Electroconvulsive Therapy (ECT) Devices for Class II Intended Uses

Draft Guidance for Industry, Clinicians and Food and Drug Administration Staff

DRAFT GUIDANCE

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Physical Medicine and Neurotherapeutic Devices Branch

Preface

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Electroconvulsive Therapy (ECT) Devices for Class II Intended Uses

Draft Guidance for Industry, Clinicians and FDA Staff

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1 Introduction

This draft guidance document provides draft recommendations for 510(k) submissions and compliance with special controls being proposed to support reclassification of Electroconvulsive Therapy (ECT) Devices into class II (special controls) for severe major depressive episode (MDE) associated with Major Depressive Disorder (MDD) or Bipolar Disorder (BPD) in patients 18 years of age and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition. An ECT device is an electrical device used for treating severe psychiatric disturbances by applying a brief intense electrical current to the patient's head to induce a major motor seizure. This guidance is issued for comment purposes only.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

2 Background

FDA has issued a proposed administrative order to reclassify ECT devices for the treatment of severe MDE associated with MDD or BPD in patients 18 years of age or older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition, which are currently Class III devices, into Class II (special controls), subject to premarket notification. FDA is proposing this reclassification under the Federal Food, Drug and Cosmetic Act (FD&C Act) based on new information pertaining to the device. This draft guidance is intended to provide recommendations on how to comply with the special controls proposed in 21 CFR

876.5540(b)(1) and indicate what information is suggested for submission to FDA in a 510(k) to demonstrate that the special controls have been met.

The special controls proposed in 21 CFR 876.5540(b)(1) include a requirement that devices marketed prior to the effective date of the final reclassification must submit an amendment to their previously cleared 510(k) that demonstrates compliance with the special controls within 60 days after the effective date of the final reclassification. The recommendations in this guidance are also appropriate for submission in such amendments.

3 Scope

An ECT device, as described in 21 CFR § 882.5940, is defined as:

> (a) *Identification.* An electroconvulsive therapy device is a prescription device, including the pulse generator and its stimulation electrodes and accessories, used for treating severe psychiatric disturbances by inducing in the patient a major motor seizure by applying a brief intense electrical current to the patient's head.

The scope of this document is limited to ECT devices intended for the treatment of severe MDE associated with MDD or BPD in patients 18 years of age and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition, proposed § 882.5940(b)(1), product code GXC. ECT devices used outside of this indication are not within the scope of this guidance.

4 510(k) Submission Recommendations

The sections below provide recommendations on information to include in a 510(k) submission for an ECT device intended for the treatment of severe MDE associated with MDD or BPD in patients 18 years of age or older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition. The sections below also include recommendations about how to comply with the proposed special controls, and how to demonstrate such compliance within a 510(k) submission.

4.1 Device Description

You should identify your device by the regulation and product code described in **Section 3 (Scope)**. In addition, we recommend that your device description contain the following information:

- **General Information:** You should identify classification name (e.g., electroconvulsive therapy device), the CFR classification regulation number under which you believe the device and any components/accessories are regulated, common name (e.g., electroconvulsive therapy device, (ECT)), trade or proprietary name, including a listing of all model numbers, and a clear description of the proposed device's intended use. In addition, you should specify whether this device has been previously submitted to FDA and, if so, if it was for identical or different indications.

If the device has been previously cleared by FDA for different indications, specify for which indications.

- **Device components and accessories.** You should provide a description of how the ECT device interconnects (e.g., cables and connectors) with other components or accessories.

  Examples of components and accessories commonly used with ECT devices including the following:

  Stimulation Electrodes: You should specify the materials, construction, type (e.g., adhesive or hand-held), and dimensions of the electrodes provided with, or recommended for use with, your device.

  Electrode Lead Wires and Patient Cables: You should describe the length(s), construction, materials, and connections between the stimulator device and the electrodes.

  Electrode Gel: Electroconductive media used with ECT devices are regulated as class II devices under 21 CFR 882.1275.

  Electroencephalography (EEG) Component: EEG components of ECT devices are regulated as Class II devices under 21 CFR 882.1400.

  Electrocardiography (ECG) Component: ECG components of ECT devices are regulated as Class II devices under 21 CFR 870.2340.

  For any devices labeled for use specifically with your ECT devices that have received prior marketing clearance, you should identify the name of the manufacturer and, if applicable, include reference to the 510(k) number through which marketing clearance was obtained.

- **Photograph or engineering drawings of the device.** You should also provide a photograph or engineering drawing of the device and a functional block diagram (including all accessories).
- **User interface.** You should describe the user interface, including user controls, displays and functions. You should describe how stimulation is initiated and controlled and describe whether individual output stimulus parameters (e.g., amplitude, pulse width, frequency, train duration) can be adjusted by the user or whether only the percent maximum charge or energy can be adjusted. A description of all output displays should be provided.
- **Programmability**. You should indicate any fixed or default programs and whether the device can be custom programmed by the user. If programmable, the extent of the device's programmability should be provided.
- **Technical specifications.** You should provide a detailed table summarizing the device technical specifications (i.e., product specifications, such as the examples

below, including parameter ranges and accuracy, and any other functional, physical, and environmental specifications of the device), including:

- Output stimulation specifications and operating limitations (See Sections 4.2 and 4.3 of this guidance);
- Power source specifications:
  - For AC line-powered devices, you should specify the line voltage and frequency, and the method of line current isolation
  - For battery powered devices, you should identify the number, size, chemistry, and type (primary cell or rechargeable) of batteries to be used with the device and the estimated longevity of the battery. You should also provide a description of battery indicators (e.g., low battery and charging indicators); and
- A description of all possible device settings.

- **Patient contacting materials.** You should identify the components of the device that are patient contacting. For each component, you should identify the generic material of construction, the supplier, and the unique material identifier.
- **Software.** You should provide a complete description of software and the appropriate software documentation as described in Section 5.7 of this guidance.

4.2 Comparison to Predicate Device

You must provide information on how your device is similar to and different from the legally marketed predicate device ("predicate device") in accordance with 21 CFR 807.87(f). We recommend that you provide a side-by-side comparison in a comparison table whenever possible. You should provide a discussion elaborating on the similarities and differences identified in the comparison table. Your discussion should include an explanation of how your device is substantially equivalent, referencing performance data as necessary. If there are technical differences between your device and the predicate device, you should also provide a rationale for why such differences do not raise different questions of safety and effectiveness .

Table 1 shows the minimum recommended comparison information to provide in your submission.

Table 1. Device Output Parameters (See Appendix A. Definitions of Output Specifications)

Descriptive Information	Proposed Device	Predicate Device
Waveform(s) (e.g., pulsed monophasic, pulsed biphasic)[a]		
Shape		
Current or Voltage Regulated?		
Maximum Output Voltage (volts) (+/- ____%)		
Maximum Output Current (mA) (+/- ____%)		
Frequency (Hz)		
Pulse Duration (ms)		
Minimum Electrode Surface Area (cm^2)		
Pulse Delivery Mode		
Maximum Pulse Train Duration (seconds)		
Number of Trains per Activation		
Maximum Total Charge Delivered (mC)[b] (+/- ____%)		
Isolation Resistance from Ground (MΩ)		
Maximum Total Energy Delivered (J)[c] @ 220 Ω (+/- ____%)		
Impedance Monitor (static and/or dynamic)		
High/Low Impedance Shut Down Level(Ω)[d]		

[a] Output specifications should be provided for each different output waveform.
[b] The maximum total charge in predicate devices is 576.0 mC.
[c] The maximum total energy in predicate devices is 101.4 J into a 220 Ω load.
[d] Recommended allowable bounds for dynamic impedance is 100 to 600 Ω.

If the ECT device includes other components such as electrode gels (21 CFR 882.1275), EEG (21 CFR 882.1400), and ECG (21 CFR 870.2340), a comparison of the technical characteristics of the components should also be made to an appropriate legally marketed predicate device.

4.3 Technical Parameters

FDA is proposing to require as a special control that sponsors identify the technical parameters of the device, including waveform, output mode, pulse duration, frequency, train delivery, maximum charge and energy, and the type of impedance monitoring system necessary to characterize and compare the device performance. FDA is further proposing a special control that non-clinical testing confirm the electrical characteristics of the output

waveform. In order to adequately characterize your device output, the technical parameters of the device, as listed in Table 1, should be provided. See Appendix A for definitions. You should also provide the following documentation for each output waveform associated with these output parameters:

a. Minimum and maximum output values;

b. Increments for increasing output value;

c. Accuracy (i.e., (+/- ____%);

d. Stimulus ramp up and down times;

e. A description of how the output values were verified, including the number of devices tested (minimum of 10 devices is recommended)

f. For each output mode, you should provide an oscilloscope tracing (or an accurate diagram) describing the electrical output waveform. For each output mode, we recommend you provide tracings to describe the individual pulse output waveform under loads of 100, 220, and 600 ohms. FDA also recommends you provide one tracing showing the series of pulses into a 220 ohm load. With each tracing, we recommend you include:

   i. name of the output mode

   ii. clearly labeled amplitude and time axes

   iii. identification of the amplitude baseline (i.e., with no output)

   iv. listing of all output parameter settings (e.g., amplitude, pulse width, frequency).

4.4 Biocompatibility

FDA is proposing to require as a special control that components (and accessories) of the device that come into human contact must be demonstrated to be biocompatible. You should select biocompatibility tests appropriate for the duration and nature of contact with your device. For stimulation electrodes, we recommend you conduct testing for external devices in contact with the skin for a limited duration (i.e., less than 24 hours). If identical materials and identical material processing are used in a predicate device with the same type and duration of patient contact, you may identify the predicate device in lieu of providing biocompatibility testing.

4.5 Electrical and Mechanical Safety

FDA is proposing to require as a special control that performance data must demonstrate electrical and mechanical safety and the functioning of all safety features built into the device including the static and dynamic impedance monitoring system. The sections below provide recommendations regarding performance data for electrical and mechanical safety.

4.5.1 General Equipment Safety

We recommend that you demonstrate the electrical and mechanical safety of the device by performing electrical and mechanical safety testing as described in the FDA-recognized standard, IEC 60601-1, Medical Electrical Equipment – Part 1: General requirements for basic safety and essential performance, or by an equivalent method.

You should provide a detailed discussion of the extent to which this standard was used to guide the device design and protect against electrical and mechanical hazards. The discussion should include specific criteria such as:

- power supply – supply type, rated voltage, rated current, frequency, etc.;
- accuracy of controls and protection from delivering hazardous outputs;
- protection under fault-conditions;
- protection against unwanted or excessive radiation;
- excessive temperature;
- environmental testing;
- mechanical hazards associated with moving parts and overall device construction; and
- protection from leakage current under normal and single-fault conditions.

If the device is intended for use with rechargeable batteries, we recommend that your 510(k) identify the method used to isolate the user from AC line current, and that you follow IEC 60601-1, *Medical Electrical Equipment - Part 1: General Requirements for Safety,* or an equivalent method to show that the levels of patient leakage current, measured under both normal and single fault conditions, are acceptable. You should also specify whether the device can be used during recharging.

4.5.2 Device Specific Safety Features

To demonstrate the functioning of safety features, FDA recommends you describe all such features built into the device, including how they function (e.g., hardware and/or software), and provide testing to demonstrate that they function as specified, including but not limited to:

- disabling or limiting runaway pulse trains
- patient isolation from line currents
- preventing unintended DC current
- limiting maximum output

- providing shut-offs for high or low impedance with dynamic impedance monitoring
- visual and/or audible indicators for stimulus delivery
- manual abort treatment capability

4.6 Electromagnetic Compatibility (EMC)

FDA is proposing to require as a special control that appropriate analysis/testing must validate electromagnetic compatibility (EMC). EMC encompasses both emissions (interference with other electronic devices) and immunity (interference with device performance created by emissions from other electronic devices). We recommend that you evaluate the EMC of your device for all device output modes in accordance with IEC 60601-1-2, *General requirements for basic safety and essential performance – Collateral standard: Electromagnetic compatibility – Requirements and tests*. You should also provide:

- a clear summary of all EMC testing (emissions and immunity) of this device with the test results and data to support any claims for immunity to electromagnetic interference (EMI);
- a brief explanation of how each EMC test was performed and how the testing for each mode addresses the risks for EMI and demonstrates EMC to the claimed levels;
- a brief explanation of how the testing addresses the timing of the device for therapy delivery;
- explanations and justifications for any deviations from the referenced standards or modifications to the device tested; and
- pass/fail criteria for each EMC tests, how these were quantified and measured, and justifications for these criteria.

4.7 Software Life Cycle and Risk Management

FDA is proposing to require as a special control that appropriate software verification, validation, and hazard analysis be performed. We recommend that you submit information for software-controlled devices as described in *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089543.htm). As described in the Software Guidance, the documentation that FDA recommends you submit is determined by the "level of concern" for your software device. The level of concern is related to the risks associated with software failure. FDA believes that the software used to operate an ECT device presents a "major level of concern" because a failure or latent design flaw could either directly result in major injury to the patient or could indirectly result in major injury to the patient through incorrect or delayed information or through the action of a care provider.

We recommend that you provide a full description of the software/firmware supporting the operation of the subject device following the Software Guidance, commensurate with a major level of concern. This recommendation applies to original device/systems as well as to any software/firmware changes made to already-marketed devices. Changes to software must be revalidated and re-verified in accordance with Design Controls, 21 CFR 820.30, and documented in the Design History File, per 21 CFR 820.30(j). Some software changes may warrant the submission of a new 510(k).

We advise you to consider whether you can conform to any recognized software standards and provide statements or declarations of conformity as described in the FDA Guidance, *Use of Standards in Substantial Equivalence Determinations* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073752.htm).[1] .Please visit the following website to search for the FDA-recognized standards involving medical devices containing software: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073752.htm.

If the device includes off-the-shelf software, you should provide additional information as recommended in the FDA document titled *Guidance for Industry, FDA Reviewers and Compliance on Off-the-Shelf Software Use in Medical Devices* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073778.htm).

4.8 Electrodes

FDA is proposing to require as a special control that performance data must demonstrate electrical performance, adhesive integrity, and physical and chemical stability of the stimulation electrodes. To assure that the device performs as intended, we recommend that you evaluate and document the electrodes' biocompatibility (see Section 4.4), electrical performance, adhesive performance, stability, and, if applicable, suitability for reuse (see Section 4.9.1.8).

4.8.1 Electrical Performance

The stimulation electrode design should ensure that the energy from the waveform/pulse generator is efficiently transferred to the patient. For both recording and stimulation applications, we recommend that you perform impedance testing to assure that the electrode has conductive properties appropriate to the device's intended use. The construction of ECT stimulation electrodes should ensure that the electrodes distribute electrical current reasonably uniformly across the electrode-skin interface, and avoid "hot spots" that may result in user discomfort or skin burns.

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[1] In addition, FDA has developed updated draft guidance on the use of standards, *Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices – Draft Guidance for Industry and Food and Drug Administration Staff* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm396209.htm). When final, this guidance will represent FDA's current thinking on this topic.

The electrode lead wires and patient cables intended for use with a medical device are subject to the mandatory performance standard set forth in 21 CFR Part 898. The end of the lead remote from the patient shall be constructed so that the lead cannot become connected to earth ground via an exposed conductive surface or to mains power via direct connection to an electrical outlet. The electrode lead wires and patient cables must be in compliance with the test requirements and test methods of subclause 8.5.2.3 of IEC 60601-1 (2005), *"Medical Electrical Equipment - Part 1: General Requirements for Safety,"* Amendment No. 1 (1991), and Amendment No. 2 (1995), see 21 CFR 898.12(a). Your 510(k) should contain information sufficient to demonstrate conformance to this standard.

4.8.2 Adhesive Performance

The electrode design should ensure that the electrodes will adhere to the patient's skin for a duration of use compatible with the intended use of the device. We recommend that you perform testing to assure that the electrode's adhesive performance meets the specified design requirements and user needs.

4.8.3 Stability

ECT electrode materials should be stable and resist physical and chemical breakdown as a result of conducting electrical current and extended periods of storage over a range of environmental conditions. We recommend that you perform testing to establish, for labeling purposes, the device's shelf life and storage conditions, and in cases where the electrodes are reusable, use life.

4.9 Labeling

FDA is proposing to require as a special control specific labeling requirements for both the instructions for use and patient labeling. Premarket notification submissions must include labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). The following suggestions are aimed at assisting you in preparing labeling that satisfies the proposed special control requirements, as well as the requirements of 21 CFR Part 801.

Labeling must include adequate information for practitioners to safely and correctly use the device; this information should include indications, effects, routes, methods, frequency and duration of administration and any relevant hazards, contraindications, side effects and precautions (21 CFR 801.109(d)).

Proposed labels, labeling, and advertisements sufficient to describe the ECT device, its intended use, and the directions for use should be provided with a specific intended use statement and any warnings, contraindications, or limitations clearly displayed.

4.9.1 Instructions for Use

The labeling should include an operator's manual (Instructions for Use) with clear and concise instructions that delineate the technological features of the specific device and how the ECT device is to be used. Instructions should encourage use of local/institutional training programs approved by the relevant institutional and professional organizations.

FDA recommends that the operator's manual for physician use include information in each of the following categories:

4.9.1.1 Device Use

- Brief description of the device and its accessories, including illustrations, features, functions, output modalities, and specifications

- Description of all user-accessible controls, including indicators, markings, labels on the device, and accessories that provide information on the function or meaning of each control, display, output jacks, etc.

- Directions for cleaning and maintenance, where appropriate

- Storage information

- Electrical safety requirements. Electrical safety requirements for the ECT device should be stated clearly in the product labeling. A list of technical standards to which the device has been tested and shown to comply should also be provided.

4.9.1.2 Intended Use

The labeling should include an intended use statement with specific indications of the intended patient population meeting DSM-V[2] criteria for MDE associated with MDD or BPD. In addition, the indications for use should specify that the device is indicated for severe MDE in treatment-resistant patients. The indications for use should specify the conditions of use and the patient population. For example, ECT devices are intended only for use in patients 18 years of age and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition. In addition, you should specify whether the device is intended to be used as sole therapy or as an adjunct to other therapies, including medications in the specified population. The labeling should also contain a description of the clinical trial population that identifies the population studied according to treatment severity and resistance.

FDA recommends that physician labeling include a discussion of the benefits and risks to be considered when choosing the proper stimulation parameter. Physician labeling should include instructions to the physician to provide such labeling to the patient. Table 2 summarizes stimulation parameters, indicating preferred modalities of treatment and those associated with increased cognitive and memory adverse events.

[2] American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.

Table 2. Stimulation Parameters and Effect of Cognitive/Memory Adverse Events

Stimulation Parameter	Associated with Increased Cognitive/Memory Adverse Events	Preferred Modality of Treatment to Minimize Cognitive/Memory Adverse Events
Waveform	Sinusoidal	Brief pulse
Electrode Placement	Bitemporal, unilateral dominant	Unilateral non-dominant hemisphere
Stimulus intensity (especially with bilateral treatment)	Increased intensity of treatment	Decreased intensity of treatment (e.g., < 3 times seizure threshold, with bitemporal electrode placement)
Frequency of treatments	Increased frequency of treatment	Decreased frequency (e.g. 2 times per week or less) of treatment or holding treatment

4.9.1.3 Contraindications

Each contraindication in the labeling should describe the consequences of contraindicated use. Contraindications should include:

- Severe and unstable cardiovascular conditions (e.g. recent myocardial infarction, unstable angina, congestive heart failure, critical aortic stenosis, uncontrolled hypertension/hypotension)
- Cerebrovascular conditions (e.g. aneurysm, arteriovenous malformation)
- Increased intracranial pressure
- Space-occupying cerebral lesions (e.g. tumors)
- Recent stroke (hemorrhagic or ischemic)
- Severe and unstable pulmonary conditions (e.g. chronic obstructive pulmonary disease, asthma, pneumonia)[3]

[3] American Psychiatric Association. 2001. The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training and Privileging—A Task Force Report, 2nd ed. American Psychiatric Press, Washington, DC. p. 30.

4.9.1.4 Warnings

FDA is proposing a special control that would require labeling for ECT devices to include a prominently placed warning:

Warning: ECT device use may be associated with: disorientation, confusion, and memory problems.

FDA is also proposing a special control that would require labeling for ECT devices to include the following warning, prominently placed, unless performance data demonstrating a beneficial effect of longer term use, generally considered treatment in excess of three months, is provided:

Warning: When used as intended this device provides short-term relief of symptoms. The long-term safety and effectiveness of ECT treatment has not been demonstrated.

Longer term use is generally considered treatment in excess of three months.

In addition, the warnings section of the operator's manual should address the concerns described below.

- **Cognitive/Memory Decline.** Labeling must include a bolded warning regarding the disorientation, confusion, and memory problems (see above).

  The labeling should also provide additional information on cognitive/memory risks including a warning that ECT device use may be associated with:

  - Disorientation and confusion
  - Anterograde (short-term) verbal memory
  - Retrograde (long-term) autobiographical memory

- **Medical/Physical.** FDA recommends including a warning that ECT device use may be associated with (in order of frequency of occurrence):

  - Pain/somatic discomfort (including headache, muscle soreness, and nausea)
  - Skin burns
  - Physical trauma (including fractures, contusions, injury from falls, dental and oral injury)
  - Prolonged or delayed onset seizures
  - Pulmonary complications (insufficient, or lack of breathing, or inhalation of foreign substance into the lungs)

- Cardiovascular complications (heart attack, high or low blood pressure, and stroke)

- Death

- **Psychiatric.** FDA recommends including a warning that ECT device use may be associated with:

  - Risk of Ineffective Therapy: The labeling should include appropriate warnings for use in patient populations where efficacy has not been established and where treatment may represent a risk to the patient. ECT device use may be associated with ineffective treatment of your primary psychiatric condition, or may lead to worsening of psychiatric symptomatology.

  - Treatment-emergent mania: The labeling should include appropriate warnings regarding the occurrence of manic symptoms (including euphoria and/or irritability, impulsivity, racing thoughts, distractibility, grandiosity, increased activity, talkativeness, and decreased need for sleep) following treatment.

  - Risk of Relapse: The labeling should include appropriate warnings for use that effectiveness greater than one month after treatment completion has not been established.

4.9.1.5 Precautions

The following precautions should be provided.

- **Lack of Evidence for Efficacy or Safety in Specific Patient Populations.** Labeling should include Precautions for the use of ECT devices in the treatment of patients with psychiatric conditions where safety and efficacy has not been established. This may include patients with:

  - age less than 18

  - schizophrenia

  - schizophreniform disorder

  - schizoaffective disorder

  - biopolar mania or mixed states

- **Maintenance Treatment.** Labeling should include a precaution that describes the limitations of available information on the safety and effectiveness of long-term treatment with the ECT device, also known as maintenance ECT.

4.9.1.6 Procedure Cautions and Risk Mitigation

Specific procedural warnings and cautions for the use of the ECT device should be provided

in a separate section of the operator manual and should address concerns such as the risk of inadvertent discharge or excessive stimulation discharge.

In addition, to mitigate the risks of ECT, FDA is proposing a special control that would require labeling to include the following specific recommendations to the device user:

i. Conduct of a pre-ECT medical and psychiatric assessment (including pertinent history, physical examination, anesthesia assessment, dental assessment, and other studies as clinically appropriate)

ii. Use of patient monitoring during the procedure (i.e., electrocardiography, heart rate, blood pressure, ventilation, oxygen saturation)

iii. The appropriate use of general anesthesia, including neuromuscular blocking agents, by a licensed anesthesia provider during the ECT procedure

iv. pre-ECT dental assessment and the use of mouth protection (bite blocks) during the procedure

v. Electroencephalography (EEG) monitoring until the continuous seizure has terminated

vi. Instructions on electrode placement, including adequate skin preparation and the use of conductivity gel during electrode placement

vii. Monitoring cognitive status

- Cognitive function should be evaluated before beginning ECT and monitored throughout the course of treatment via formal neuropsychological assessment using validated psychometric instruments for evaluating specific cognitive functions (e.g., attention, memory, executive function).
- Assessment should also include patient self-report of perceived cognitive difficulties via standardized self-report inventory and/or structured clinical interview
- All assessments should be conducted by a qualified, appropriately trained, mental health professional licensed by the state
- These results should be routinely reviewed during the course of treatment and influence appropriate clinical decision-making (e.g., holding or terminating treatment, changing ECT treatment parameters).

4.9.1.7 Clinical Testing and Reported Adverse Events

FDA is proposing a special control that would require labeling to include information related to generic adverse events associated with ECT treatment, as well as a detailed summary of the clinical testing, which includes the clinical outcomes associated with the use of the device, and a summary of adverse events and complications that occurred with the device. A specific section of the operator's manual should present a summary of adverse events and complications that occurred with the ECT device in clinical studies as well as a summary of the device effectiveness in clinical studies. Reports of cognitive and memory impairment should be cited in number, type, and severity as these are frequently associated with ECT

treatment. In addition, the number and incidence of deaths, completed suicides, suicide attempts, seizures or worsening of depression should be provided. Effects on cognitive function using targeted measures of analysis should be reported.

4.9.1.8 Reuse of the Device

FDA is proposing a special control that would require labeling to include, where appropriate, validated methods and instructions for reprocessing of any reusable components. If the electrodes are not limited to single-patient use, we recommend that the labeling include instructions for handling, transport, cleaning, and biological decontamination to ensure the safety and protection of patients and health care or other personnel who perform these tasks. You should evaluate the potential for skin reactions and disease transmission, as well as demonstrate that the cleaning and biological decontamination of the electrodes provides sufficient protection and does not impact their functional performance. In general, we believe pre-gelled electrodes cannot be cleaned and decontaminated in a manner that assures prevention of cross-contamination skin reactions or disease transmission; therefore, we recommend that these electrodes be limited to single-patient use. For recommendations regarding the development and validation of reprocessing instructions in your proposed device labeling, please refer to the guidance *Processing/Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling* (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf).

4.9.1.9 Training

FDA is proposing a special control that would require device labeling to indicate the appropriate training necessary for safe use of the device. Training recommendations may include participation in a recognized device use training course, documented adequate supervised device use (under a qualified clinician), or training as recommended by state licensing boards and/or appropriate professional organizations.

4.9.2 Patient Labeling

FDA is proposing to require patient labeling as a special control for ECT devices. The proposed special controls would require patient labeling provide prospective patients with information that will assist them in understanding who may benefit from treatment with the device, what those potential benefits are, relevant contraindications, warnings, precautions, adverse effects/complications, how the device operates, the typical course of treatment, and other available treatments. Providing such information to the patient prior to scheduling treatment is an important tool to help ensure effective communication between the patient and practitioner concerning the safe use of the device and the purposes for which it is intended. Each patient should have access to clear information in plain language to assist with forming realistic expectations of the treatment and its potential complications. Clearly written patient labeling can help patients understand which types of potential side effects, e.g., disorientation, confusion, memory problems, may be important to report to their health care provider. The patient labeling should use terminology that is well known and understood by the average layperson.

We recommend you follow the general format and relevant principles discussed in the CDRH guidance document entitled, *Guidance on Medical Device Patient Labeling* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070782.htm) In addition, we recommend patient labeling for ECT devices include the following information specific to these devices and their intended uses:

4.9.2.1 Purpose of the device and indications for use

To demonstrate compliance with the special controls, patient labeling should contain a description of the device, its intended use and intended patient population, as well as when the device should not be used (contraindications). The labeling should also include information from clinical studies describing appropriate candidates for the procedure.

Further, patient labeling should describe in lay terms how the device operates to achieve its effects and the typical course of treatment, such as in the following suggested phrasing:

- "The device applies a controlled electric current and prevents the electrical current (amplitude, waveform, duration of exposure) from exceeding limits specified by the manufacturer. The treatment involves the application of a controlled electric current that leads to a 'convulsion' or a 'seizure'.

- For it to be effective, multiple treatments with ECT may be necessary.

- Patients should discuss the number of treatments and treatment schedule with their physicians. It is important to continue with the recommended follow-up treatments to help prevent the depression from returning.

- ECT device treatment effects are often temporary, and patients may need to continue other forms of depression therapy."

ECT informational material should be discussed with a designated and competent family member or other individual who could also discuss any informed consent with the patient.

4.9.2.2 Benefits and Risks of the Device

FDA is proposing a special control that would require patient labeling to provide information on potential device benefits. The labeling should provide patients and their caregivers with balanced, accurate information about the expected benefits from using the device, and describe the probability of such benefits based upon your clinical trial. The information provided should be sufficient to help patients make informed treatment decisions based on accurate information regarding the expected benefits of ECT treatment along with the risks involved.

FDA is also proposing a special control requiring patient labeling to describe the known risks of ECT treatment. Absent performance data demonstrating that these risks do not apply, the proposed special controls would require the following statements to be included in your patient labeling::

- *ECT treatment may be associated with disorientation, confusion and memory loss, including short-term (anterograde) and long-term (autobiographical) memory loss following treatment. These side effects tend to go away within a few days to a few months after the last treatment with ECT. However, some patients have reported a permanent loss of memories of personal life events (i.e., autobiographical memory). Improvements in the way ECT is applied to patients currently, with controlled electric currents and electrode placement, can minimize but not completely eliminate, these risks.*

- *Patients treated with ECT may also experience manic symptoms (including euphoria and/or irritability, impulsivity, racing thoughts, distractibility, grandiosity, increased activity, talkativeness, and decreased need for sleep) or a worsening of the psychiatric symptoms they are being treated for.*

- *The physical risks of ECT may include the following (in order of frequency of occurrence):*

    - *Pain/somatic discomfort (including headache, muscle soreness, and nausea)*

    - *Skin burns*

    - *Physical trauma (including fractures, contusions, injury from falls, dental and oral injury)*

    - *Prolonged or delayed onset seizures*

    - *Pulmonary complications (insufficient, or lack of breathing, or inhalation of foreign substance into the lungs)*

    - *Cardiovascular complications (heart attack, high or low blood pressure, and stroke)*

    - *Death*

FDA is proposing a special control to require that patient labeling include a summation of the clinical testing, which includes the clinical outcomes associated with the use of the device, and a summary of adverse events and complications that occurred with the device.

FDA is also proposing to require as a special control that patient labeling for ECT devices include a prominently placed warning:

Warning: ECT device use may be associated with: disorientation, confusion, and memory problems.

In addition, FDA is proposing a special control that would require labeling for ECT devices to include the following warning, prominently placed, unless performance data demonstrating a beneficial effect of longer term use, generally considered treatment in excess of three months, is provided:

Warning: When used as intended this device provides short-term relief of symptoms. The long-term safety and effectiveness of ECT treatment has not been demonstrated.

Longer term use is generally considered treatment in excess of three months.

4.9.2.3 Alternative Treatments

FDA is proposing a special control that would require patient labeling to describe currently-available alternative treatments, including medications, devices and psychotherapy. FDA recommends that patients speak with their health care providers to determine if they are suitable alternatives for them.

5 Animal and Clinical Testing

ECT devices will generally not be subject to animal or clinical testing if they are similar to legally marketed ECT devices in design and technology and are indicated for severe MDE (associated with MDD or BPD) in patients 18 years of age and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition. However, new or modified indications for use or technological characteristics may require the submission of animal or clinical testing to demonstrate substantial equivalence.

It is important to note that ECT devices for other indications are outside the scope of this guidance but likely *would* require clinical testing.

5.1 Animal Testing

For devices with notable dissimilarity from legally marketed ECT devices (e.g., in design or technology), nonclinical testing in animals may be appropriate to confirm the safety of the procedure and evaluate the functional characteristics of the device design. Such testing must comply with 21 CFR Part 58, which prescribes Good Laboratory Practices for nonclinical studies. If you are considering animal testing, we encourage you to contact the review branch early in the product development process to discuss your study design.

5.2 Clinical Evidence

Clinical testing will not generally be needed for new devices if the proposed device is sufficiently similar to the predicate device in terms of indications, device specifications, and energy output, such that reliance on bench and/or animal testing may be sufficient to demonstrate substantial equivalence. In cases where clinical testing is needed, FDA recommends that the clinical study be designed to demonstrate that your device is as safe and effective as the predicate device when used as described in the Indications for Use statement.

Clinical evidence may be requested in situations such as the following:

- indications for use dissimilar from legally marketed devices of the same type;[45]

- new technology, i.e., technology different from that used in legally marketed devices of the same type, yet does not raise different questions of safety or effectiveness; or

- cases where engineering and/or animal testing raise issues that warrant further evaluation with clinical evidence to establish substantial equivalence.

FDA will consider alternatives to clinical testing when the proposed alternatives are supported by an adequate scientific rationale.

FDA believes prospective clinical trials for ECT devices should support changes in stimulation parameter outputs (i.e. current, voltage, frequency, phase duration, charge density, and pulse width). If your device's electrical output to the patient exceeds that of previously cleared predicate ECT devices, the 510(k) submission should include appropriate supporting data to show that you have considered what consequences and effects this change or new use might have on the safety and effectiveness of the device (21 CFR 807.87(g)). We recommend a prospective clinical trial to provide the evidence of safety and effectiveness.

5.3 Significant Risk and Investigational Device Exemption (IDE)

FDA believes that ECT devices carry significant risks to patients,[6] and therefore require the filing of an IDE application, under 21 CFR 812.20(a)(1) when used for unapproved uses. FDA believes any clinical investigation of an investigational ECT device in accordance with the recommendations of section 5.2 of this guidance will generally constitute a significant risk investigation as defined in 21 CFR 812.3(m)(4). Sponsors of clinical investigations of devices must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

5.4 Clinical Protocol

The clinical study should be designed to address the concerns provided below. To ensure optimal study design, we recommend that you request the Agency's review of your protocols prior to initiating clinical studies for your device through our pre-submission (pre-sub) process. For information on the pre-sub process, see guidance *Requests for Feedback on*

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[4] ECT devices that are indicated for schizophrenia, bipolar manic states, schizoaffective disorder, schizophreniform disorder, and catatonia are proposed to be classified as Class III devices, requiring PMAs.

[5] Under section 513(i) of the FD&C Act, to be found substantially equivalent, a device must have the same intended use as a legally marketed device. If an indication for use is determined to be a new intended use, the device will be found not substantially equivalent.

[6] See *Significant Risk and Nonsignificant Risk Medical Device Studies* at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf.

Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf).

Indication for use: The indication for use should identify the patient population for whom the device is intended, including the age, DSM-V diagnosis, treatment severity, and level of treatment resistance.

Inclusion and Exclusion Criteria: The inclusion and exclusion criteria should characterize the population to be studied. Your inclusion and exclusion criteria should specify the DSM-V diagnosis, medication resistance and treatment severity. Due to safety concerns, we recommend you exclude subjects who have metal implanted in the head, excluding the mouth (e.g., implanted brain stimulators), significant cardiovascular disease (including uncontrolled hypertension, hypotension, arrhythmias or critical aortic stenosis), significant pulmonary disease, history of adverse reaction to general anesthetic agents, history of seizure disorder, cerebrovascular disease, dementia, delirium, head trauma, increased intracranial pressure, or central nervous system (CNS) tumors.

In addition, you should address other subject characteristics, including:

- age
- comorbid psychiatric and neurological disorders
- pregnancy
- length of current episode, single or recurrent episode
- baseline depression severity, based on validated depression assessment tool
- risk of suicide, based on a validated suicide severity scale
- prior treatment with antidepressant therapies [Dose, duration and outcome of antidepressant trials should be documented using a structured format, such as the antidepressant treatment history form (ATHF)[7]
- the presence of neurostimulator devices
- significant heart disease, cerebrovascular disease, history of epilepsy, dementia, head trauma, increased intracranial pressure, or central nervous system (CNS) tumors.

Treatment parameters: Treatment parameters should be standardized and should be specified in detail in your protocol. You should include a description of the determination of

[7] Oquendo M, et al. A computer algorithm for calculating the adequacy of antidepressant treatment in unipolar and bipolar depression. J Clin Psychiatry 2003;64:825-33.

seizure threshold and determination of applied stimulation. In addition, you should specify all the technical treatment parameters for stimulation, the site of electrode placement, the number and frequency of treatments and overall duration of treatment exposure. FDA recommends you provide details about whether treatment sessions will be individualized (i.e., whether treatment parameters will be adjusted based on the study subject response, or other variables).

Study design: For devices intended to treat neuropsychiatric indications (such as depression) FDA recommends either a prospective randomized sham-controlled study or a prospective randomized concurrent controlled trial comparing the device to a legally-marketed predicate device for the same indications for use. We also recommend that you perform the study in multiple centers to analyze for a treatment by site interaction. Depending on the characteristics of the patient population, the randomized phase should be of sufficient duration to demonstrate a clinically meaningful effect. If your study incorporates a cross-over phase, (i.e., subjects originally receiving control treatment switched to receiving investigational treatment or vice versa), you should provide detailed criteria pertaining to the cross-over.

Due to the possible variation of neuropsychiatric symptoms over time, we recommend that you incorporate a screening and/or baseline phase, prior to the randomized phase of the study. During this phase, clinical indicators of symptomatology should be assessed to provide assurance that the patient's depression has stabilized. During the baseline phase, concurrent medication therapies may either be stabilized or withdrawn depending on how you wish to study your device. The screening phase should be of sufficient duration to allow stabilization of the patient's symptoms and, if appropriate, concurrent therapies.

If you plan to study patients on concurrent medications, you should describe how you plan to deal with changes in medications or doses. If you plan to study your device on patients who have been withdrawn from standard therapies, you should follow the drug manufacturer's guidelines for the appropriate time period for each medication that will assure that the medications have been washed out.

Given the inherent risks of ECT device use, we recommend you incorporate a prospective lead-in phase design, in order to recruit only subjects who have demonstrated non-response to medication therapy.

We also recommend that you design your study to incorporate a sufficient period of follow up after the completion of the randomized phase of the study to evaluate the durability of effect. FDA recommends a post treatment follow-up period to assess patient response or remission, the incidence of suicide, and any long-lasting adverse effects. We recommend that the follow-up include assessment of both the active and control groups when feasible, for example, if both groups are receiving best medical therapy.

Device effectiveness: You should specify the primary and secondary effectiveness endpoints for the study. Endpoints should be chosen to assure a clinically meaningful effect.

Validated assessment scales should be used as the primary endpoint. FDA recommends that a comparison of the proportion of subjects who meet the criteria of response and remission in

both the active and control groups be performed. In addition, FDA recommends that you assess a patient reported outcome such as quality of life as one of your secondary endpoints. Additional outcome measures should include patient global impression of improvement and clinician global impressions of improvement and severity.

Device safety: Clinical studies conducted in the US must comply with the applicable reporting requirements of 21 CFR 812.150(b).[8] For clinical studies of ECT devices, device safety data should include the incidence of serious adverse events (e.g., medical/physical complications such as adverse reaction to anesthetic agents/neuromuscular blocking agents, cardiovascular complications, death, physical trauma, prolonged (or tardive) seizures, pulmonary complications, or stoke), cognitive/memory dysfunction (i.e., global cognitive function global memory function, anterograde verbal memory, retrograde impersonal memory, and retrograde personal (autobiographical) memory, subjective memory), and device malfunction resulting in patient or operator injury. For depression, due to the possibility of suicidal ideation or behavior in the study population, FDA recommends that the protocol include a suicide severity rating scale, such as the Columbia Suicide Severity Rating Scale[9], to assess both suicide intent and behavior. You should also collect incidence of common adverse events such as alterations in blood pressure, physical trauma, dental/oral trauma, headache, muscle soreness, nausea and vomiting, application site skin burns or pain/discomfort, and discontinuation rate due to adverse events.

If possible, you should collect systematic safety outcomes data for cognitive/memory dysfunction (i.e., global cognitive function global memory function, anterograde verbal memory, retrograde impersonal memory, and retrograde personal (autobiographical) memory, subjective memory) using validated and standardized assessment tools, administered by appropriately trained and licensed personnel. These assessments should be conducted for at least 12 months after ECT treatment.

You should also determine the severity and duration of each adverse event. To achieve that goal, your data should include information about any intervention that was performed, whether and when the event was resolved, and whether the event was device related.

Training: You should describe any training provided to study investigators, including both training on the use of the device and on any assessment tools. Supporting information to substantiate an adequate level of training should be stated, such as a pre-study reliability certification program and reliability assessment for clinical raters during the study.

5.5 Reporting of Statistical Outcomes for Clinical Study Results

The following study design features should be stated clearly in the study protocol document.

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[8] Studies conducted under an approved IDE must meet all recordkeeping and reporting requirements described in 21 CFR 812.150. Studies allowed under the abbreviated IDE requirements (as defined in 21 CFR 812.3(m)(4)) must comply with the recordkeeping and reporting requirements described in 812.2(b).

[9] See http://www.cssrs.columbia.edu

Sample Size Estimation: FDA recommends you provide justification for your sample size estimates. We recommend you provide clearly defined null and alternative hypotheses, pre-specified type I and II error rates, clinically acceptable differences to be detected in the superiority trial, or non-inferiority margin in the non-inferiority trial, and an estimation of sample size that accounts for study subject loss to follow-up and drop-out. FDA also recommends you discuss how to adjust for a type I error rate in any interim analyses based upon a clearly defined group sequential trial design, if applicable.

Hypotheses: You should specify your null and alternative hypotheses. Your statistical hypothesis should describe the specific statistical model proposed for the main analysis and any relevant secondary analyses.

Randomization and Blinding: You should describe an *a priori* method of randomization and provide a method to ensure integrity of the study blind in detail. We recommend you include an assessment of the effectiveness of the blinding, such as asking patients to guess their treatment group. In addition, we recommend that you perform sensitivity analyses, such as examining the correlation between adverse events and the observed treatment effect to examine the possibility of unblinding due to adverse events.

Effectiveness Assessments: You should include an overall assessment of safety and effectiveness. In your assessment, you should report:

- the primary efficacy endpoint which should be based on a validated assessment tool;
- the secondary efficacy endpoints which should also be based on validated assessment tools (Your secondary endpoints should assess any benefits for which you plan to claim effectiveness.); and
- the standardized effect size for continuous outcome measures and/or the number-needed-to-treat (NNT) for categorical endpoints (whichever measure or endpoint you report, you should include it for the study population and the control group).

5.5.1 Statistical Analysis Plan

Analysis populations: The preferred analysis population for a superiority study is the intent-to-treat population, consisting of all patients as originally randomized. For non-inferiority studies with an active control, you should base the determination of effectiveness on the collective results from per-protocol, intent-to-treat, and as-treated analysis populations. A per-protocol population refers to patients with no protocol violations and complete follow-up. As-treated, although similar to intent-to-treat, refers to all patients, but is grouped according to the treatment actually received not the randomization assignment.

Primary and secondary endpoints: You should report the primary and secondary endpoints, comparing the results of the active group to the control group. For depression studies, we recommend that you report change as a continuous measure, as well as the rate of response, defined as a 50% reduction on the assessment scale, and also the rate of remission.

If you wish to make any labeling claims based on your secondary endpoints, you should prespecify a statistical method to control multiplicity, such as a hierarchical testing order or the step-down method of Holm.

Missing data: Your study analysis plan should include methods for handling missing data. This includes imputation methods, such as multiple imputation, and sensitivity analyses, such as imputing various proportions of missing outcomes (of a binary endpoint) as "successes" or "failures."

Covariate Analysis: We recommend you specify methods for handling significant covariates in the statistical model. For any covariate term included in the proposed statistical model to evaluate effectiveness, we recommend you investigate a treatment group by covariate interaction. If such an interaction term is found to be statistically significant, your statistical summary should include a discussion of the implication of the statistically significant interaction on the overall interpretation of the study results.

Treatment by site interactions: Multicenter studies should include a measure to assess any significant treatment by center interaction on the primary effectiveness measure. We recommend both treatment and control groups be studied at the same site(s). We also recommend you apply an appropriate randomization blocking procedure to balance the number of subjects in each participating center between control and treatment groups in order to facilitate an assessment of the poolability of data across centers. In addition, your statistical analysis section should include a discussion of the importance of any statistically significant treatment-by-site interaction to the overall interpretation of the study results.

Bayesian Methods: If Bayesian statistical methods are used, we recommend you specify the prior information and conduct simulation analysis to estimate the probability of Type I error rate and the required sample size.

FDA recommends you identify the type of patient population (e.g., intent-to-treat, per protocol, evaluable, complete, or others) used in each statistical analysis.

5.6 Reporting Results from Journal Articles or Meta-analyses

If applicable, safety results obtained with the ECT device that were reported in the medical literature should be summarized and included in the 510(k). In addition, effectiveness data for your ECT device for your indications for use that are available from journal articles or meta-analyses may be submitted as supportive information. FDA recommends you provide a comprehensive analysis of the available current, peer-reviewed literature that relates to the advantages and disadvantages of your device. Because the body of literature on ECT is expansive, and varies in scientific quality, we recommend that your analysis rate the strength of the scientific evidence in each study[10]. We also suggest that your review focus on recently

[10] An example of a method of evaluating literature is by methods described by the Agency for Healthcare Research and Quality, **"Evidence Report/Technology Assessment, Number 47, *Systems to Rate the Strength of Scientific Evidence*"** (West, et al. 2002).

conducted studies, utilizing more current standard of practice techniques and stimulation parameters.

For each reviewed publication, the following information should be reported:

- indication for use and intended use
- patient population studied, including age, summary of psychiatric disorder(s), antidepressant or other medications, any prior ECT treatment, duration and frequency of previous treatments, and relevant baseline psychiatric characteristics
- use or non-use of drugs during the study
- electrode placement, and stimulation used for treatment
- nature of and type of control group (e.g., concurrent, patients as own control, historical control, randomization, sham treatment, double masking)
- patient assessments used (pre- and post-treatment)
- statistical analyses used and results
- duration of patient follow-up
- adverse events and treatment-emergent pathologies reported, and how this information was obtained
- long-term effects on retrograde memory and cognitive function and the assessment measures used
- safety and effectiveness results of study and conclusion.

Appendix A. Definitions of Output Specifications

For the purposes of this guidance document, the following definitions of output specifications are used:

- **Brief Pulse**: A rectangular pulse with a pulse duration of 0.5 to 2.0 milliseconds.

- **Charge:** The total charge is the integral of the current magnitude over the duration of the stimulus train. For constant-current, rectangular-pulse trains the total charge is equal to the product of the pulse current amplitude, width, pulse repetition frequency, and train duration.

  Total Charge = Current Amplitude x Pulse Width x Train Duration x Frequency x 2 [only multiply by 2 for biphasic waveforms to account for pulse-pairs (see Figure A2)]

- **Charge Density:** Charge referred to the unit area of the electrode. It is calculated by dividing the charge by the electrode surface area.

- **Dynamic Impedance:** The impedance during delivery of the output stimulus. It is measured during the delivery of energy by monitoring voltage and current. Dynamic monitoring helps to ensure safety since impedances may change during stimulus delivery.

- **Energy:** The total energy is the integral of the power delivered during the stimulus train, which for constant current rectangular pulses is equal to the product of the total charge, the current amplitude, and the dynamic impedance. For reporting purposes the Energy should be calculated using a dynamic impedance of 220 Ω.

  Energy = Charge x Current Amplitude x Dynamic Impedance

- **Frequency:** For *monophasic* waveforms the frequency is the number of pulses per second (see Figure A1). For *biphasic* waveforms the frequency is the number of pulse-pairs per second (see Figure A2). The unit of measure is Hertz (Hz).

- **Impedance Monitor.** Devices can make make static electrode impedance measurements, which are made before or after the delivery of energy, and/or dynamic electrode impedance measurements, which are made during the delivery of energy by monitored voltage and current. Dynamic monitoring is safer when impedances change during shock delivery.

- **Number of Pulses in a Train:** The number of pulses in a train can be calculated as follows,

  Monophasic Waveform: Train Duration x Pulse Frequency

  Biphasic Waveform: Train Duration x 2 x Pulse-pair Frequency

- **Pulse:** A rapid, transient change in the amplitude of a signal from a baseline value to a higher or lower value, followed by a rapid return to the baseline value. (see Figures A1 and A2)

- **Pulse-pairs**: Symmetrical biphasic pulses are referred to as pulse-pairs (see Figure A2).

- **Pulse Width:** The time elapsed from the beginning to the end of all phases plus the interphase interval within one pulse (see Figures A1 and A2).

- **Static Impedance:** The impedance before or after the delivery of energy. It is measured during self-test procedures.

- **Train Duration:** A train is a finite series of pulses and the train duration is the time period in which these finite series of pulses are delivered (See Figures A1 and A2).

- **Ultra Brief Pulse**: A rectangular pulse with a pulse duration of less than 0.5 milliseconds.

- **Waveform**: Shape of the shortest repetitive component of the output wave (e.g., rectangular). The waveform can be *monophasic* (See Figure A1 below) or *biphasic* (See Figure A2 below). A monophasic waveform can have either positive of negative pulses. A biphasic waveform has a positive and a negative pulse and is *symmetrical* if the positive and negative pulses of stimulation are of the same duration, magnitude and shape. Alternating current sinusoidal waveforms are a specific type of biphasic waveform.

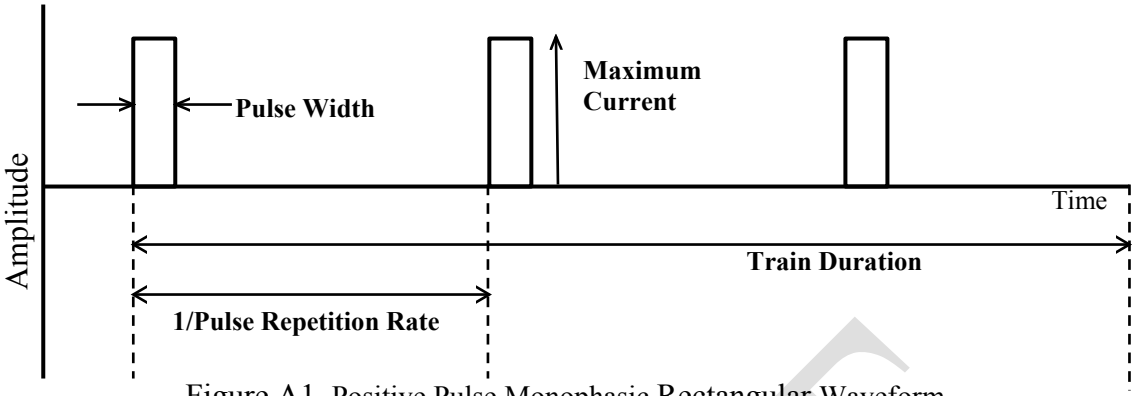

Figure A1. Positive Pulse Monophasic Rectangular Waveform

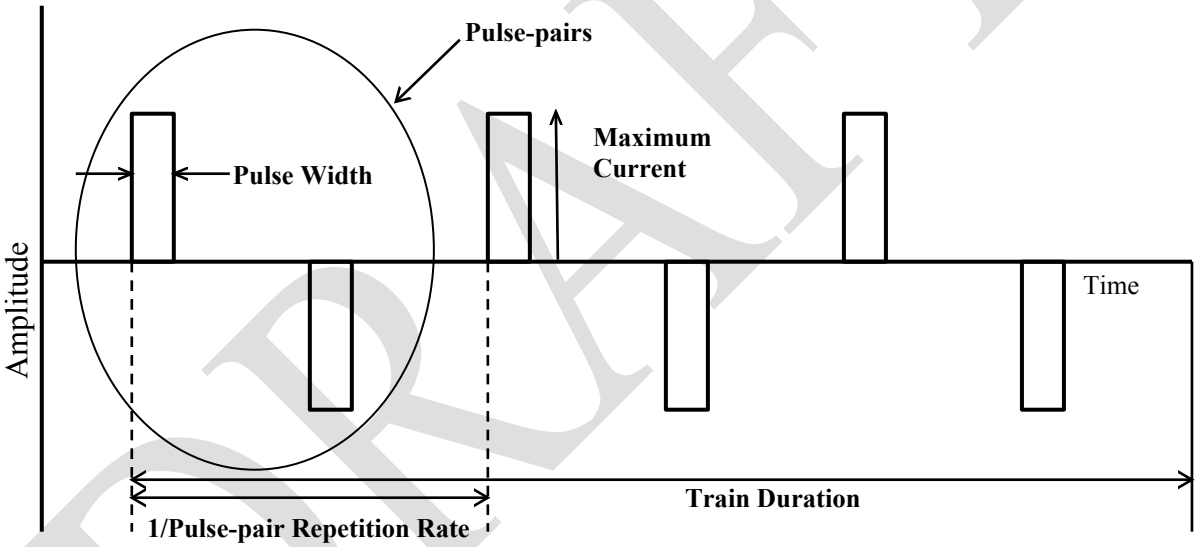

Figure A2. Biphasic Rectangular Waveform