DE NOVO CLASSIFICATION REQUEST FOR reSET

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Computerized behavioral therapy device for psychiatric disorders. A computerized behavioral therapy device for psychiatric disorders is a prescription device intended to provide a computerized version of condition-specific behavioral therapy as an adjunct to clinician supervised outpatient treatment to patients with psychiatric conditions. The digital therapy is intended to provide patients access to therapy tools used during treatment sessions to improve recognized treatment outcomes.

NEW REGULATION NUMBER: 21 CFR 882.5801

CLASSIFICATION: II

PRODUCT CODE: PWE

BACKGROUND

DEVICE NAME: reSET

SUBMISSION NUMBER: DEN160018

DATE OF DE NOVO: May 16, 2016

CONTACT: Pear Therapeutics, Inc.
745 Atlantic Ave.
Boston, MA 02111

INDICATIONS FOR USE

reSET is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician. reSET is indicated as a 12 week (90 days) prescription-only treatment for patients with substance use disorder (SUD), who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse. It is intended to:

- increase abstinence from a patient's substances of abuse during treatment, and
- increase retention in the outpatient treatment program.

LIMITATIONS

For prescription use only.

The reSET device is not intended to be used as a stand-alone treatment device or to be used as a substitute for medication.

The reSET was not demonstrated to be effective for patients reporting opioids as their primary substance of abuse.

The safety and effectiveness of reSET has not been established in patients enrolled in opioid treatment programs.

The benefit of treatment with reSET on abstinence was not evaluated beyond 12 weeks of treatment. The ability of reSET to prevent potential relapse after treatment discontinuation has not been studied.

Patients in the control arm of the supporting clinical trial, who were treated with typical outpatient therapy, were not eligible to receive contingency management incentives that patients treated with the desktop-based version of reSET received. The benefit of reSET without the use of contingency management incentives has not been evaluated.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

reSET™ is a digital therapy comprised of a patient application and clinician dashboard intended to deliver cognitive behavioral therapy (CBT) to patients with SUD to increase abstinence from substance use and increase retention in outpatient therapy programs. CBT is a psychosocial intervention that aims to change a patient's thinking and behavior, and it has been studied in psychiatric disorders such as major depressive disorder (*Psychiatr Clin North Am.* 2010; 33: 537–55). reSET is based on a specialized version of CBT known as the community reinforcement approach (CRA), which was originally developed for alcohol dependence and cocaine use (*Behav Res Ther.* 1973; 11:91-104; *Exp. Clin. Psychopharmacol* 2000; 3:205–2). The community reinforcement incorporates a range of therapeutic modalities including CBT to make substance-free lifestyle rewarding, skill building to promote behavioral change, and contingency management to reward and incentivize abstinence and replace the satisfaction obtained from substance abuse. CBT and CRA are considered valid models for substance abuse therapy and other psychiatric disorders.

reSET consists of several therapy lessons (modules) that are intended to teach the user the following skills to aid in the treatment of substance use disorder:

- Identifying situations and triggers that make substance use more likely
- Avoiding substance use,

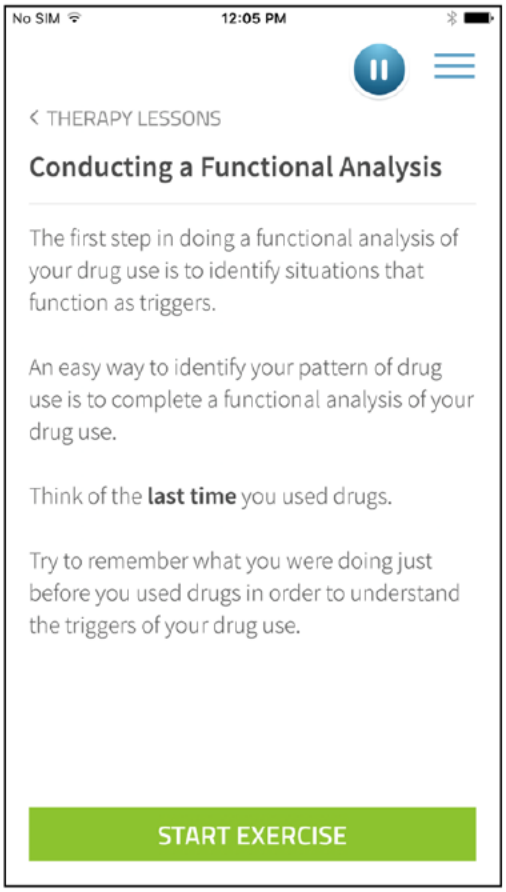
- Coping with thoughts about substance use,
- Recognizing negative thinking and identifying techniques to move to positive thinking
- Making decisions about substance use
- Taking responsibility for choices made and evaluating the consequences of those choices

Each therapy lesson is comprised of a cognitive behavioral therapy component and skill building exercises related to the above areas. The content of the therapy lessons is delivered primarily via text, and may include videos, animations and graphics. All text and video within reSET is narrated in English.

Following most therapy lessons, the patient undergoes fluency learning, a method of questioning that intended to promote learning and improve both short-term and long-term retention of material. Within the fluency learning section of reSET, patients are asked between 4-10 multiple choice and fill-in-the-blank questions about the key concepts presented in the lesson. An example of screenshots from the device is provided in the figure below.

Figure 1: Example of reSET's multiple choice questions

A



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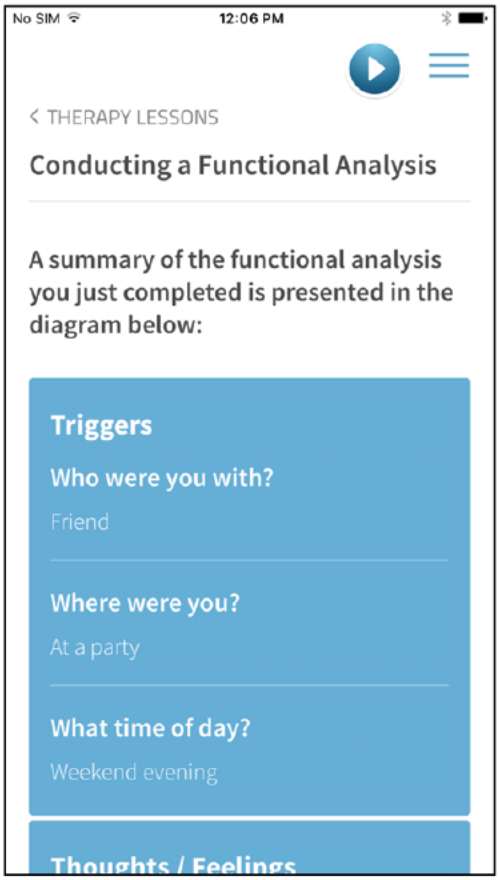

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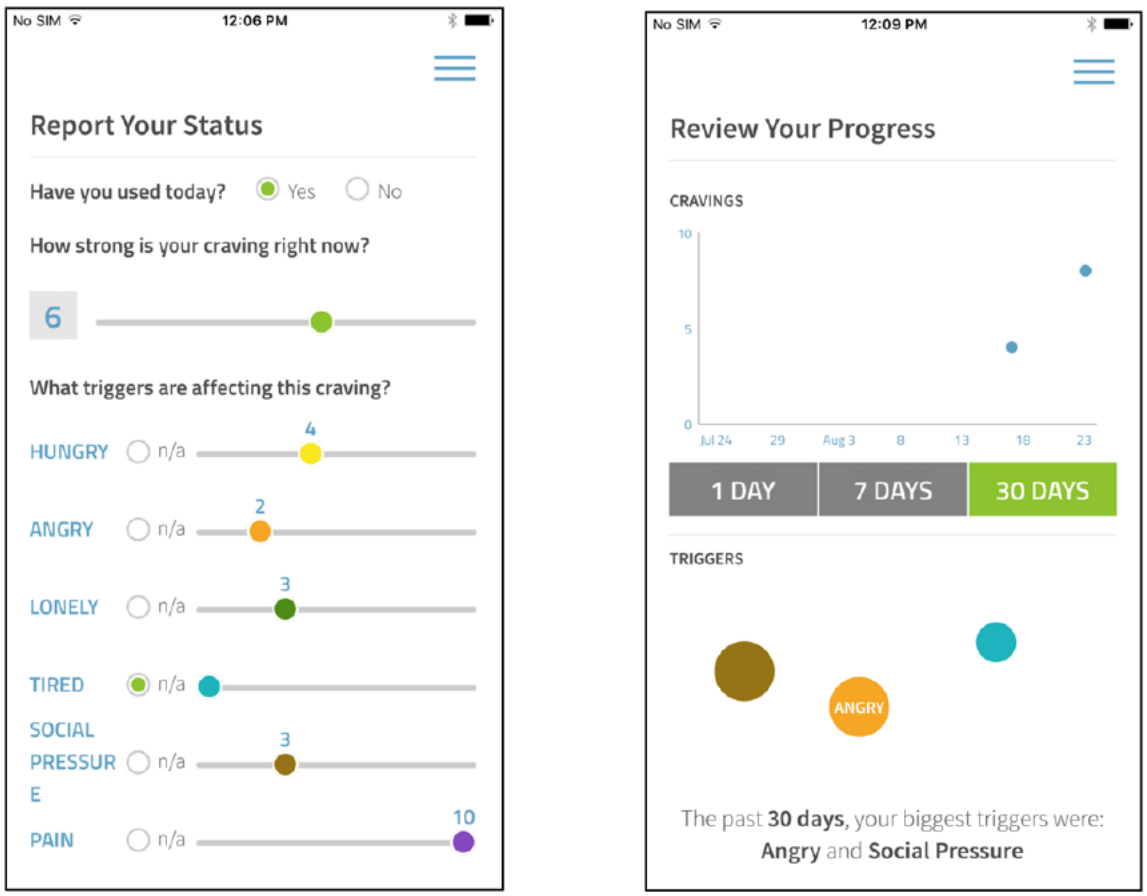


Figure 1. The reSET® device. A. Screencap showing the first screen of the "Conducting a Functional Analysis" core therapy lesson. This therapy lesson contains an interactive exercise intended to help patients analyze and better understand their patterns of drug use. **B.** Summary screen from the "Conducting a Functional Analysis" core therapy lesson. This screen displays patient-entered answers to questions that are asked during the interactive exercise within the module. **C.** Report Your Status screen. Patients can choose to report whether they have used on a given day and record any cravings and triggers. **D.** Review your Progress screen. Patients can review their self-reported cravings and triggers over a 1, 7, or 30-day time-period.

When a question is answered incorrectly, the patient is presented with the correct response and the question is recycled back into the queue and asked again. In order to successfully complete the fluency learning section, patients must answer each question correctly three times, providing a repetitive component that reinforces concept mastery. If the patient completes the lesson and demonstrates proficiency, they can "spin the wheel" for virtual rewards that may be incorporated into a contingency management program at the treating physician's clinic.

Therapy Lessons

reSET is comprised of 62 lessons, including one on-screen User Guide that explains how to use the reSET app and 61 therapy lessons. When a patient uses reSET for the very first time, he or

she must step through the User Guide session to ensure they understand how to use the app. The 61 therapy lessons are split into 31 core therapy lessons and 30 supplemental therapy lessons. The therapy lessons include categories related to life skills, treatment, mood matters, social connections, sexual health, and hepatitis C and HIV**.**

The therapy lessons in the core therapy lesson group are focused on building basic cognitive behavioral and relapse prevention skills (e.g., functional analysis of drug use and self-management planning, drug refusal skills). The therapy lessons in the supplemental group cover a range of topics that can be relevant for patients with SUD such as managing relationships, building communication skills, and time management. They also provide more in-depth training on HIV, hepatitis and STI prevention as well as support for those patients living with HIV and Hepatitis C.

Once the initial User Guide lesson has been completed, the patient gains access to the next core therapy lesson. In the core therapy lessons, a patient can only advance to the next lesson after successfully completing the prior lesson. At any time, patients can choose to review a completed lesson. Once a patient successfully completes all the core therapy lessons, they gain access to all the supplemental therapy lessons. These lessons do not have a set order of completion, and patients can choose lessons that are relevant to managing their disease or as recommended by their clinician.

reSET recommends that patients should complete 4 lessons per week. Each lesson is intended to take between 10-20 minutes to complete. Therapy lesson lengths vary, as do the number of fluency assessment questions the patient must take at the end of a lesson. Some therapy lessons have optional worksheets for the patient to complete that are intended to help the patient understand the key concepts taught in the therapy lesson.

The reSET application allows patients to track their their own progress on the device's therapy modules. The device additionally has a Patient Self Report interface that allows for patients to track their cravings and substance use. This information is available to the patient's treating physician through the device.

Clinician use

The clinician dashboard for reSET displays the patient's progress. The clinician can view which therapy lessons the patient has completed, as well as view patient-reported substance use, cravings and triggers. The reSET app automatically pushes an assessment every four days to ask if the patient has taken any drugs or alcohol in the past 4 days, and if so, on which days. The patient is also asked to report whether they have had any cravings for drugs and alcohol and if so, to rate the intensity of the cravings. This reSET initiated, self-report data will display on the clinician's dashboard. Patients may also log their drug and alcohol use at any time into reSET along with tracking their cravings and distinct triggers. These use, craving and trigger data are presented to the clinician. The clinician can also enter in-clinic data inputs such as urine drug screens and appointment attendance.

Contingency management

reSET is intended be used in conjunction with a contingency management incentives system. reSET provides virtual "rewards" when the patient completes a lesson successfully as well as when their urine drug screen, or other objective test, is negative for substances. Clinics may convert the virtual "rewards" into tangible rewards according to their own procedures.

SUMMARY OF NONCLINICAL/BENCH STUDIES

SOFTWARE

The De Novo request provided appropriate software documentation consistent with a "Moderate" level of software concern as discussed in the FDA Guidance Document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005.

Software validation and verification testing demonstrated that the device met its design, implementation, and cybersecurity requirements.

SUMMARY OF CLINICAL INFORMATION

A multi-site, un-blinded, randomized clinical trial (National Institute of Drug Abuse CTN0044) was conducted to characterize reSET's probable benefits and risks.

Study overview

Study participants received 12 weeks of either treatment as usual (TAU), reflecting standard treatment at each site, or reduced TAU supplemented with a desktop-based version of reSET, which could be accessed at the clinic or at home (rTAU + reSET). Randomization was stratified by site, primary substance of abuse of stimulant/non stimulant, and abstinence/non-abstinence at baseline.

Inclusion criteria

- Male and female patients (≥ 18 years) accepted for outpatient, substance abuse treatment at a participating community treatment program (CTP) study site.
- Self-report any substance use problem, including alcohol as long as they also report other substance use in addition to alcohol.
- Report use of a drug of abuse within 30 days prior to screening or (2) have exited a controlled environment (e.g., detoxification unit, hospital, or correctional facility) within 30 days of screening and report use of a drug of abuse within 60 days prior to screening.
- Participants must be within the first month of initiating treatment at a collaborating CTP to ensure that scheduled psychosocial interventions can be initiated early on in treatment for all participants.
- Self-report a planned substance abuse treatment episode of at least 3 months.

- Participants with prior substance abuse and/or psychiatric treatment episodes were not excluded.

Exclusion criteria

- Individuals were excluded if they were participants in Opioid Treatment Programs (OTPs) and/or receiving opioid replacement medication, as TAU differs considerably in OTPs relative to other outpatient programs. If participants in CTPs received some non-opioid pharmacotherapy for their substance use disorder or psychiatric disorder, this was systematically tracked and considered in planned analyses as appropriate.
- Individuals were excluded if they planned to move out of the area within 3 months.
- Individuals were excluded if they had insufficient ability to provide informed consent to participate.
- Individuals were excluded if they lacked sufficient ability to use English to participate in the consent process, the interventions or assessments

Treatment

- *Treatment as Usual (TAU)*: patients in the TAU arm received standard treatment provided by each collaborating CTP. All CTPs included in the study routinely offered group or individual therapy sessions at least twice a week. Therapy sessions were between 2-3 hours in duration for an estimated 4-6 hours per week. No contingency management incentives were included in this arm. Participants were asked to provide urine drug and breath alcohol tests at each twice-weekly visit

- *Reduced TAU (rTAU) + reSET*: patients in the rTAU + reSET arm received reduced TAU and reSET. TAU was identical to that described above; however, reSET reduced face-to-face therapy session of TAU by 2 hours per week. Participants randomized to the reSET + rTAU arm were asked to complete a minimum of 2 modules of reSET per visit for a minimum aggregate of 4 modules per week. Participants were asked to complete all 32 core modules during weeks 1-8 of treatment. During weeks 9- 12, participants were asked to select from the 30 supplemental modules. They were also able to repeat any of the core modules during this time.

- Patients in the rTAU + reSET cohort were eligible to receive contingency management rewards for module completion and negative drug screens. Patients in the TAU cohort were not eligible to receive these rewards.

Primary outcome measures

- *Abstinence at weeks 9-12*: abstinence from all drugs of abuse and heavy drinking days (5 or more drinks per day for men, 4 or more for women) in the interval between the two biweekly study visits, measured in "half week" intervals. Both self-report and urine drug screens were used to measure abstinence. Urine drug screen results were interpreted as follows:

Table 1: Urine drug screen interpretations. Timeline follow-back (TLFB) represents patient self-reported substance use since the time of last assessment.

		Urine Drug Screen		
		Positive	**Negative**	**Missing**
Self Report	**Positive**[a]	+	+	+
	Negative[b]	+	-	Missing
	Missing[c]	+	Missing	Missing

[a] Positive self report indicates ≥1 reported non-abstinent day in the half-week.

[b] Negative self report indicates all days in the half-week were reported abstinent.

[c] Self report is missing if there is no TLFB data for ≥1 day in the half-week.

- *Retention in outpatient therapy:* the time to drop-out from treatment, treated as time-to-event data (time until last face to face contact).

Analysis cohorts

- Cohort 1: All comers
- Cohort 2: Excluding patients who reported opioids as their primary substance of abuse
- Cohort 3: Excluding patients with any opioid use during the trial

Table 2: Analysis cohort sample sizes

SAMPLE SIZES	TAU	rTAU + reSET	Total
Cohort 1: all comers	252	255	507
Cohort 2: excluding primary opioids	193	206	399
Cohort 3: excluding all opioids	153	152	305

Results

- *Abstinence*: Abstinence rates were determined for weeks 9-12 using repeated measures logistic Generalized Estimating Equations (GEE) model with factors for treatment, time and treatment X time ("treatment times time") interaction. Missing data were treated as failures. The analysis results of abstinence for cohort 1 and 2 are presented below, additionally compared by abstinence at baseline. The abstinence analyses were completed in the context of a GEE model that incorporates within-subject variability across the observation window and estimates abstinence at specified time points based on the model the analyses yields percentages rather than absolute numbers. The number of patients reported in the table below represents the number of patients in that entire group (e.g., N=252 patients in Cohort 1 were in the TAU group overall; N=139 patients were abstinent at baseline in the Cohort 1 TAU group).

Table 3: Abstinence rates in Cohorts 1 (N=507) and 2 (N=399)

Abstinence	Cohort 1 (All Comers)			Cohort 2 (Excluding Primary Opioids)		
Abstinence Weeks 9-12	**TAU**	**rTAU + reSET**	**p value**	**TAU**	**rTAU + reSET**	**p value**
Overall	16.0% (252)	29.7% (n=255)	0.0076	17.6% (193)	40.3% (206)	0.0004
Abstinent at baseline	40.9% (139)	54.1% (n=136)	0.0961	45.7% (102)	65.1% (105)	0.0170
Non-abstinent at baseline	3.0% (113)	10.1% (n=119)	0.0099	3.2% (91)	16.1% (101)	0.0013
Consecutive Abstinent half-weeks (overall) - mean	2.8 (252)	4.9 (n=255)	0.0005	2.8 (193)	5.2 (206)	0.0006
Total Abstinent half-weeks (overall) - mean	8.6 (252)	10.9 (n=255)	0.0019	8.8 (193)	11.9 (206)	0.0003

Patients who received rTAU + reSET had statistically significant increased odds of remaining abstinent at the end of treatment:

Cohort 1: Odds ratio=2.22, 95% CI (1.24, 3.99); p=0.0076
Cohort 2: Odds ratio=3.17, 95% CI (1.68, 5.99); p=0.0004.

Cohort 3 (all opioids excluded, N=153 TAU, N=152 rTAU+reSET) had similar abstinence to cohorts 1 and 2, with abstinence rates in the rTAU + reSET arm of 38.5% compared to 17.5% in the TAU arm (Odds Ratio=2.95, 95% CI=1.43, 6.09, p=0.0034).

- *Abstinence: patients who were abstinent at baseline:* Patients who were abstinent at baseline were significantly more likely to remain abstinent throughout the study than patients who were not abstinent at baseline for both patients who received TAU and patients who received rTAU + reSET.

Table 4: Subgroup analysis, abstinence rates in patients who were abstinent at baseline for Cohort 1 (N=507, all comers),

Endpoint	Time Point	rTAU + reSET (n=136)	TAU (n=139)	Odds Ratio (95% CI)	P-value*
Abstinence: Abstinent at Baseline	Week 9-12	54.1%	40.9%	1.70 (0.91, 3.18)	0.0961
Endpoint	**Time Point**	**rTAU + reSET (n=119)**	**TAU (n=113)**	**Odds Ratio (95% CI)**	**P-value***
Abstinence: Non-Abstinent at Baseline	Week 9-12	10.1%	3.0%	3.59 (1.36, 9.48)	0.0099

Table 5: Subgroup analysis, abstinence rates in patients who were abstinent at baseline for Cohort 2 (N=399, excluding primary opioids)

Endpoint	Time Point	rTAU + reSET (n=105)	TAU (n=102)	Odds Ratio (95% CI)	P-value*
Abstinence: Abstinent at Baseline	Week 9-12	65.1%	45.7%	2.22 (1.15, 4.27)	0.017
Endpoint	**Time Point**	**rTAU + reSET (n=101)**	**TAU (n=91)**	**Odds Ratio (95% CI)**	**P-value***
Abstinence: Non-Abstinent at Baseline	Week 9-12	16.1%	3.2%	5.74 (1.99, 16.60)	0.0013

Table 6: Abstinence subgroup analysis, abstinence rates in patients who were abstinent at baseline for Cohort 3 (N=305, excluding all opioids)

Endpoint	Time Point	TAU (n=84)	rTAU + reSET (n=80)	Odds Ratio (95% CI)	p-value*
Abstinence: Abstinent at Baseline	Week 9-12	41.5%	68.8%	3.11 (1.49, 6.52)	0.0026
Endpoint	**Time Point**	**TAU (n=69)**	**rTAU + reSET (n=72)**	**Odds Ratio (95% CI)**	**p-value***
Abstinence: Non-Abstinent at Baseline	Week 9-12	3.7%	10.4%	3.04 (0.89, 10.43)	0.0765

Abstinence analysis by primary substance is shown below for all comers (Cohort 1). Patients who primarily abused opioids did not show an abstinence benefit with reSET.

Table 7: Abstinence rates by primary substance of abuse, with missing data treated as failures (Cohort 1)

Primary Substance (total n)	TAU (n=250)	rTAU+reSET (n=247)	Odds Ratio (95% CI)	p-value[2]
Alcohol (n=104)	n=46	n=58		
Abstinence rates (Weeks 9-12)	32.2%	53.9%	2.45 (0.86, 6.98)	0.0925
Cocaine (n=102)	n=49	n=53		
Abstinence rates (Weeks 9-12)	16.5%	36.7%	2.93 (1.00, 8.62)	0.0510
Marijuana (n=114)	n=60	n=54		
Abstinence rates (Weeks 9-12)	12.3%	24.4%	2.31 (0.82, 6.48)	0.1118
Stimulants (n=69)	n=36	n=33		
Abstinence rates (Weeks 9-12)	42.2%	61.0%	2.14 (0.60, 7.63)	0.2411
Opiates (n=108)	n=59	n=49		
Abstinence rates (Weeks 9-12)	15.9%	5.7%	0.32 (0.11, 0.96)	0.0415

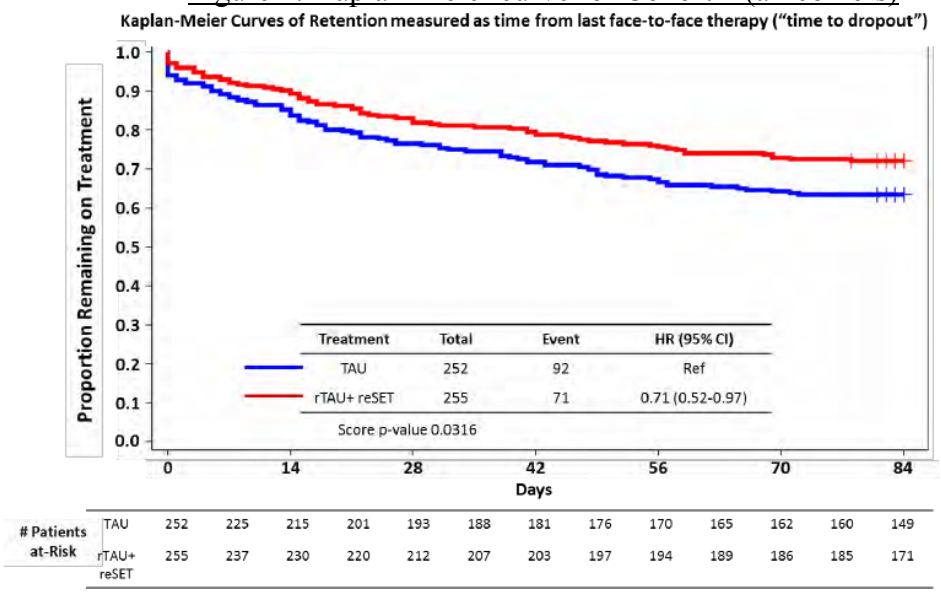
- *Retention*: Retention (time to withdrawal) in outpatient therapy was analyzed using the Kaplan-Meier method. The probability of retention was estimated at weeks 2, 4, 6, 8, 10 and 12. The retention between the rTAU + reSET and TAU arms were compared using a logrank test. Statistically significant improvement in retention was observed in Cohort 1 and Cohort 2 in the rTAU + reSET arm compared to the TAU arm (Cohort 1 p=0.0316; Cohort 2 p=0.0042, cohort 3 p=0.0113).

Table 8: Retention rates for Cohorts 1, 2, and 3

RETENTION (# dropouts/total, % dropouts)	TAU	rTAU + reSET	p-value
Cohort 1: all comers	92/252, 36.5%	71/255, 27.8%	0.0316
Cohort 2: excluding primary opioids	71/193, 36.8%	49/206, 23.8%	0.0042
Cohort 3: excluding all opioids	59/153, 38.6%	38/152, 25.0%	0.0113

The Kaplan-Meier curve for cohort 1 is shown below:

Figure 2: Kaplan-Meier curve for Cohort 1 (all comers)



Adverse events

In the entire clinical study, the number of patients with any adverse event was 13% (n=66). The number of patients with any event was 29 (11.5%) in TAU and 37 (14.5%) in reSET + rTAU (p = 0.3563). None of the adverse events in the reSET arm were adjudicated by the study investigators to be device-related. The events evaluated were typical of patients with SUD, including cardiovascular disease, gastrointestinal events, depression, mania, suicidal behavior, suicidal ideation and attempts.

Summary

In summary, the study supporting the reSET device as an adjunct to 12-week TAU showed statistically-significant increases in abstinence and retention in outpatient therapy in an all-comers cohort. Subgroup analysis demonstrated that patients who primarily abused opioids had a statistically significant reduction in abstinence with reSET compared to TAU. Abstinence at the start of treatment strongly predicted abstinence at 12 weeks.

LABELING

The labeling for the reSET device meets the requirements of 21 CFR 801.109 for prescription devices. The physician and patient labeling include:

- Information to mitigate the risks of use error, including a user guide with screenshots demonstrating how the user should interact with the device;
- A description of the device's therapy lessons or modules;
- A warning that the device should not be used as a standalone therapy and does not represent a substitution for a patient's medication; and

- A description of the mobile devices on which the device has been demonstrated to be compatible.

Physician labeling includes a description of the model of cognitive behavioral therapy upon which the device is based, along with a summary of the clinical testing performed to support the device's performance claims.

Patient labeling includes a user guide that incorporates detailed screen shots instructing the user how to interact with the app.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of reSET and the measures necessary to mitigate these risks.

Identified Risk	Mitigation Measures
Device provides ineffective treatment, leading to worsening condition	Clinical data Software verification, validation, and hazard analysis Labeling
Device software failure, leading to delayed access	Software verification, validation, and hazard analysis Labeling
Use error / improper device use	Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the reSET is subject to the following special controls:

1. Clinical data must be provided to fulfill the following:
    a. Describe a validated model of behavioral therapy for the psychiatric disorder; and
    b. Validate the model of behavioral therapy as implemented by the device.

2. Software must be described in detail in the software requirements specification (SRS) and software design specification (SDS). Software verification, validation, and hazard analysis must be performed. Software documentation must demonstrate that the device effectively implements the behavioral therapy model.

3. The following labeling must be provided:
    a. Patient and physician labeling must include instructions for use, including images that demonstrate how to interact with the device.
    b. Patient and physician labeling must list compatible devices.
    c. Patient and physician labeling must include a warning that the device is not intended for use as a standalone therapy.
    d. Patient and physician labeling must include a warning that the device does not represent a substitution for the patient's medication.
    e. Physician labeling must include a summary of the clinical testing with the device.

BENEFIT/RISK DETERMINATION

The risks of the device are based on data collected in a clinical study described above. No device-related adverse events were observed in the supporting clinical trial. The risks associated with the device include:

- **Device provides ineffective treatment, leading to worsening condition.** This risk is mitigated by basing the device's treatment on a validated method of behavioral therapy; collecting clinical data demonstrating that the device's therapy is effective in the intended use population; software verification, validation, and hazard analysis demonstrating that the model of therapy was correctly implemented on the device; and labeling. Patients with substance use disorder have a high relapse rate, and those who were abstinent at the start of treatment were much more likely to remain abstinent than those who were non-abstinent at the start of treatment.
- **Device software failure, leading to delayed access.** This risk is mitigated by performing appropriate software verification and validation testing to demonstrate that the device's behavioral therapy has been correctly implemented so that the user can access it when needed.
- **Use error / improper device use.** This risk is mitigated by labeling that:
    - Provides adequate instructions for use, including images that demonstrate how the patient should interact with the device, so that the user can have appropriate access to the device's therapy.
    - Provides a list of compatible devices in the labeling so that users know the appropriate devices on which they can access the therapy.
    - Provides warnings that the device is not intended for use as a standalone therapy and is not intended to replace care by the patient's physician so that the device is used in the appropriate context, because patients with substance use disorder typically have medical and psychiatric comorbidities that may be detected and addressed in face-to-face clinician therapy sessions.
    - Provides warnings that the device is not intended to replace a patient's medication.

The probable benefits of the device are also based on data collected in a clinical study as described above. The benefits of the device include:

- In all comers, increased likelihood of abstinence (using a GEE analysis model) after 12 weeks of treatment with the device + outpatient therapy (29.7% abstinent) as compared to patients who only received standard outpatient therapy (16% abstinent). This likelihood is increased in patients who do not self-identify as primarily using opioids (40.3% abstinent with device + outpatient therapy vs. 17.6% with standard therapy alone), and in patients who were already abstinent at the start of therapy (54.1% abstinent with device + outpatient therapy vs. 40.9% with standard therapy alone). Increased abstinence with the device was not observed in patients who self-identified as primary opioid users (5.7% abstinent with device + outpatient therapy vs. 15.9% with standard therapy alone).

- Increased duration of retention in the patient's 12-week outpatient therapy program as compared to patients who only received standard outpatient therapy.

Additional factors to be considered in determining probable risks and benefits for the reSET include:

- The reSET device mobile app was not studied in the clinical trial described above. Rather, a desktop-based version of the device was studied. This desktop-based version of the device had equivalent content to the reSET app and was evaluated in a side-by-side comparison to ensure the equivalency of the content and format. Therefore, the reSET app is likely to provide similar benefit as the therapy provided by the desktop-based version.

- The majority of patients accessed the desktop-based version of the device on-site at their treating clinic the majority of the time. This represents an additional opportunity for interaction with clinical staff, who may have been able to detect obvious impairment and other issues, which may itself have a therapeutic effect. Patients in the control group of the clinical trial did not have this additional opportunity for interaction with the clinical staff. To help address this concern, a subanalysis was performed to examine abstinence rates of those who accessed the desktop-based version of reSET within the treatment center as compared to those who used the device in offsite. Among those who accessed the device offsite, there was a statistically significant increase in abstinence rates in the intervention group compared to TAU group ($p=0.0029$). It is thought that this off-site access condition is more representative of the intended use of the reSET device. Additionally, it should be noted that a similar analysis was done to examine abstinence rates in those who accessed the device onsite only. In contrast to the hypothesis that interaction with study staff may have an effect of the trial outcome measures, results comparing abstinence rates among the on-site and offsite groups showed greater abstinence rates in both the desktop-based version of reSET and TAU groups of the offsite arm.

- Patients in the control arm of the clinical trial were not eligible to receive financial contingency management incentives that patients treated with the desktop-based version of reSET received. Patients in the reSET study arm were eligible to receive vouchers that

either stated congratulatory messages (e.g. "good job") or were exchangeable for prizes of typically around $1, occasionally around $20, and rarely $80-$100 based on negative drug screen results and completion of the device's modules. Device labeling has specifically stated that the device is intended as an adjunct to a Contingency Management System. Information and recommendations for implementation of similar "Contingency Management System" were provided as part of the Clinical Directions for Use. As a default, a system of virtual feedback will be used if other rewards are not selected by the practitioner.

- Substance use disorder is a complex, chronic, relapsing condition for which available treatments for have modest effects with significant failure rates. Treatment may need to be maintained over long time periods due to the chronic nature of SUD. Treatment for SUD may be broadly divided into pharmacologic and non-pharmacologic. Pharmacologic interventions include medications such as disulfiram, naltrexone, or baclofen; these medications may not be well tolerated in all patients due to side effects or may have reduced efficacy due to compliance issues. Psychosocial treatments include individual and group counseling.

These additional factors could have the potential to influence the effectiveness of the reSET device's therapy. However, comparison of device therapy modules between TES and reSET, subanalysis of patients who accessed TES at the clinic and offsite, and labeling information related to contingency management are adequate to ensure that the benefits for using the reSET device as labeled outweigh the risks.

Patient Perspectives

Patient perspectives considered for the reSET included patient satisfaction surveys on a 1-10 scale. The following responses were collected from 233 out of the 255 participants (91.4%) in the reSET arm:

- Patients considered the system and education useful (8.64/10, with 1 being "not useful" and 10 being "very useful")

- Patients considered themselves satisfied with the computerized system used in the study (8.86/10, with 1 being "not at all satisfied" and 10 being "very satisfied")

- Patients considered the device's counseling and education to be easy to understand (3.14/10, with 1 being "very easy" and 10 being "very difficult.")

Patient perspectives were collected on the desktop-based version of the reSET device and did not include an assessment of patient perspectives on the smartphone-based version of the device.

Benefit/Risk Conclusion

Any abstinence in an SUD patient population is beneficial, and increased time in retention allows for additional therapeutic interactions between patients and clinicians, which may permit the clinician to address the comorbidities that are known to exist in a high rate in this population.

Provided that these results are taken in context as an adjunct use device in a SUD population, these results suggest an additional therapeutic option for this patient population.

In conclusion, given the available information above, the data support that for treatment of substance use disorder as an adjunct to contingency management and outpatient therapy for patients with substance use disorder who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse, the probable benefits outweigh the probable risks for the reSET. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the reSET is granted and the device is classified under the following:

Product Code: PWE
Device Type: Computerized behavioral therapy device for psychiatric disorders
Class: II
Regulation: 21 CFR 882.5801