1. To inform the FDA’s decision on reclassification, the key risks presented by ECT must be identified, and a determination must be made regarding how and whether sufficient information exists to establish controls to mitigate those risks. The FDA has identified the following key risks of ECT (in alphabetical order) in the FDA’s review of the Public Docket, the Manufacturer Docket, the Manufacturer and User Facility Device Experience (MAUDE) Database, and in FDA’s literature review:
   
a. Adverse reaction to anesthetic agents/neuromuscular blocking agents  
b. Alterations in blood pressure  
c. Cardiovascular complications  
d. Cognition (disorientation and confusion)  
e. Death  
f. Dental/oral trauma  
g. Device malfunction  
h. Memory dysfunction (particularly retrograde autobiographical memory, anterograde memory)  
i. Pain/somatic discomfort  
j. Physical trauma  
k. Prolonged seizures  
l. Pulmonary complications  
m. Skin burns  
n. Stroke

Is this a complete and accurate list of the most significant risks presented by ECT? Comment on whether you disagree with inclusion of any of these risks, or whether you believe any other risks are among the most significant risks presented by ECT.

2. Below are potential regulatory controls FDA could apply to ECT to mitigate medical/physical risks of ECT (i.e. adverse reaction to anesthetic agents/neuromuscular blocking agents, alterations in blood pressure, cardiovascular complications, death, dental/oral trauma, pain/somatic discomfort, physical trauma, prolonged seizures, pulmonary complications, skin burns, stroke):

   a. Restricting ECT device use to physicians with specific training and/or experience with the administration of ECT;

   b. Physician labeling recommendations for:

      i. pre-ECT assessment (including pertinent history, physical examination, EKG, echocardiogram, chest x-ray, pulmonary function tests, lab tests, and neuroimaging)
ii. ECT procedure monitoring (including EKG, blood pressure, pulse, respiratory rate and oxygen saturation)

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

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

v. Electroencephalography (EEG) monitoring during and after the procedure

vi. Adequate skin preparation and the use of conductivity gel during electrode placement

c. Patient labeling requiring use of a checklist of all known risks of ECT, with each item to be signed off by both patient and physician prior to initiating treatment

d. Requirement for further premarket studies (either pre-clinical [bench, animal] or clinical) for significant changes in device technology or new indications for use (IFU)

Please discuss each of these potential controls and whether it, either alone or in combination with others, adequately mitigates the medical/physical risks of ECT.

3. Below are potential regulatory controls FDA could apply to ECT to mitigate risks of adverse cognitive and memory effects (especially with respect to anterograde and retrograde memory functioning):

a. Physician labeling recommendations for:
   i. Exclusive use of brief pulse (1-1.5 msec) waveform stimulus
   ii. Use of ultrabrief pulse (0.3 msec) stimulus
   iii. Exclusive use of unilateral nondominant electrode placement
   iv. Use of bifrontal electrode placement
   v. Limiting frequency of treatment to a maximum of twice weekly during a course of ECT
   vi. Monitoring cognitive status prior to ECT and throughout the course of treatment

b. Patient labeling requiring use of a checklist of all known risks of ECT, with each item to be signed off by both patient and physician prior to initiating treatment.

c. Requirement for further premarket studies (either pre-clinical [bench, animal] or clinical) for significant changes in device technology or new IFU

Please discuss each of these potential controls and whether it, either alone or in combination with others, adequately mitigates the cognitive and memory risks of ECT.
4. Regarding neuropathological changes, the manufacturer and public dockets both indicated “brain damage” as a potential risk associated with ECT. However, FDA’s review of the literature did not identify evidence of gross anatomical, histological, or immunohistochemical evidence, or evidence from biomarkers of injury, to support this association. Please discuss whether the existing clinical data support brain damage as a potential risk of ECT and if so, how this risk can be mitigated.

5. Currently cleared IFUs for ECT devices include the following:

   a. Depression (unipolar and bipolar)
   b. Schizophrenia
   c. Bipolar manic (and mixed) states
   d. Schizoaffective disorder
   e. Schizophreniform disorder
   f. Catatonia

Please provide your overall recommendation for the classification (Class II or III) of the ECT device for each of the above indications.