

Resource Document on the FDA Final Order to Reclassify ECT Devices

Approved by the Joint Reference Committee, February 2019

"The findings, opinions, and conclusions of this report do not necessarily represent the views of the officers, trustees, or all members of the American Psychiatric Association. Views expressed are those of the authors." -- *APA Operations Manual*.

Prepared by the Ad Hoc Work Group on ECT Reclassification

Background

On December 26, 2018, the Food and Drug Administration (FDA) issued a final order regarding the reclassification of devices for administration of electroconvulsive therapy (ECT).ⁱ On the basis of device risk and the steps needed to give reasonable assurance of safety and effectiveness, the FDA categorizes medical devices into one of three classes (Class I, II, or III), with Class I devices generally posing the lowest risk to the patient.ⁱⁱ As part of a broader statutory requirement to re-categorize class III devices that were marketed prior to May 28, 1976,ⁱⁱⁱ the FDA evaluated evidence related to the effectiveness and safety of ECT, convened a meeting of its Neurological Devices Advisory Panel to evaluate the effectiveness and safety of ECT devices, published a draft order on the reclassification of ECT devices and reviewed over 3,400 public comments related to the draft order. The American Psychiatric Association (APA) participated in this process by providing testimony at the Neurological Devices panel hearing and by submitting detailed [comments](#) on the draft order.^{iv}

The final order on the reclassification of ECT devices provides regulatory guidance on the statements that ECT device manufacturers can make about the uses of their products in the United States. Although the FDA clearly states that "FDA is not permitted to limit or interfere with the authority of a healthcare professional to administer any legally marketed device to a patient for any condition or disease within a legitimate clinician-patient relationship," a number of questions have arisen about the implications of the final order for clinicians, clinical researchers, patients and their families. This resource document is intended to address these questions.

Summary of the FDA Final Order

The FDA found that there was sufficient evidence for safety and effectiveness to categorize ECT devices within class II for depression and catatonia. Specifically, ECT devices are classified as class II devices "for the treatment of catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition."^v The FDA did not define treatment-resistance or specify who might require a rapid response due to the severity of their psychiatric or medical condition, leaving these definitions to the evaluating clinician.

The class II category permits device manufacturers to market ECT devices for the above diagnoses provided that "special controls" are used to assure safety and effectiveness. Special controls include device-related characteristics and specific requirements for product labeling.^{vi} With the reclassification of ECT devices to class II for the circumstances noted above, the FDA specifies a number of "controls," or

standards, for manufacturers to demonstrate related to technical aspects of the ECT device.^{vii} As an additional special control, the FDA also specifies that device manufacturers must list a number of items in their product labeling including:

- Information related to generic adverse events associated with ECT treatment
- Instructions to ECT device users on:
 - Pre-ECT medical and psychiatric assessment
 - Patient monitoring during the procedure
 - General anesthesia and neuromuscular blocking agent use
 - Mouth/dental protection during the procedure
 - EEG monitoring during an ECT-induced seizure to the point of seizure termination
 - Stimulus electrode placement, including adequate skin preparation and use of conductive gel
 - Cognitive status monitoring of the patient prior to beginning ECT and during the course of treatment
- Clinical training needed by users of the device
- Patient population in which the device is intended to be used
- Operation of the device and the typical course of treatment
- Validated methods and instructions for reprocessing of any reusable components
- A detailed summary of device technical parameters and clinical testing.

In addition to standard product labeling, the FDA can also require that patient labeling be developed by device manufacturers as a special control.^{viii} Medical device patient labeling can be developed in a number of formats (e.g., patient brochures, patient leaflets, user manuals, videotapes) and "informs patients or their lay caregivers about proper use, risks, and benefits of the device in language they can understand." Patient labeling materials are meant for use by patients or lay caregivers without professional input. They can also be used or suggested to patients or lay caregivers in the context of professionally delivered education, although such use is not required. In terms of patient labeling for ECT devices, the FDA directs manufacturers to include:

- Information on relevant contraindications, warnings, and precautions
- A summary of the clinical testing, including summaries of clinical outcomes, adverse events and complications that occurred with the device
- Information on how the device operates and the typical course of treatment
- Potential benefits and alternative treatments
- Known risks of treatment including disorientation, confusion and memory loss (short-term (anterograde) and long-term (autobiographical) memory loss following treatment
- Manic symptoms or a worsening of the psychiatric symptoms that are being treated
- Pain or somatic discomfort such as 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
- Cardiovascular complications and
- Death

The final order also specifies that both the product labeling and patient labeling are to include a warning that "ECT device use may be associated with disorientation, confusion, and memory problems." In addition, the final order specifies that labeling should note that "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."

In the FDA final order, ECT devices are noted to be in "Class III (premarket approval) for the following intended uses: schizophrenia, bipolar manic states, schizoaffective disorder, schizophreniform disorder, and catatonia or a severe MDE associated with MDD or BPD in: (i) Patients under 13 years or (ii) Patients 13 years and older who are not treatment-resistant or who do not require a rapid response due to the severity of their psychiatric or medical condition." A class III designation would also apply to any other indication, with the exception of depression or catatonia. Thus, before a device could be marketed for use in these other indications, a device manufacturer would need to submit a premarket approval application (PMA) and have it approved by the FDA.

Implications of the FDA Final Order

Clinical indications for ECT

The ability of a psychiatrist to treat patients who have a clinical indication for ECT is not affected by the class designation of ECT devices. The class II designation "for the treatment of catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition" is relevant to ECT device manufacturers in delineating the indications that they can include in their product marketing. The final order is quite specific in noting that "FDA is not permitted to limit or interfere with the authority of a healthcare professional to administer any legally marketed device to a patient for any condition or disease within a legitimate clinician-patient relationship" and that "FDA does not regulate off-label use of ECT by physicians." In this regard, "off-label" use of ECT is similar to "off-label" use of medications.

The FDA does note that "healthcare professionals should carefully consider all ECT device labeling, including potential adverse events, warnings, and medical conditions that can increase patient risk when deciding if ECT is appropriate for their patients, including those with comorbid conditions. The healthcare professional is responsible for providing appropriate ongoing medical management to mitigate any patient specific risks associated with comorbid conditions." Consequently, as with any patient for whom ECT is being recommended or administered,^{ix} the psychiatrist will want to document the rationale for ECT as well as the major target symptoms that ECT is intended to address and their severity. Similarly, the relevant benefits and risks of treatment as compared to other treatment options should be documented and reviewed with the patient as part of the informed consent process.^x In discussing potential benefits of treatment for "off-label" uses, discussion of the evidence can point to information from case series, observational studies and early studies of ECT that contribute to our knowledge on the treatment of these disorders, even though the effectiveness evidence reviewed by the FDA was not viewed as sufficiently robust to warrant inclusion of additional indications in class II. Expert consensus, as reflected in APA's 2001 ECT Task Force Report^{xi} and correspondence with the FDA,^{xii} also supports the clinical appropriateness of ECT in patients under age 13 and in individuals with schizophreniform disorder, schizophrenia, schizoaffective disorder, and manic episodes as well as in other clinical circumstances.

Concomitant physical health conditions

The documented safety of ECT^{xiii,xiv} and information on possible side effects of ECT treatment will not typically be affected by the patient's psychiatric diagnosis. When patients have concomitant physical health conditions that place them at increased risk of complications, including those conditions that are listed as warnings or contraindications in the device labeling, these should be discussed and documented in considering the benefits and risks of treatment.^{xv} Although there are no absolute contraindications to the use of ECT, an increase in risk may be associated with conditions such as severe or unstable cardiac, pulmonary or neurological disorders. For many such conditions, appropriate medical consultations, adjustments in the treatment technique or in the patient's medications during treatment may help in mitigating such risks.

Informed consent

A review of informed consent documents is suggested to determine whether any additions are needed. The sample consent documents that are available in APA's 2001 Task Force Report on The Practice of Electroconvulsive Therapy^{xvi} already incorporate the majority of the potential risks of ECT that the FDA has included in their requirements for device manufacturers related to product labeling. However, it may be warranted for informed consent documents to mention adverse reactions to anesthetic agents and neuromuscular blocking agents, delayed seizures, manic symptoms and worsening of psychiatric symptoms that are the focus of ECT treatment. Given the labelling warning about disorientation, confusion and memory problems, psychiatrists may also wish to review this section of their informed consent documents. It is also suggested that the informed consent be reviewed with the patient whenever risks and/or benefits of ECT substantively change as treatment proceeds or when treatments move from treating an acute episode to prophylactic or maintenance use. In addition, any State regulatory requirements regarding consent for ECT should also be followed. Patient labeling materials that have been developed by device manufacturers in response to the FDA final order are not required to be used; however, clinicians may find them to be useful as supplemental educational materials for patients and for families as part of the informed consent process.

Monitoring of cognitive effects of ECT

As part of the FDA's special controls noted above, device manufacturers are required to include suggested instructions for users of the device in the product labeling. Psychiatrists administering ECT should take these suggestions into account in regard to their ongoing practice. The recommendations for cognitive assessment in APA's 2001 ECT Task Force Report are consistent with the FDA labeling requirement for device manufacturers on "cognitive status monitoring prior to beginning ECT and during the course of treatment via formal neuropsychological assessment for evaluating specific cognitive functions (e.g., orientation, attention, memory, and executive function)." There are a number of formal (i.e., structured and systematic) approaches for assessing cognitive function that clinicians can use to fulfill these monitoring requirements. Although any formal approach can be used that assesses these cognitive domains, examples of commonly used scales include the Mini-Mental State Examination (MMSE)^{xvii, xviii} and the Montreal Cognitive Assessment (MoCA).^{xix, xx} The MoCA includes tasks related to orientation and memory as well as attention and executive function (trail making test, design copy, clock face, naming animals). It has been shown to be a highly sensitive screening instrument in severe mental illness^{xxi} and depression.^{xxii} In addition, the MOCA is highly correlated with the global cognitive score in patients with depression^{xxiii} and is sensitive to ECT-induced cognitive deficits in visuo-executive, memory and language.^{xxiv} If screening neuropsychological assessment identifies cognitive difficulties or changes in cognition with treatment, more detailed testing or adjustments to ECT treatment parameters can be considered.

Maintenance treatment

The importance of maintenance treatment following an acute course of ECT is implied by the FDA labelling requirement related to short-term symptom relief with ECT. The acute effects of ECT in relieving severe psychiatric symptoms are of crucial importance to patients and a major benefit of ECT treatment. Nevertheless, a significant fraction of patients who receive an acute ECT course may relapse even when treated with maintenance medication.^{xxv, xxvi, xxvii, xxviii} Thus, it is imperative that ECT be viewed as one component of a comprehensive approach to treatment that may also include pharmacotherapy, psychotherapy, and other somatic or psychosocial interventions. Furthermore, many patients may benefit from maintenance ECT^{xxix, xxx, xxxi} and the FDA leaves the use of maintenance ECT to the discretion of the treating psychiatrist.

Training for ECT practitioners

Recommendations for training in ECT have been outlined in the APA's 2001 ECT Task Force Report, which emphasized the importance of didactic instruction related to ECT as well as directly supervised

clinical experience in evaluating patients for ECT, obtaining informed consent, determining the optimal electrode placement and stimulus parameters for the individual patient, determining the number and frequency of ECT treatments, assessing for therapeutic outcomes, identifying adverse effects of treatment, and providing post-ECT management. Ongoing participation in continuing medical education activities related to ECT is important for keeping knowledge and skills about ECT up to date.

Investigational device exemptions for ECT-related research

For psychiatrists who are also involved in research related to ECT, prospective studies on indications not listed in class II will need to follow FDA rules regarding investigational device exemptions (IDEs).

Obtaining additional information

If other questions arise related to the implications of the FDA final order for psychiatrists and for patients, these can be directed to the Practice Management Helpline at (800) 343-4671.

Summary

- The FDA reclassification of ECT devices provides device manufacturers with regulatory guidance on the statements that they can make about uses of their products in the United States.
- The ability of a psychiatrist to treat patients who have a clinical indication for ECT is not affected by the re-classification of ECT devices, because the FDA cannot limit or interfere with the authority of a healthcare professional to administer any legally marketed device to a patient for any condition or disease within a legitimate clinician-patient relationship.
- As part of the informed consent process, ECT practitioners should continue to discuss and provide education to patients and families about the benefits and risks of ECT, including factors such as concomitant physical health conditions that may influence treatment planning. A review of informed consent documents is suggested to determine if any revisions are indicated.
- Formal neuropsychological assessment of specific cognitive functions (e.g., orientation, attention, memory, and executive function) before, during and after an ECT course can be accomplished using any structured and systematic scale that assesses these domains. Examples include, but are not limited to, the MMSE and the MOCA.
- It is imperative that acute and maintenance treatment with ECT be viewed as one component of a comprehensive approach to care that may also include pharmacotherapy, psychotherapy and other somatic or psychosocial interventions.

ⁱ Food and Drug Administration. Neurological devices; Reclassification of electroconvulsive therapy devices; effective date of requirement for premarket approval for electroconvulsive therapy devices for certain specified intended uses. Accessed on January 16, 2019 at

<https://www.federalregister.gov/documents/2018/12/26/2018-27809/neurological-devices-reclassification-of-electroconvulsive-therapy-devices-effective-date-of#footnote-1-p66103>

ⁱⁱ U.S. Department of Health and Human Services. Food and Drug Administration. Overview of Medical Device Classification and Reclassification. Accessed on January 31, 2019 at <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm378714.htm>

ⁱⁱⁱ Federal Food, Drug, and Cosmetic Act. Sections 513 and 515(i)(2) (21 U.S.C. 360).

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- ^{iv} Letter from the American Psychiatric Association to Commissioner Robert M. Califf, M.D. of the U.S. Food and Drug Administration dated March 10, 2016. Accessed on January 31, 2019 at <https://www.regulations.gov/document?D=FDA-2014-N-1210-0908>.
- ^v Federal Food, Drug, and Cosmetic Act. 21 CFR Part 882.5940 (b)
- ^{vi} U.S. Department of Health and Human Services. Food and Drug Administration. Regulatory Controls. Medical Devices. Accessed on January 16, 2019 at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/GeneralandSpecialControls/ucm2005378.htm#special>
- ^{vii} Federal Food, Drug, and Cosmetic Act. 21 CFR Part 882.5940 (b)
- ^{viii} U.S. Department of Health and Human Services. Food and Drug Administration. Center for Devices and Radiological Health. Guidance on Medical Device Patient Labeling; Final Guidance for Industry and FDA Reviewers. Issued on April 19, 2001. Accessed on January 31, 2019 at <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM070801.pdf>
- ^{ix} American Psychiatric Association. The Practice of Electroconvulsive Therapy Recommendations for Treatment, Training, and Privileging (A Task Force Report of the American Psychiatric Association). 2nd Ed. Washington DC: American Psychiatric Association, 2001
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- ^{xi} American Psychiatric Association. The Practice of Electroconvulsive Therapy Recommendations for Treatment, Training, and Privileging (A Task Force Report of the American Psychiatric Association). 2nd Ed. Washington DC: American Psychiatric Association, 2001
- ^{xii} Letter from the American Psychiatric Association to Commissioner Robert M. Califf, M.D. of the U.S. Food and Drug Administration dated March 10, 2016. Accessed on January 31, 2019 at <https://www.regulations.gov/document?D=FDA-2014-N-1210-0908>.
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- ^{xv} American Psychiatric Association. The Practice of Electroconvulsive Therapy Recommendations for Treatment, Training, and Privileging (A Task Force Report of the American Psychiatric Association). 2nd Ed. Washington DC: American Psychiatric Association, 2001
- ^{xvi} American Psychiatric Association. The Practice of Electroconvulsive Therapy Recommendations for Treatment, Training, and Privileging (A Task Force Report of the American Psychiatric Association). 2nd Ed. Washington DC: American Psychiatric Association, 2001
- ^{xvii} Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975 Nov;12(3):189-98.
- ^{xviii} The MMSE is copyrighted and information about use, including administration instructions and alternative versions, can be accessed at <https://www.parinc.com/Products/Pkey/238>.
- ^{xix} Montreal Cognitive Assessment. Accessed on January 16, 2019 at <https://www.mocatest.org/>
- ^{xx} The MoCA is copyrighted and users can register to use the MoCA without charge at <https://www.mocatest.org/>. This website also provides information on administration instructions and alternative versions.

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