



# FDA Perspective: Regulatory Considerations for Digital Mental Health Therapeutics

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# Current Digital Mental Health Therapeutics

21 CFR 882.5801 - Computerized behavioral therapy device for psychiatric disorders - Rx only	
reSET	Substance use disorders (not currently on opioid replacement therapy, do not abuse alcohol solely, or do not abuse opioids as primary substance of abuse)*
reSET-O	Increase retention of patients with opioid use disorder in outpatient treatment as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management*
Somryst	Chronic insomnia*
MamaLift Plus	Mild to moderate postpartum depression*
Rejoyn	Major Depressive Disorder (MDD) symptoms (on antidepressant medication)*
Daylight	Generalized anxiety disorder*
21 CFR 882.5803 - Digital therapy device for Attention Deficit Hyperactivity Disorder	
EndeavorRX	Improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined type Attention Deficit and Hyperactivity Disorder (ADHD)*
EndeavorOTC	Improve attention function as measured by computer-based testing in patients 18 and older with primarily inattentive or combined type ADHD, who have a demonstrated attention issue*
Prismira	Improve attention function in adults ages 22-55 years old with primarily inattentive or combined-type ADHD*

21 CFR 882.5801, 2025, <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-882/subpart-F/section-882.5801>  
 21 CFR 882.5803, 2025, <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-882/subpart-F/section-882.5803>  
 FDA 510(k) Database, 2025 (<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm>)

\*Note: This is not the complete indication for use statement.

# Special Controls for Current Regulations

Risk	Special controls (Mitigation measures)
<b>21 CFR 882.5801</b>	
Ineffective treatment, leading to worsening condition	Clinical performance data Software verification, validation, and hazard analysis Labeling
Software failure leading to delayed access	Software verification, validation, and hazard analysis Labeling
Use error or improper device use	Labeling
<b>21 CFR 882.5803</b>	
Ineffective treatment, leading to worsening condition	Clinical performance testing Labeling
Device software failure leading to delayed access	Clinical performance testing Labeling
Treatment results in: <ul style="list-style-type: none"> <li>- Frustration, emotional reaction, dizziness, nausea, headache, eye-strain, or joint pain</li> <li>- Seizure</li> <li>- Screen addiction</li> <li>- Decreased sleep quality</li> </ul>	Clinical performance testing Software verification, validation, and hazard analysis Labeling

De Novo Classification Request for ReSet, 2017, [https://www.accessdata.fda.gov/cdrh\\_docs/reviews/DEN160018.pdf](https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160018.pdf)

De Novo Classification Request for EndeavorRX, 2020, [https://www.accessdata.fda.gov/cdrh\\_docs/reviews/DEN200026.pdf](https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN200026.pdf)

# Evidence Considerations

## RCT

- Reasonable control arm
- Best practices for blinding

## Subject selection criteria

- Adequate criteria to define the intended patient population

## Study endpoints

- Appropriate outcome measures
- Defined endpoints

## Study duration

- Appropriate timeframe to demonstrate clinical benefit

# Benefit Considerations: GenAI-enabled Digital Mental Health Therapeutics

- Effective treatment for mental health conditions or symptoms
- Level of evidence to show clinically significant results for a mental health condition or symptoms under the conditions of use (e.g., adjunctive vs. standalone)
- Unique device specific considerations for generative AI enabled digital mental health therapeutics
- Use with or without oversight of a health care provider

# Risk Management Process

- AAMI/ANSI/ISO 14971:2019
- Medical Devices- Application of Risk Management to Medical Devices

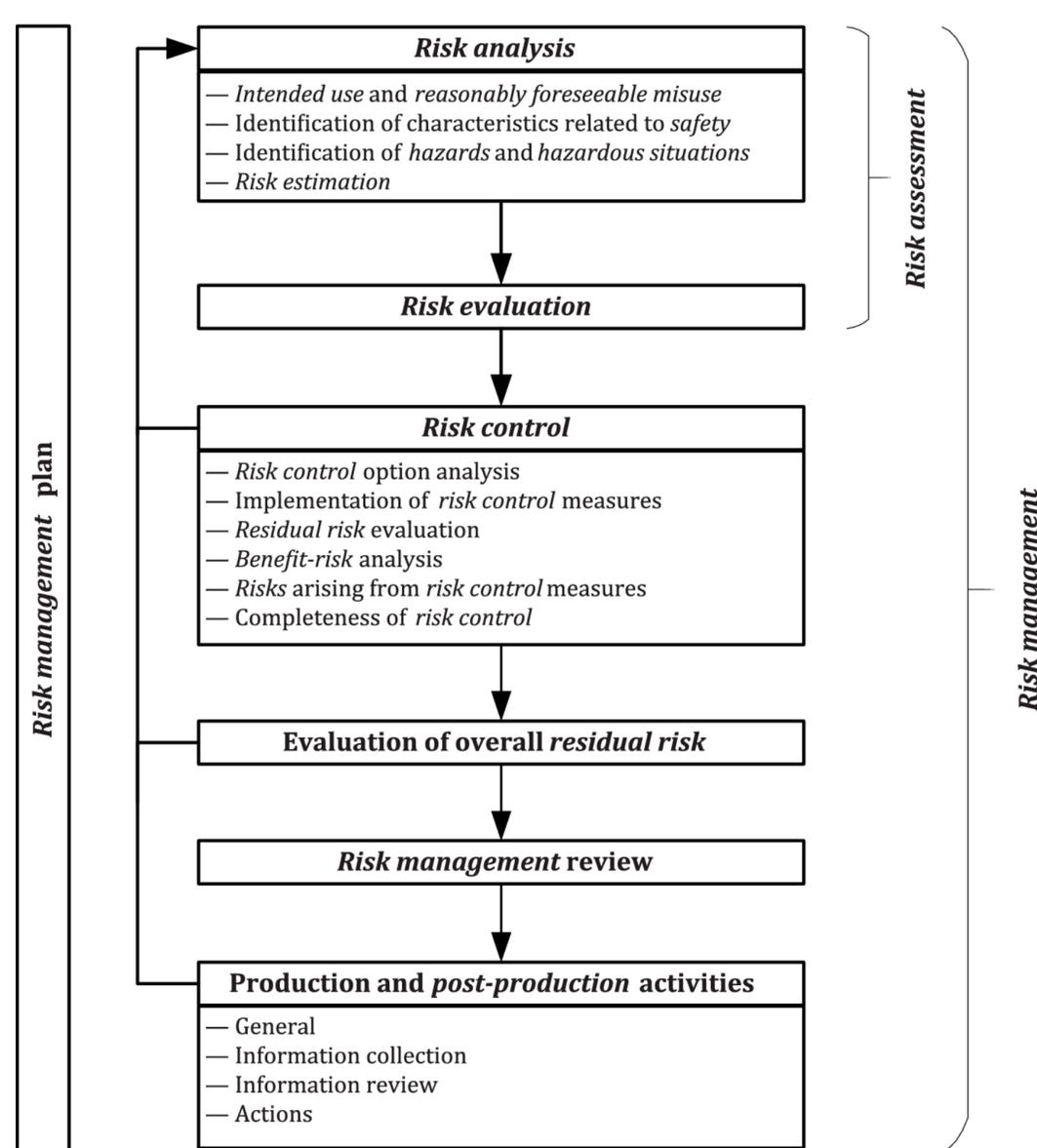


Figure 1 — A schematic representation of the risk management process

# Examples of Risk Considerations

Risk Management – GenAI Enabled Digital Mental Health Therapeutics (EXAMPLES)			
Hazard	Hazardous Situation	Clinical Harm	Risk Control
<ul style="list-style-type: none"> <li>Missed crisis identification or inadequate response</li> </ul>	<ul style="list-style-type: none"> <li>Missed or delayed diagnosis of crisis</li> <li>Inadequate or inappropriate response to suicide, physical harm, or harm to others</li> <li>Failure to report a patient’s potential harm to others</li> </ul>	<ul style="list-style-type: none"> <li>Death/Suicide</li> <li>Physical harm to self</li> <li>Harm to others</li> </ul>	Examples: <ul style="list-style-type: none"> <li>Crisis escalation plan</li> <li>Automatic emergency detection/ management module</li> </ul> <p style="text-align: center;">?</p>
<ul style="list-style-type: none"> <li>Misidentification of medical symptoms</li> </ul>	<ul style="list-style-type: none"> <li>Failure to identify general medical conditions that mimic mental health symptoms</li> <li>No in person physical exams or assessments by a clinician</li> </ul>	<ul style="list-style-type: none"> <li>Medical condition goes untreated</li> <li>Worsening of the medical condition</li> <li>Deterioration of biological systems</li> </ul>	?
<ul style="list-style-type: none"> <li>Inadequate or incorrect clinical therapeutic content or guidance</li> </ul>	<ul style="list-style-type: none"> <li>Improper or inadequate therapeutic content provided (potentially due to hallucination/confabulation)</li> <li>Failure to recognize clinically significant symptom worsening</li> <li>Inadequate adjustment to symptom changes</li> <li>Patient does not comply with clinician prescribed treatment plan</li> </ul>	<ul style="list-style-type: none"> <li>Worsening of mental health disorder or symptoms</li> <li>Suicide or self-harm</li> </ul>	?

# Risk Controls, Mitigations, Testing and Monitoring

- Risk mitigations during device development/product lifecycle
  - Best practices focused on mental health indications
  - Human Factors
    - Understand how patients and clinicians use the device
    - Iterative testing with intended users
  - Safety by design
    - Model input, model training, reinforcement and fine-tuning strategies (noting training level of human therapists, if utilized), model specification, system prompts
    - Risk escalation plans (e.g., 988, when a human/therapist may be notified)
- Verification & Validation of risk control measures
  - Benchmark testing, unit testing, red teaming, human factors
  - Clinical performance testing
- Post-market monitoring

