & Johnson Company	Associate R&D Engineer	▪ Directed cross-functional project teams from concept through to product launch ▪ Designed Class III medical device implants & associated instruments utilizing PRO-E ▪ Worked with molding engineers and materials scientists developing absorbable polymers into implantable devices ▪ Coordinated testing with contract facilities and orthopedic

			surgeons ▪ Facilitated team meetings and authored product life cycle documentation per FDA and ISO requirements ▪ Maintained project schedules and budgets ▪ Worked with patent attorneys to file and research IP ▪ Led divisional implementation and personnel training for a corporate "Design for the Environment" initiative
Aug 1996 – Mar 1999	Mitek Products, Inc., a Johnson & Johnson Company	Senior Engineering Technical Assistant	▪ Supervised and trained R&D technicians and temporary technicians ▪ Managed Development Lab which included equipment upgrades, lab layout, test scheduling, etc. ▪ Interacted directly with engineers, interdepartmental project teams, suppliers, and orthopedic surgeons to develop medical devices ▪ Led development of components/sub-assemblies within project teams ▪ Planned and implemented hands-on surgeon product evaluation labs, both internationally and domestically ▪ Continued to perform previous responsibilities of R&D Technician
Feb 1995 – Aug 1996	Mitek Products, Inc., a Johnson & Johnson Company	R&D Technician	▪ Established and defined newly created position of R&D Technician ▪ Led set-up of an R&D test lab which included equipment procurement, floor plan design, etc. ▪ Designed, developed, and implemented test methods and protocols which included simulated use and in vitro testing utilizing cadaver and animal models ▪ Performed all aspects of product and materials testing, including failure mode investigation ▪ Designed and machined basic test fixtures and devices using AutoCAD, PRO-E, and model shop equipment
Feb 1995 – Aug 1996	Mitek Products, Inc., a Johnson & Johnson Company	Quality Control Technician	▪ Inspected all product lines from incoming stock to final release ▪ Assisted in setup and supervision of new 2nd shift production group ▪ Processed and provided corrective actions for product complaints ▪ Performed internal Quality Audits per Standard Operating Procedures and FDA/ISO requirements ▪ Trained and supervised QC technicians ▪ Coordinated calibration and maintenance of all QC equipment
Feb 1990 –	Nova	Quality Control	▪ Provided training and guidance for QC technicians and

Feb 1992	Biomedical	Technician, Consumables Division	assemblers ▪ Responsible for in process and final inspection of prototype and released product ▪ Utilized precision inspection equipment including: Comparators, Coordinate measuring systems, Toolmaker's microscopes, etc.

Higher Education

College/University	Subject(s)	Degree/Qualification
Northeastern University, Boston, MA, USA	Mechanical Engineering	Bachelor of Science (Cum Laude) / Mechanical Engineering
Wentworth Institute of Technology	AutoCAD training.	Certificate for proficiency in AutoCAD design software.
Worcester Polytechnic Institute	Project Management and 12 related professional development courses; including "Project Management for Professionals", "Microsoft Project", Geometric Dimensioning and Tolerancing", etc.	Certificate in Project Management; 16.8 Continuing Education Credits (CEC).

Additional qualifications and training (especially quality management, conformity assessment according to EC directives 93/42/EEC, 90/385/EEC and 98/79/EC)

From – to	Training Organization	Title of Course	Qualification
1992-1995	American Society for Quality Control	Various ISO related training courses, including ISO 9000.	Training provided overview of ISO 9000 and other ISO Standards. Passed Exams.
1992-1995 (Continuous Quality Control Training)	Mitek, Inc., a J&J Co.	Training to Standard Operating Procedures (SOP) for conducting internal audits and supplier audits	Qualified to conduct internal and supplier audits per FDA/ISO requirements
1995-2003 (Various training sessions)	Mitek, Inc., a J&J Co.	Training to SOP for Risk Management per ISO 14971	Qualified to lead ISO 14971 based risk management team activities for product design and development.
June 1996 (2 Days)	MTS, Inc. On-site training by Senior Technician, Jay McHugh	Materials Test Machine Training; Testworks Software and Load Frame Training.	Proficiency in maintenance & operation of electromechanical test equipment.

April 1997 (4 Days)	Instron, Inc. Canton, MA	Materials Test Machine Training; Series IX and Wave Maker Software, and Load Frame Training.	Certified in Servo-hydraulic & Electromechanical materials testing proficiency.
April 23-24, 1998 (5 Days)	Rand Technologies	Pro/Engineer Basic II	Proficiency in using Pro/E 3-D modelling design software. Passed Exam.
Sept 1998 (2 Days)	Machine Shop Training by Pat Luongo	Machine Shop Training	Training toward proficiency in operating machine shop equipment as well as understanding applications in Medical Device manufacturing.
July 1999 (2 Days)	Alpine Analytics / Manugistics	Training for STATgraphics Plus	Certificate training for proficiency in the use of STATgraphics Plus for statistical analysis of results specific to medical devices industry. Passed Exam.
Feb 18-19, 1999 (14 Hours; 1.4 CEU)	Performance Training Associates, Inc	Industrial Electricity I & II	1.4 Continuing Education Units toward proficiency in electric circuits for manufacturing applications.
Oct 30 to Nov 3, 2000 (5 Days)	PTC Precision Learning	Fundamentals of Design	Training for techniques in designing and developing devices for manufacture. Passed Exam.
Feb 2002 (1 Day)	Johnson & Johnson	Medical Professionals Training	Operating Room Sterile Procedures and Conduct
Oct 2002 (4 Days)	Johnson & Johnson	ISO 140001 Environmental Management	Internal companywide leader for Environmental Management at Mitek, Inc.; Training conducted over 4 days at New Brunswick, NJ J&J Headquarters.
May 2003 (2 Days)	Advanced Design, Inc (ADI) Burlington, MA	Wildfire Design Software Training	Training in Wildfire 3-D modelling software from Parametric Technology Corp.
2004 to 2006 (Regular Continuous Training)	Scandius Biomedical, Inc	Training to Standard Operating Procedures for preparing Technical Documentation.	Qualified to prepare 510(k) per FDA and Technical Documentation per MDD requirements.
2004 to 2006 (Regular Continuous Training)	Scandius Biomedical, Inc.	Training to Standard Operating Procedures for conducting internal audits and participating in external audits.	Qualified to conduct internal audits per FDA/ISO requirements and to participate in external FDA/NB (MDD/ISO 13485) audits.
Jan 2005 (3 Days)	SolidVision, Inc	SolidWorks release 2005 training.	Training for SolidWorks 2005 3-D modelling design software.

June 2005 (2 Days)	Medical Design & Manufacturing (MD&M)	Medical Design & Manufacturing East Convention	Attended convention related to medical device manufacturing to speak with and learn about suppliers, design systems, rapid prototyping, and other medical device industry related areas.
November 2005 (4 Days)	Arthroscopy Association of North America (AANA)	Fall AANA Course	Attended symposia related to current orthopedic practices and conducted surgeon training on innovative ACL repair system via cadaver lab sessions.
March 2006 (4 Days)	American Academy of Orthopaedic Surgeons (AAOS)	Spring AAOS Meeting, Chicago, IL	Attended Instructional Courses, Lectures, Poster Sessions, and conducted Surgeon Skill Training toward innovative ACL repair system.
August 2006 (Four Days)	BSI Product Services	Whittlebury Hall, Towcester, UK Medical Device Technical Specialist Training	Training for BSi Healthcare Procedures; including auditing, reviewing, project management, CE certificates, etc.
September 18 - 21 2006 (4 Days)	BSI Management Systems Inc.	Medical Devices Directive (93/42/EEC)	MDD & application of CE Mark, assessment of clients against the QA modules of 93/42/EEC.
Oct. 2006 (2 hours)	Orthopaedic / Dental Team – Sunita Ahir	Artificial Knee Joints – history, design and failure modes.	Understanding of Level III Orthopaedic Standards.
Oct. 2006 (One Day)	Orthopaedic / Dental Team – Louise Jennings	University of Leeds – Wear Testing Lab.	Understanding of ISO 14242 (hips) and ISO 14243 (knees).
Jan. 2007 (½ Day)	Orthopaedic / Dental Team – Chris Brodrick	Metal, Ceramic and Plastic materials used in Orthopaedics.	Understanding of ISO and ASTM material standards.
Feb. 2007 (2 Hours)	Orthopaedic / Dental Team – Vicky Medley	Bone Cement, Cementing Techniques and Accessories.	Understanding and shortcomings of ISO 5833.
Mar. 2007 (½ Day)	Orthopaedic / Dental Team – Suzanne Halliday	2006 Annual Reports from Eight National Joint Registries.	Understanding of failure mechanisms of joint replacement implants.
May 2007 (2 Hours)	Orthopaedic / Dental Team – Gabriel Adusei	Dental Composite Materials.	Awareness of ISO4049:2000, ISO 11405:2003, ISO 14569-1:1999 and EN ISO 6874:2005
August 29, 2007 (5 Hours)	BSI Management Systems, Inc.; Tom Karman, Angie Combs	BSi Medical Devices Assessors Training	BSI Internal Training toward auditor proficiency updates to MDD updates to Risk Management, & several other auditor related concepts. Passed Exam.

September 10, 2007 (1.5 Days)	BSI Product Services, Healthcare; David Marshall, Andre Routh	EN ISO 14971:2007 Training	Training toward proficiency in Risk Management per EN ISO 14971:2007
September 12, 2007 (1 Day)	BSI Product Services, Healthcare; Jane Arnold-Round; Senior Regulatory Consultant	EN 12442 / ISO 22442 Training; Medical Devices Utilizing Animal Tissues	Training toward proficiency in Animal Tissue per EN ISO 10993
September 13, 2007 (1 Day)	BSI Product Services, Healthcare; Dr. John Lang DABT; Medwise International Consultancy Limited	EN ISO 10993 Workshop Training Biological Evaluation of Medical Devices	Training toward proficiency in biocompatibility per EN ISO 10993
September 14, 2007 (1/2 Day)	BSI John Worroll & John Howlett	MDD training	Training on auditing proficiency and other MDD requirements.
July 14th, 2008 (Four Days)	BSI Product Services	Robinson College, Cambridge, UK Medical Device Technical Specialist Training	Training for BSi Healthcare Procedures; including auditing, reviewing, project management, CE certificates, etc. Specialized topics; advanced therapy medicinal products, client scheme management, Mutual Recognition Agreements
January 25th, 2009 (1/2 Day)	BSI Product Services	Training for 2007/47/EC	Training for MDD amending directive 2007/47/EC
August 3rd, 2009 (Four Days)	BSI Product Services	Hatfield, UK Medical Device Technical Specialist and Scheme Manager Training	Training for BSi Healthcare Procedures; including auditing, reviewing, project management, CE certificates, etc. Specialized topics; biocompatibility & toxicity, clinical data & statistics, drug consultations, phthalates, software

August 20th, 2009 (2 hours)	BSI Product Services	Hong Kong CAB training	Training for Hong Kong Conformity Assessment Body (CAB) requirements
June 21st, 2010 (Four Days)	BSI Product Services	Moor Hall, Cookham, UK Medical Device Technical Specialist and Scheme Manager Training	Training for BSi Healthcare Procedures; including auditing, reviewing, project management, CE certificates, etc. Specialized topics; Asia/EMEA/ROW regulatory updates, active devices, IVD training, combination products, animal tissue training
December 14th, 2010 (3 Day)	Ethicon, Inc Regulatory Affairs	Regulatory Affairs Overview Training	Training on Ethicon devices and regulatory procedures
April 11th, 2011 (1 Day)	Mentor Worldwide, LLC	Regulatory Affairs Overview Training	Training on Mentor devices and regulatory procedures
September 28th, 2013 (Four Days)	Regulatory Affairs Professional Society (RAPS)	2013 RAPS Regulatory Convergence, Boston, MA, USA	Healthcare conference with lectures, workshops and exhibitors covering medical devices, pharmaceuticals and biologics.
December 14th, 2010 – Present	Johnson & Johnson	Compliance Wire Training	Healthcare compliance training, standards and operating procedures
September 18th, 2015	BSI Group	BSI Medical Devices Roadshow	Notified Body sponsored training on MDD requirements and medical device regulations framework
August 2nd, 2016	TÜV SÜD	TÜV SÜD Training Roadshow	Notified Body sponsored training on MDD requirements and future regulation changes; MEDDEV 2.7.1r4, MDR
Q1/Q2 2017	TÜV SÜD	TÜV SÜD / J&J MDR Meetings	Notified Body meetings face-to-face with J&J regarding MDR interpretations and requirements.
Q2 2017 / Q1 2018	BSI	BSI / J&J MDR Meetings	Notified Body meetings face-to-face with J&J regarding MDR interpretations and requirements.
May 15, 2018	BIOMEDevice / MD&M	BIOMEDevice Conference	Panel discussions, technical sessions, case studies related to surgical robotics, medical AI, software validation and other topics.

Patents and publications

- US Patent 6,773,436 Absorbable bone anchor

- US Patent 7,217,279 Suture loop anchor
- US Patent 7,875,064 Absorbable bone anchor
- European Patent EP1297788 Absorbable bone anchor
- US Patent Applications:
    - 2011/0087283 Absorbable bone anchor
    - 2007/0185494 SUTURE LOOP ANCHOR
    - 2006/0247641 Method and apparatus for the repair of a rotator cuff (RTC) tendon or ligament
    - 2005/0107828 Suture loop anchor
    - 2005/0019368 Bioabsorbable suture anchor system for use in small joints
    - 2004/0243180 Absorbable bone anchor
    - 2003/0065331 Absorbable bone anchor

End 10.10. CV of Medical Operations (MO) Evaluator

9.8. CER Revision History

Revision history for CER SCN073157

Revision Number	Date (DD Month YYYY)	Description of Change
A	02 April 2020	• Initial CER for the Ethicon Megadyne Electrosurgical Generator (new line extension device) • New CER #SCN073157 Rev A,1 for Megadyne Electrosurgical Generators: Megadyne Electrosurgical Generator (existing) and ETHICON Megadyne Electrosurgical Generator (new line extension) • CE plan for update to MEDDEV 2.7.1 Rev 4.

9.9. CER Approval Signatures (E-Signatures)

Medical Affairs Evaluator

Approver Name/Title	Signature
Medical Evaluator Giovanni A. Tommaselli, MD Medical Director, Lifecycle Management – Ethicon, a Johnson & Johnson Medical Devices Company	e-signature in CHANGE MANAGEMENT SYSTEM

Regulatory Affairs Evaluator

Approver Name/Title	Signature
Regulatory Evaluator Emily Nesbitt Associate Director Regulatory Affairs	e-signature in CHANGE MANAGEMENT SYSTEM

Medical Operations Evaluator

Approver Name/Title	Signature
Medical Operations Evaluator Karl Reese Director, Medical Operations (Global Surgery & Robotics)	e-signature in CHANGE MANAGEMENT SYSTEM

Reference Attachment 100503719 for Declaration of Interest (DOI) Forms.