REGULATORY UPDATE TO THYMATRON® SYSTEM IV INSTRUCTION MANUAL
Caution: Federal law restricts this device to sale by or on the order of a licensed physician.

ECT is a complex medical procedure. Its proper and safe conduct requires a staff of licensed healthcare professionals who are trained and experienced with the associated procedures, have received clinical privileges for ECT from the appropriate hospital committee, and have carefully read and are thoroughly familiar with the medical literature concerning the risks, benefits, complications, and methods of ECT. This literature includes the major textbooks of ECT, publications about ECT that have appeared in the major journals of psychiatry, the Journal of ECT, and the American Psychiatric Association's The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training and Privileging – A Task Force Report (2001) . As with other aspects of medical practice, knowledge about ECT continues to change, and clinicians are responsible for maintaining awareness of these changes from these publications and other sources.

It is essential that doctors planning to use the Thymatron® System IV read and follow the warnings and recommendations of the Task Force Report of the American Psychiatric Association as set forth in "The Practice of Electroconvulsive Therapy" (APA, 2001), which states, in part, that "A small minority of patients treated with ECT later report devastating cognitive consequences. Patients may indicate that they have dense amnesia extending far back into the past for events of personal significance or that broad asof cognitive function are so impaired that the patients are no longer able to engage in former occupations...in some patient self-reports of profound ECT-induced deficits may reflect objective loss of function...In rare cases, ECT may result in a dense and persistent retrograde amnesia extending to years..."

INDICATIONS FOR USE

The U.S. Food and Drug Administration has indicated ECT for use in the treatment of severe major depressive episodes associated with major depressive disorder (MDD) or bipolar depressive 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.

The Thymatron® System IV is intended to be used to administer electroconvulsive therapy (ECT) to patients suffering from mental disorders in which a rapid, definitive response is desired. ECT is most often indicated in patients who have not responded to adequate courses of appropriate pharmacotherapies but is also indicated as the primary treatment for patients in whom a rapid or high probability of response is desired (as when they are severely medically ill or in danger of harming themselves) or who are known by their treatment history to respond only to ECT, or who have expressed a valid preference for ECT over alternate therapies.

SAFETY INFORMATION

Please read the following important safety requirements before using the Thymatron® System IV ECT Instrument.

WARNINGS

WARNING: Do not remove the top or bottom covers of the Thymatron® System IV. There are no user serviceable parts inside. Any servicing must be performed by qualified service personnel.

WARNING: Do not use any cables or lead wires that appear to be damaged.

WARNING: The Thymatron® System IV is defibrillator protected.
Nevertheless, for safety reasons, all cable connections between the Thymatron® System IV ECT Instrument and the patient must be disconnected prior to initiation of the defibrillation stimulus.

WARNING: Avoid the risk of accidental shock to medical personnel. Do not contact the patient, or any conductive surface touching the patient, unless wearing electrically insulated gloves. If holding the patient's jaw or touching the patient's head during the electrical stimulus, make sure to use electrically insulating gloves.

WARNING: Administering ECT to a patient with an implanted DBS device can damage the DBS device or cause it to malfunction and cause injury to the patient.

WARNING: Specific patient conditions may be associated with substantially increased risk from ECT. These include unstable or severe cardiovascular conditions (recent myocardial infarction, unstable angina, poorly-compensated
congestive heart failure, severe valvular cardiac disease), vascular aneurysms susceptible to rupture with increased blood pressure, increased intracranial pressure, recent cerebral infarction, severe chronic obstructive pulmonary disease, asthma, pneumonia and anesthesia risk level ASA 4 or 5.

PRECAUTIONS

CAUTION: Do not subject the Thymatron® System IV to extreme moisture, and do not use it after it has been partially or totally immersed in liquid or when a significant amount of liquid has been spilled on it. Power the unit off and have it checked by a qualified technician before powering it on or using it again.

CAUTION: Only use the Thymatron® System IV with the Somatics' Treatment or Monitoring Cables.

CAUTION: The Treatment and Monitoring Cables are not interchangeable and cannot be inserted into the wrong front panel connector. Attempting to force the Treatment Cable into the connector intended for the Monitoring Cable (and vice versa) will damage both the connector and the cable.

CAUTION: The ECG function of the Thymatron System IV is used only to obtain a heartrate to help assess the efficacy of the seizure; it is not intended to be used to make diagnoses. Do not use the Thymatron System IV ECG function to monitor the patient's heart for any other purpose.

CAUTION: The EMG function of the Thymatron System IV is used only to obtain an estimate of the motor seizure duration to help assess the efficacy of the seizure; it is not intended to be used to make diagnoses. Do not use the Thymatron System IV EMG function to monitor the patient's nerve activity for any other purpose.

CAUTION: Do not dispose of your Thymatron® System IV in the general waste. As per Directive 2002/96/EC for the disposal of electrical and electronic equipment, please contact the manufacturer for instructions.

CAUTION: Prior to initiating ECT on a patient with a cochlear implant, healthcare professionals should discuss the issue with an otolaryngologist or audiologist and review the cochlear implant Instructions for Use.

CAUTION: Thymapad® electrodes are single-use only and must be discarded after the treatment. The Thymatron® System IV Treatment Cable, Monitoring Cable and lead wires can be cleaned by wiping them off with a Germicidal Disposable Cloth. Steel stimulus electrodes may be cleaned with soapy water or alcohol. The Thymatron® has no special requirements for restricted environment during transport or storage, beyond Standard Sub-clause 10.1 criteria.

ADVERSE EVENTS

Like any therapy, ECT has risks. Certain patients will experience adverse events in conjunction with electroconvulsive therapy. Patients should be made aware of these risks and confirm that they fully understand them prior to consenting to therapy.

The most common reported adverse effects of ECT are:

- Headache.
- Muscle soreness; Mild to moderate pain/discomfort, including jaw pain.
- Nausea.
- Disorientation immediately after seizure induction.
- Memory dysfunction (see further discussion below).

Recent estimates in the medical literature of the mortality rate associated with ECT treatment are 1 per 10,000 patients or 1 per 80,000 treatments.
Other serious adverse events have occurred, including adverse reaction to anesthetic agents / neuromuscular blocking agents; adverse skin reactions (e.g., skin burns); cardiac complications, including arrhythmia, ischemia/infarction (i.e., heart attack), acute hypertension, hypotension, and stroke; cognition and memory impairment; brain damage; dental/oral trauma; general motor dysfunction; physical trauma (i.e., if inadequate supportive drug treatment is provided to mitigate unconscious violent movements during convulsions); hypomanic or manic symptoms (e.g., treatment-emergent mania, postictal delirium or excitement); neurological symptoms (e.g., paresthesia, dyskinesias); tardive seizures; prolonged seizures; non-convulsive status epilepticus; pulmonary complications (e.g., aspiration/inhalation of foreign material, pneumonia, hypoxia, respiratory obstruction such as laryngospasm, pulmonary embolism, prolonged apnea); visual disturbance; auditory complications; onset/exacerbation of psychiatric symptoms; partial relief of depressive anergia enabling suicidal behavior; homicidality; substance abuse; coma; falls; and device malfunction (creating potential risks such as excessive dose administration).

Certain patients are more likely to experience severe adverse events, including those with pre-existing cardiac illness, compromised pulmonary status, a history of brain injury, or medical complications after earlier courses of anesthesia or ECT. Concurrent administration of antipsychotic (neuroleptic) medication may increase the risks of adverse cardiac, pulmonary, and neurological events, and falls. Concurrent administration of stimulants may increase the risks of cardiac and neurological complications, such as prolonged seizure. All of this information should be assessed in developing the treatment plan for a particular patient.

Cognitive side effects are experienced in varying types and severity by ECT patients. Studies have shown that the methods used in ECT administration have a significant impact on the nature and magnitude of cognitive deficits. In general, the American Psychiatric Association recognizes that the following treatment parameters are each independently associated with more intense cognitive side effects:

- Bilateral electrode placement;
- Sine wave stimulation;
- High electrical dosage relative to seizure threshold;
- Closely spaced treatments;
- Larger numbers of treatments;
- Concomitant psychotropic medications;
- High dosage of barbiturate anesthetic agents.

ECT may result in anterograde or retrograde amnesia. Such post-treatment amnesia typically dissipates over time; however, incomplete recovery is possible. In rare cases, patients may experience permanent memory loss or permanent brain damage.

ECT—and use of the Thymatron® System IV specifically—has been shown to be effective in treating major depressive episodes associated with major depressive disorder (MDD) or bipolar depressive 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. A few studies performed with the device are highlighted below, with additional references provided in the bibliography.

TECHNIQUE OF ECT

Users of Thymatron ECT devices should carefully follow the specific ECT treatment techniques and procedures outlined in Chapters 6-11 of the American Psychiatric Association's The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training and Privileging – A Task Force Report (2001)

EFFICACY, SAFETY, AND SIDE-EFFECTS

EFFICACY

A randomized, double-blind, controlled trial of ECT in 230 patients with major depression treated with a Thymatron found 3 different electrode placements equally and significantly effective in reducing depression scale scores, with the greatest effect achieved with traditional bitemporal ECT (Kellner et al, 2010).

A randomized, controlled trial of ECT in 489 major depressive patients, with or without atypical features, treated with a Thymatron DGx. Both the atypical and the typical groups experienced significant improvement in depression (Husain et al, 2008).

A randomized, controlled trial of ECT in 253 unipolar depressed patients with and without psychosis treated with a Thymatron. An 87% overall remission rate was obtained that was greater and more complete in the psychotic depressives (Petrides et al, 2001).

SAFETY

Somatics' safety experience with the Thymatron ECT device since 1984 when FDA approved the Somatics Thymatron ECT device for marketing shows that more than 4,300 Thymatron devices have been sold worldwide. During that time Somatics has maintained complete safety files on the Thymatron device, including those required by the FDA's Good Manufacturing Practice regulation, the Canadian Standards Association, and international testing agencies for the CE mark. In the ensuing 34 years there has been no occurrence of a reportable adverse event (death or serious injury) related to the use of a Thymatron ECT device, no reported occurrence of catastrophic ECT component failure, and no product recall issued.

SIDE-EFFECTS

Numerous studies have been conducted to assess the potential adverse events of ECT on cognition and brain structure. The following is a sample of the many that were conducted with the Thymatron device.

14 patients undergoing bilateral ECT were assessed for cognitive performance by psychometric testing on day before ECT and after the 3rd, 6th, and last ECT treatments. Pre-ECT and post- ECT concentrations of neuron-specific enolase (NSE) and protein S-100, two indicators of brain tissue damage, were not significantly different and the authors concluded that modern ECT does not induce brain tissue damage detectable by changes in NSE or S-100 protein (Agelink et al, 2001).

A Thymatron was used to treat 83 unipolar depressives who had been evaluated at baseline on tests of behavioral and semantic memory. One year after a course of bilateral or unilateral ECT neither behavioral memory nor semantic memory scores were reduced from baseline—in fact, bilateral ECT was associated with significantly improved semantic memory (Schat et al, 2007).

Proton magnetic resonance spectroscopic imaging was used to study hippocampal effects of the Thymatron ECT device as reflected in N-acetylaspartate signals. In 17 patients receiving either unilateral or bilateral ECT, all of whom improved with treatment. No differences were found from 30 control subjects in hippocampal N-acetylaspartate signals, thus providing no evidence for ECT-induced hippocampal atrophy or cell death (Ende et al, 2000).

REFERENCES

Kellner CH, Knapp R, Husain MM et al (2010)
Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial
Br J Psychiatry 196:226-34.

Husain MM, McClintock SM, Rush AJ et al (2008)
The efficacy of acute electroconvulsive therapy in atypical depression.
J Clin Psychiatry 69:406-11.

Petrides G, Fink M, Husain MM et al (2001)
ECT remission rates in psychotic versus nonpsychotic depressed patients: a report from CORE
J ECT 17:244-53.

Agelink et al (2001)
Relation between electroconvulsive therapy, cognitive side effects, neuron specific enolase, and protein S-100.
J Neurol Neurosurg Psychiatry 71:394–396

Schat et al (2007)
Changes in Everyday and Semantic Memory Function After Electroconvulsive Therapy for Unipolar Depression.
JECT 23:153-157

Ende et al (2000)
The Hippocampus in Patients Treated With Electroconvulsive Therapy
Arch Gen Psychiatry 57:937-943

DISCLAIMER / WARRANTIES

Please note that nothing in this manual constitutes, or should be construed as, a claim by Somatics LLC that confusion, cognitive impairment, or memory loss (short-term, long- term, recent, remote, transient, or persistent), or structural brain change (brain damage) cannot occur as the result of ECT or the general anesthesia administered with ECT.

Many patients experience temporary loss of recent or remote memories with ECT, particularly with traditional bilateral ECT. A few patients have reported experiencing persisting loss of memories or memory functions after ECT. Mental and physical illnesses, anesthesia, medications, and postponement of treatment each have their own adverse effects, which can be substantial.

The outcome of ECT treatment depends on many clinical aspects outside the ECT device, including the physical, psychiatric and emotional condition of the patient prior to and at ECT, details of the ECT treatment other than the ECT device settings, including anesthesia and medication exposure. By using the Thymatron System IV, the user accepts responsibility for describing details of those and of pre-existing conditions including brain injury and atrophy, and cognitive difficulties, and for disclosing all appropriate information about risks of ECT to patients, their families and their guardians (if any).

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