TITLE PAGE

Protocol Number:	**810P204**
Title:	Exploratory Neuroimaging Study to Evaluate the Effect on Brain Activity of SPN-810 for Impulsive Aggression (IA) in Patients with Attention-Deficit/Hyperactivity Disorder (ADHD) in Conjunction with Standard ADHD Treatment
Sponsor:	Supernus Pharmaceuticals, Inc. [redacted]
IND number:	106,515
Investigational Medicinal Product:	Molindone Hydrochloride Extended-Release Tablets (SPN-810)
Indication:	Treatment of Impulsive Aggression (IA) in subjects with Attention-Deficit/Hyperactivity Disorder (ADHD) in conjunction with standard ADHD treatment
Medical Monitor	[redacted]
Phase:	2
Protocol Version:	3.0
Release Date:	12 Apr 2019
Good Clinical Practice (GCP) Statement:	This study is to be performed in full compliance with International Conference on Harmonization (ICH) GCP and all applicable local regulations. All required study documentation will be archived as required by regulatory authorities.

PROTOCOL SIGNATURE PAGE

I, the undersigned, have read this protocol and agree to conduct this trial in accordance with all stipulations of the protocol and in accordance with ICH GCP and all applicable local guidelines, including the Declaration of Helsinki and all its accepted amendments to date.

Principal Investigator's Signature	Date
Print Name	
Site Number	

SUPERNUS PHARMACEUTICALS, INC. PROTOCOL APPROVAL PAGE

[redacted]

Authors:

Reviewers:

Approved By:

CLINICAL PROTOCOL SYNOPSIS

Name of Company: Supernus Pharmaceuticals, Inc.	**IND Number:** 106,515
Name of Product: Molindone Hydrochloride Extended-Release Tablets (SPN-810)	**Name of Active Ingredient:** Molindone hydrochloride
Protocol Number: 810P204	**Phase of Development:** 2

Title of the Study: Exploratory Neuroimaging Study to Evaluate the Effect on Brain Activity of SPN-810 for Impulsive Aggression (IA) in Patients with Attention-Deficit/Hyperactivity Disorder (ADHD) in Conjunction with Standard ADHD Treatment.

Objectives:

Primary Objective:

The primary objective is to evaluate the effect of SPN-810 treatment on brain activity in subjects aged 8-12 years with ADHD and IA using functional Magnetic Resonance Imaging (fMRI).

Secondary Objectives:

Secondary objectives are to evaluate the effect of SPN-810 treatment on:

- The functional connectivity between brain regions using resting-state fMRI (rs-fMRI)
- The concentration of neurotransmitters glutamate and gamma-aminobutyric acid (GABA) using Magnetic Resonance Spectroscopy (MRS)
- Safety of SPN-810

Tertiary Objectives:

Tertiary objectives are to evaluate the following:

- [redacted]
- Effect of SPN-810 treatment on the Clinical Global Impression-Severity (CGI-S) and -Improvement (CGI-I) scores
- Effect of SPN-810 on the Retrospective-Modified Overt Aggression Scale (R-MOAS) score

Study Design:

A multi-center, double-blind, randomized (1:1), placebo-controlled, parallel-group, 2-arm study

Number of Subjects:

The study will screen approximately 40 male and female subjects, aged 8-12 years inclusive, with ADHD and IA, to achieve an approximate enrollment of 30 subjects.

Criteria for Inclusion:

Healthy male or female subjects, aged 8-12 years, inclusive, at the time of screening with primary diagnosis of ADHD and currently receiving monotherapy treatment with an optimized US Food and Drug Administration (FDA)-approved ADHD medication. IA will be confirmed at screening using the R-MOAS and the Vitiello Aggression Scale. Subjects who qualified to participate in one of the ongoing double-blind Phase 3 studies (CHIME-1 and CHIME-2) but screen failed (i.e., non-compliance with the electronic diary or currently on ADHD treatment with more than one FDA-approved medication) will be eligible to enroll in Study 810P204 if they meet the study criteria.

Criteria for Exclusion:

Current or lifetime diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia or related disorder, personality disorder, Tourette's disorder, fetal alcohol syndrome, or psychosis not otherwise specified. Currently meeting DSM criteria for autism spectrum disorder, pervasive developmental disorder, obsessive-compulsive disorder, post-traumatic stress disorder. Known or suspected IQ <70, pregnancy, substance or alcohol abuse. Known history of implanted brain stimulator, vagal nerve stimulator, ventriculoperitoneal shunt, cardiac pacemaker, orthodontic braces, or implanted medication port. Visual and hearing (≥25 dB) impairment. Pre-existing medical or psychological conditions that preclude being in the MRI scanner (e.g., claustrophobia, morbid obesity, or marked anxiety about the procedure).

Treatment, Dose, and Mode of Administration:

Molindone Hydrochloride Extended-Release Tablets, dosage forms of 3 mg and 9 mg or matched placebo. Treatment to be administered orally twice daily, with or without food. Subjects will be up-titrated over a period of approximately 15 days to the final dose.

- Treatment 1: placebo
- Treatment 2: 36 mg

Duration of Treatment and Study Duration:

Total subject duration on study: approximately 9 weeks

- Pre-treatment Phase: Up to 30 days
  - Screening: 1 day
  - Baseline MRI: 1 day
- Treatment Phase: 28 days
  - Titration period: 14 days
  - Maintenance period: 14 days
- Taper/Conversion Phase: 7 days

Pre-treatment Phase:

Screening (Visit 1):

Subjects will be screened approximately 30 days before titration. Prior to conducting any screening procedures, written Informed Consent/Assent must be obtained from the subject's parents or legal representative, and the subject (when required). During the Screening Visit (Visit 1), the R-MOAS and the Vitiello Aggression Scale will be administered to determine the subject's eligibility for study treatment by evaluating the severity and the subtype of aggression, respectively. Only subjects whose scores indicate impulsivity will be included in the study. At Screening the ADHD diagnosis will also be confirmed with the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) diagnostic tool, according to DSM-5 criteria. During the screening visit, subjects will also have their head shape scanned (approximately 2 minutes) using a noninvasive handheld 3D scanning system from Caseforge.

Baseline MRI (Visit 2):

After completing the screening procedures, subjects who satisfy the inclusion and exclusion criteria will proceed to the Baseline MRI visit (Visit 2) at the Imaging Center where the pre-treatment scans will be performed, which includes the aggression task (PSAP), resting state BOLD, structural scans and MR spectroscopy.

- *Habituation Phase:*

Prior to the MR imaging session in the magnet, subjects will practice the Point Subtraction Aggression Paradigm (PSAP) Task outside of the MRI environment, which will be followed by a mock MRI acquisition to habituate the subject to the horizontal position and MRI scanner sounds. During the mock session, subjects will learn to keep their head still via feedback from the sensor based on the MoTrak head motion feedback system.

- *MR Imaging Session:*

After a short break, the subject will be placed on the MR scanner bed and positioned in the 32-channel head coil using the Caseforge customized helmet, such that the subject can see the projection screen at the back of the magnet via a mirror system. The subject will be given ear plugs, have a respiratory belt placed around their chest, may have a pulse sensor placed on their toe, and given the button box for the PSAP Task and the emergency squeeze ball. Subjects will undergo an approximately 1-hour long MR imaging session with the following acquisitions: 3-plane localizer, followed by two 12-minute fMRI sessions of the PSAP Task, a three-dimensional magnetization-prepared rapid acquisition with gradient echo (3D MPRAGE) anatomical scan (6 minutes), a Magnetic Resonance Spectroscopy (MRS) acquisition (8 minutes), a resting-state fMRI scan (8 minutes), and a 3-minute Fluid Attenuated Inversion Recovery (FLAIR) clinical anatomical scan. All scanning will be performed on a Siemens-Skyra 3T MRI scanner. MR imaging parameters were optimized in the 810P204a study.

PSAP

The Point Subtraction Aggression Paradigm (PSAP) is a behavioral aggression paradigm consisting of a computer game in which each participant plays against a computer to earn points. However, at the beginning of the game subjects will be told that they will be playing

against a fictitious opponent located in a different building. The subject can steal points (simulating an aggressive behavior) or have points stolen by the opponent (i.e., provocation). At the beginning of the task, subjects will be instructed that they and their opponent could earn as many points as possible that can be turned into money. The subject can press 1 of 3 buttons on a keypad (Option 1, 2 or 3) a set number of times to achieve a specific outcome.

BOLD fMRI

BOLD (blood oxygenation level-dependent) fMRI is a method used to investigate brain activity by measuring the change in blood oxygenation. When a brain area is active, the flow of oxygenated blood increases to that region in response to increased oxygen demand. Changes in the relative levels of oxyhemoglobin and deoxyhemoglobin can be detected due to their differences in magnetic susceptibility. Deoxygenated hemoglobin is paramagnetic while oxygenated hemoglobin is diamagnetic. An Echo Planar Imaging (EPI) MRI sequence is sensitive to changes in magnetization (T2*) and can therefore be used to measure blood oxygenation as a proxy for brain activity during the task.

BOLD Resting fMRI

A resting-state BOLD fMRI (rs-fMRI) will be measured (subjects will look at the image of a crosshair during an 8-minute scan) after the completion of the PSAP Task fMRI and MR spectroscopy. The rs-fMRI will be used to identify functional connectivity in brain networks in subjects "at rest." Connectivity is measured by the spontaneous fluctuations in the BOLD signal. The more synchronized these fluctuations are, the more connected the brain regions.

Randomization (Visit 3):

After the completion of the baseline procedures, eligibility will minimally require completion of (1) two PSAP sessions and (2) the MPRAGE structural scan. Eligible subjects will be randomized in a 1:1 ratio to receive placebo or 36 mg/day SPN-810 and will proceed to the Treatment Phase.

Treatment Phase:

Subjects will be titrated for 2 weeks and the final dose will be maintained for 2 weeks. Subjects will return for PK sampling at Visit 4.

At the end of the Maintenance period, subjects will return to the Imaging Center to complete the post-treatment MRI session with the same MR imaging acquisition procedures as performed at the Baseline MRI session. The visit (Visit 5) will be scheduled within 3 hours +/- 1 hour from the time the dose of study medication was taken.

Subjects who successfully complete the study will have the option to participate in the ongoing open-label extension (OLE) study (SPN-810P304). Subjects can choose to participate in the OLE at Visit 4 and will receive a blinded conversion card at the same visit. They will enter the OLE study at a dose of 18 mg/day. Subjects who choose not to enter the OLE will receive their taper card at Visit 4. All subjects will be instructed to return to the site within 1 week of Visit 5 for the end of study (EOS) procedures (Visit 6).

Endpoints:

Primary Endpoint:

- Change in the whole brain in BOLD fMRI contrast in response to the PSAP task from Baseline (Visit 2) to Visit 5.

Secondary Endpoints:

- Change in functional connectivity as reflected in the Fisher's Z-transformation of correlation coefficients between brain regions during rs-fMRI from Baseline (Visit 2) to Visit 5.
- Change in the concentrations of neurotransmitters GABA and glutamate in the anterior cingulate cortex (ACC) from Baseline (Visit 2) to Visit 5 as determined by MR spectroscopy.
- Safety endpoints:
    1. Adverse events.
    2. Safety scales (Simpson-Angus Scale, Barnes Akathisia Rating Scale [BARS], and Abnormal Involuntary Movement Scale [AIMS]).
    3. Clinical laboratory tests (hematology, chemistry, and urinalysis).
    4. Vital signs.
    5. Electrocardiograms (ECGs).
    6. Columbia-Suicide Severity Rating Scale (C-SSRS).

Tertiary Endpoints:

1. [redacted]
2. Change from baseline to Visit 4 in Investigator- rated CGI-I and CGI-S scores
3. Change from baseline to Visit 4 in the R-MOAS score

Sample size:

Approximately 30 subjects will be enrolled.

Pharmacokinetic Method:

[redacted]

Bioanalytical Analysis:

[redacted]

Analysis populations:

Safety Population: includes all subjects randomized to the study and who received at least 1 dose of study drug.

Completed Population: includes all subjects randomized to the study and have a baseline imaging scans (including the anatomical scan) and post-treatment imaging scans.

PK Population: includes all subjects in the safety population who had at least one PK sample drawn with a quantifiable concentration of molindone.

Statistical Methods:

Descriptive analysis will be performed for data collected. The mean, standard deviation, median, minimum, and maximum will be reported for continuous variables. Frequency and percentage will be summarized for categorical variables.

Imaging Analysis:

All functional imaging data will be analyzed using statistical parametric mapping software SPM12 (Wellcome Trust Centre for Neuroimaging, Institute of Neurology; London, UK), Analysis of Functional Neuroimages (AFNI, NIH, USA), and in-house software developed in Dr. Todd Parrish's lab at Northwestern University, Chicago, by Dr. Lana Kaiser, and at Supernus. Additional software that may be used includes FSL (Oxford, Cambridge, UK), Freesurfer (MGH, USA), and Matlab (Mathworks, USA).

While performing the PSAP Task, neuronal activation is anticipated in the ACC, ventromedial PFC (VmPFC), amygdala, insular regions, and ventral striatum including the nucleus accumbens, etc. Therefore these regions of interest (ROIs) will be emphasized during the imaging analysis.

Primary Analysis:

Both primary and secondary analyses will be based on the completed population.

The primary endpoint will be analyzed by assessing the difference in the change in BOLD fMRI contrast related to the response to the PSAP Task from Baseline (Visit 2) to Visit 5 between each treatment group (SPN-810 36 mg group and placebo).

Secondary Analysis:

Secondary endpoints will be the difference in the change in functional connectivity values (Fisher's Z-transformation of the correlation coefficient) between relevant brain regions obtained during resting state, from Baseline (Visit 2) to Visit 5 between each treatment group (SPN-810 36 mg group and placebo). The relevant variables for the correlation matrices will be calculated by Northwestern University.

Concentrations of GABA and Glu in the ACC will be analyzed descriptively. The statistics will be assessed by treatment group, at Baseline (Visit 2) and at Visit 5. The 2-sided 95% CI for the mean difference between two treatment groups, pre- and post-treatment will be examined.

Details of the analyses will be provided in the SAP.

Safety Analysis:

Safety analysis will be based on the safety population. All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and will be summarized at subject and event levels by System Organ Class (SOC), Preferred Term (PT), and study treatment. The treatment-emergent AEs will be analyzed similarly by severity, and study drug relatedness. The descriptive statistics will be summarized for continuous measures, and percentage will be reported for categorical measures from the clinical laboratory results, AEs, vital signs, ECGs, and findings from the physical examinations.

Pharmacokinetic Analysis:

[redacted]

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

LIST OF ABBREVIATIONS

ACC	Anterior Cingulate Cortex
AC-PC	Anterior Commissure-Posterior Commissure
ADHD	Attention-Deficit/Hyperactivity Disorder
ADR	Adverse Drug Reaction
AE	Adverse Event
AIMS	Abnormal Involuntary Movement Scale
ANCOVA	Analysis of Covariance
BARS	Barnes Akathisia Rating Scale
BID	Twice a Day
BMI	Body Mass Index
BOLD	Blood Oxygenation Level-Dependent
CFB	Change from Baseline
CFR	Code of Federal Regulations
CGI-S	Clinical Global Impression – Severity of Illness
CGI-I	Clinical Global Impression – Improvement
CNS	Central Nervous System
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
C-SSRS	Columbia-Suicide Severity Rating Scale
ECG	Electrocardiogram
ECRF	Electronic Case Report Form
EOS	End of Study
EPI	Echo Planar Imaging
EPS	Extrapyramidal Symptoms
FDA	Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging
FOCP	Females of Childbearing Potential
GABA	Gamma-aminobutyric acid
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
Glu	Glutamate
IA	Impulsive Aggression
IAF	Informed Assent Form
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IQ	Intelligence Quotient
IRB	Institutional Review Board
LAR	Legal Authorized Representative
MedDRA	Medical Dictionary for Regulatory Activities

MINI-KID	Mini International Neuropsychiatric Interview for Children and Adolescents
MPRAGE	Magnetization-Prepared Rapid Acquisition with Gradient Echo
MRS	Magnetic Resonance Spectroscopy
MTA	Multimodal Treatment Study of Children with ADHD
OFC	Orbitofrontal Cortex
OLE	Open-Label Extension
PFC	Prefrontal Cortex
PSAP	Point Subtraction Aggression Paradigm
R-MOAS	Retrospective-Modified Overt Aggression Scale
rs-fMRI	Resting State Blood Oxygenation Level-Dependent Functional Magnetic Resonance Imaging
SADR	Suspected Adverse Drug Reaction
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SPECT	Single-Photon Emission Computed Tomography
TE	Echo Time
TEAE	Treatment-Emergent Adverse Event
TID	Three Times a Day
TR	Repetition Time

1 INTRODUCTION

1.1 Background

Human aggressive behavior is complex, heterogeneous, and multifactorial, but can generally be divided into 2 subsets: functional, adaptive aggression and pathological, maladaptive aggression (Miczek et al. 2014). Adaptive aggression is a behavior that is considered contextually appropriate, constrained by certain rules and rituals, and may occur to ensure the integrity or survival of the individual (e.g., the ritualized violence seen in sport, or an adolescent fighting those who would attempt to steal his or her possessions) (Miczek et al. 2014; Connor, 2002). In contrast, maladaptive aggression is defined as being out of context, unstructured, and/or outside of the norms of community behavior (e.g., explosive aggression intended to harm another person, often elicited by minimal or routine environmental cues) (Miczek et al. 2014; Connor, 2016). Maladaptive aggression can be proactive or premeditated, but the more common form of pathological aggression is characterized as reactive or impulsive (Miczek et al. 2014; Miles et al., 2016). Whereas premeditated aggression is planned, covert, and associated with the anticipation of a positive outcome for the aggressor, impulsive aggression (IA) is unplanned, explosive in nature, and often accompanied by negative emotions in the aggressor (Barratt et al., 1999; Gurnani, 2016; Connor, 2016). Maladaptive aggression, including IA, is one of the most common reasons that children are referred to mental health settings. Limited research that has been conducted into the subtypes of human aggression, most has been in children and adolescents (Connor, 2002; Vitiello & Stoff, 1997).

1.2 Impulsive Aggression in the Context of Psychiatric Disorders

IA is a common comorbidity that has been compared to fever or pain (Saylor & Amann, 2016), as it presents in numerous disorders, but only provides information about the severity and not the type of illness (Jensen, 2007). Among psychological disorders, IA is often associated with attention-deficit/hyperactivity disorder (ADHD) (King & Waschbusch, 2010), autism spectrum disorders (Doyle & McDougle, 2012), bipolar disorder (Hoptman, 2015), schizophrenia (Hoptman, 2015), Alzheimer's disease (Bidzan et al., 2012), and post-traumatic stress disorder (PTSD) (Miles et al., 2016). In children and adolescents with ADHD, the prevalence of aggressive behavior is particularly high. The large Multimodal Treatment Study of Children with ADHD (MTA), which included pre-adolescent children aged 7 to 9.9 years with ADHD, showed that more than half of the 491 subjects (54%) had clinically significant aggression prior to treatment (MTA, 1999; Jensen, 2007; Saylor & Amann, 2016). Furthermore, aggression is often refractory to treatment in children with ADHD; in the MTA, 26% of subjects continued to exhibit moderate to high levels of aggressive behavior after 14 months of multimodal therapy (Jensen, 2007).

Children with both elevated levels of aggressiveness and ADHD are at greater risk for psychological, academic, emotional, and social problems, which can manifest as persistent behavioral problems, encounters with the justice system, poor academic achievement, disciplinary problems at school, and substance experimentation/abuse (Shelton et al., 1998; Saylor & Amann, 2016). As ADHD-related psychosocial impairment has been suggested to stem more from aggression/irritability than from ADHD symptoms themselves, treatment of

aggressive behavior should be emphasized in subjects with ADHD and IA (Saylor & Amann, 2016).

1.3 Neurobiology of Impulsive Aggression

Although the pathophysiology of IA is not fully understood, functional and neuroimaging studies have detected subtle abnormalities in the subcortical regions and frontal lobes of children with ADHD and inhibition deficits or high levels of impulsivity (Connor, 2002). For instance, magnetic resonance imaging (MRI) has shown that children with ADHD have reversed asymmetry of the head of the caudate, smaller volume of the left caudate head, and smaller volumes of white matter in the right frontal lobe when compared to controls (Semrud-Clikeman et al., 2000). Subjects in this study with reversed caudate asymmetry were more disinhibited, and more likely to have externalizing behaviors, including hyperactivity, aggression and conduct problems (Semrud-Clikeman et al., 2000). Data regarding the relationship between the neuroanatomy and behavior seen in children with ADHD and high levels of impulsivity are in agreement with the suggestion that IA may result from a functional imbalance in the central nervous system (CNS) (Connor, 2002; Blair, 2016).

Within the CNS, the functions of the prefrontal cortex (PFC) and the mesolimbic areas of the brain are generally thought to include providing “control” and “emotion,” respectively (Gan et al., 2016). Models suggest that IA results from a functional imbalance in these control mechanisms, and poor executive regulation of emotion (Ahmed et al., 2015; Bubenzer-Busch et al., 2015; Gan et al., 2016). More specifically, increased reactivity from the regions, including the amygdala, striatum, and the insula, drive excessive emotional arousal, whereas impaired functioning in the anterior cingulate cortex (ACC) and ventromedial PFC fail to adequately regulate these emotions (Bubenzer-Busch et al., 2015; Blair, 2016; Gan et al., 2016; Skibsted et al., 2017). Dysfunction in this circuit may heighten the risk of impulsive aggressive behavior (Skibsted et al., 2017). Furthermore, for patients with ADHD, impairment in regions of the PFC involved in planning behavior and attentional guidance is also implicated in their disinhibited behaviors (Bubenzer-Busch et al., 2015).

Functional neuroimaging studies have revealed some of the mechanistic details underlying human aggressive behavior. Serotonin transporter availability has been shown by positron emission tomography (PET) to be reduced in the ACC of subjects with intermittent explosive disorder (Frankle et al., 2005). This abnormality in serotonergic innervation has been suggested to affect impulse modulation, and may contribute to increased impulsivity and aggression (Frankle et al., 2005). Furthermore, PET studies measuring brain glucose utilization have also shown the orbitofrontal cortex (OFC) to have less neural activity in healthy subjects presented with images of aggressive scenarios (Pietrini et al., 2000). Subcortical regions of the brain have also been implicated in the presentation of aggressive behavior. In a single-photon emission computed tomography (SPECT) study of 40 adolescents and adults with exhibited aggressive behavior, and 40 psychiatric patients who had never demonstrated such behavior, those identified with aggressive behavior showed decreased activity in the PFC, increased activity in the anteromedial portions of the frontal lobes, increased left-sided activity in the basal ganglia/limbic system, and focal abnormalities in the left temporal lobe (Amen et al., 1996). Functional magnetic resonance imaging (fMRI) studies to analyze the neural systems behind the

basic human threat response have consistently shown that activity is increased in the amygdala, hypothalamus, and periaqueductal gray when subjects are presented with approaching threats (Mobbs et al., 2009; Coker-Appiah et al., 2013). FMRI can identify which regions of a subject's brain are activated in response to a stimulus by evaluating changes in the blood oxygenation level-dependent (BOLD) signal (Czerniak et al., 2013). Subjects with intermittent explosive disorder who are exposed to a display of angry faces during fMRI have been shown to experience increased activity in the amygdala, ACC, OFC, and ventrolateral PFC (Gan et al., 2016; Skibsted et al., 2017). Combining fMRI with the Point Subtraction Aggression Paradigm (PSAP) Task, a well-established test for evaluating behavioral responses related to aggression, has shown that provocation activates the amygdala, dorsal striatum, insula, and prefrontal areas in control subjects (Skibsted et al., 2017). In children with ADHD, fMRI has shown lower activation in the ACC and temporoparietal junction (a region associated with processes involved in theory of mind, social cognition, and attentional guidance) during the aggression phase of the modified version of the Point Subtraction Aggression game compared to controls (Bubenzer-Busch et al., 2015). Combined with established paradigms for evaluating aggression-related behavior, fMRI studies in healthy populations and clinical populations with high levels of IA have provided evidence for the brain regions involved in the manifestation of IA (Gan et al., 2016).

1.4 Treatment Options for Impulsive Aggression

Psychosocial interventions, psychostimulants, antipsychotics, and other adjunctive therapies to primary ADHD treatment are often used to control aggressive behavior in children with ADHD and IA (Pappadopulos et al., 2003; Blader et al., 2010; Gurnani et al., 2016). However, there remains an unmet need in this population, as there is currently no US Food and Drug Administration (FDA)-approved medication for the treatment of IA in children with ADHD (Stocks et al., 2012).

Molindone hydrochloride was previously marketed in the United States as Moban®, an immediate-release tablet for the management of schizophrenia in adults and adolescents, and was discontinued by the original manufacturer for reasons not related to its safety or effectiveness (Moban Prescribing Information, 2009; United States Food and Drug Administration, 2013). In a single-blind, dose-ranging pilot study, molindone at an optimized dose of 0.5 mg/kg/day was found to improve symptoms of aggressive-type behavior in children with undersocialized conduct disorder, aggressive type (Greenhill et al., 1985; Stocks et al., 2012). Molindone was also shown to be effective in treating aggressive behavior in a double-blind, 8-week, inpatient study of 31 children, aged 6-11 years, with undersocialized conduct disorder, aggressive type (Greenhill et al., 1985). Molindone is not associated with significant increases in weight/body mass index (BMI), in contrast to olanzapine (Sikich et al., 2008), and elicits little to no parkinsonism or extrapyramidal symptoms (EPS), as compared to other antipsychotics (Seeman & Tallerico, 1998; Sikich et al., 2008). The overall clinical profile of molindone has made it an attractive candidate for the treatment of IA in children with ADHD, especially with the anticipated benefits of an extended-release formulation.

1.5 Sponsor's Phase 2 and Phase 3 Studies

Three Phase 2 studies have been undertaken to develop molindone as a potential therapeutic for the treatment of IA. Study 810P201 was a proof-of-principle, open-label, parallel-group, randomized, dose-ranging, safety and tolerability study using the investigational immediate-release (IR) formulation of molindone (Molindone IR) dosed 3 times a day (TID) in children with ADHD and persistent serious conduct problems (Stocks et al., 2012). This study demonstrated that treatment with Molindone IR TID was safe and well tolerated. Preliminary efficacy results suggested that treatment with Molindone IR resulted in behavioral improvements and that those improvements were more marked in higher dose groups than in lower dose groups.

Study 810P202 was a Phase 2b multicenter, randomized, double-blind, placebo controlled trial in subjects aged 6-12 years diagnosed with ADHD and IA that was not controlled by optimal stimulant and behavioral therapy (Supernus Pharmaceuticals, 2013). SPN-810 treatment in the medium- and low-dose groups (24/36 mg, and 12/18 mg, respectively) showed a statistically significant difference from the placebo group in the change from baseline to the end of the study (6 weeks) in Retrospective-Modified Overt Aggression Scale (R-MOAS) score, suggesting improvement in aggressive behaviors.

SPN-810 exhibited a satisfactory safety and tolerability profile, with low incidence of adverse events (AEs) and no unexpected, life-threatening, or dose-limiting safety issues. The AEs reported in this study were consistent with the types of events that could be expected in a pediatric population taking low-dose antipsychotic medication and psychostimulant ADHD medication. The overall frequency of AEs was relatively low, as were discontinuations due to AEs. The frequency of AEs associated with EPS was also low, and the two serious AEs that occurred were not drug-related.

Study 810P203 was a multicenter open-label extension (OLE) to Study 810P202 in a pediatric population of subjects 6-12 years of age diagnosed with ADHD and IA. The starting dose for this OLE study was based on subjects' weight at the end of 810P202, with dosing gradually adjusted based on tolerability or effectiveness, regardless of weight group to 9, 18, 27, or 36 mg/day. Of the 121 subjects randomized into the double-blind Study 810P202, 78 continued on to the OLE study and received SPN-810 for up to 6 months.

SPN-810 was well tolerated when dosages were adjusted according to clinical response. [redacted]

[redacted].

The Sponsor is currently conducting 3 Phase 3 multicenter, randomized, double-blind, placebo-controlled trials in a population of subjects 6-12 years of age diagnosed with ADHD and IA (810P301, 810P302 and 810P304). The primary objective of all 3 studies is to assess the efficacy and safety of SPN-810 in reducing the frequency of IA behaviors in pediatric patients with ADHD when taken in conjunction with standard ADHD treatment.

1.6 Study Rationale and Appropriateness of Measurements

Results from Phase 2 studies and the associated OLE study have shown that SPN-810 added to optimized ADHD therapy resulted in remission of aggression and significantly improved impulsive aggressive behavior in children with ADHD, in addition to exhibiting a good tolerability profile in children with ADHD and associated feature of IA.

This Phase 2 (810P204) study seeks to evaluate the effect of 4-week SPN-810 treatment on brain functioning in patients aged 8-12 years with ADHD and associated feature of IA. This will be achieved using fMRI in conjunction with the PSAP Task, a behavioral aggression paradigm in which subjects are provoked by having money indirectly taken from them by a (unbeknownst to the subject) fictitious opponent during a money acquisition task.

The PSAP Task is a well-established test for evaluating aggressive behavioral responses related to IA, and has been previously used in fMRI studies to elucidate the neural activation involved in aggressive behaviors (Bubenzer-Busch et al., 2015; Cherek et al., 1997; Skibsted et al., 2017; Cunha-Bang et al., 2017; Kose et al., 2015).

The PSAP Task parameters for this study (810P204) were optimized in a non-interventional Study (810P204a) conducted in typically developed children 8-12 years old.

Prospective evaluation of subjects using well-established diagnostic tests will confirm that enrollees have both ADHD (by MINI-KID) and moderate to severe IA (by R-MOAS, CGI-S, and the Vitiello Aggression Scale). Subjects in this double-blind, placebo-controlled, 2-arm, randomized (1:1), parallel-group will receive study medication twice daily (BID) with or without food. Enrolled subjects will follow a titration schedule that has been shown to be safe, efficacious, and well-tolerated in a similar patient population in a previous Phase 2b study.

Safety will be assessed by the monitoring of AEs, vital signs, ECGs and clinical laboratory tests, as well as by the Simpson-Angus Scale, the Barnes Akathisia Rating Scale (BARS), the Abnormal Involuntary Movement Scale (AIMS), and the Columbia-Suicide Severity Rating Scale (C-SSRS).

The effect of Molindone on body composition, metabolic parameters, and prolactin will be evaluated.

2 STUDY OBJECTIVE

2.1 Primary Objective

The primary objective of Study 810P204 is to evaluate the effect of SPN-810 treatment on brain activity in subjects aged 8-12 years with ADHD and IA using fMRI.

2.2 Secondary Objectives

The secondary objectives are to evaluate the effect of SPN-810 treatment on:

- The functional connectivity between brain regions using resting-state fMRI (rs-fMRI)
- The concentration of neurotransmitters glutamate and GABA using MRS
- The safety of SPN-810

2.3 Tertiary Objectives:

Tertiary objectives are to evaluate the following:

- [redacted]
- Effect of SPN-810 treatment on CGI-S and CGI-I scores
- Effect of SPN-810 treatment on the R-MOAS score

3 INVESTIGATIONAL PLAN

3.1 Overall Study Design

This is a multi-center, randomized, double-blind, placebo-controlled, 2-arm, parallel-group study to evaluate the functional effect of SPN-810 treatment on IA in subjects aged 8-12 years diagnosed with ADHD in conjunction with approved ADHD medication. Figure 1 and Figure 2 depict the study design schematically.

This study consists of 3 phases: Pre-Treatment, Treatment, and Conversion/Taper.

The Pre-Treatment Phase comprises of Screening and a Baseline MRI Visit for a total duration of up to 30 days. Following Screening (Visit 1), eligible subjects will proceed to the Baseline MRI visit (Visit 2) at the Imaging Center, where the brain MRI scans will be performed. At Visit 3, eligible subjects will be randomized to study medication or placebo.

Eligible subjects will follow a dose-titration schedule as shown in Figure 1 and Figure 2, with dosing starting at [redacted] and increasing approximately every 2 days until the target dose (36 mg/day) is reached. The final dose will be maintained for 2 weeks (Maintenance period) during which time subjects will return for PK sampling (Visit 4) prior to receiving the final MRI scan at the Imaging Center (Visit 5). At the intervening visit during the maintenance phase (Visit 4), subjects will be given the option to taper down/discontinue study medication or convert to an ongoing OLE study (810P304) upon completion of the current study and will receive the blinded taper or the conversion study medication kit.

Subjects will return to the study site for a final EOS visit (Visit 6), after completing the 1-week Taper or Conversion phases. Subjects who choose to convert into the ongoing OLE (SPN-810 304) will enter the study at a dose of 18 mg/day SPN-810.

A subject who discontinues early in the Maintenance period, i.e., prior to Visit 5, may be allowed to participate in the OLE on a case-by-case basis after consultation by the Investigator, Medical Monitor, and Sponsor.

[redacted]

Safety will be assessed by the monitoring of AEs, vital signs, ECGs and clinical laboratory tests, as well as by the Simpson-Angus Scale, the Barnes Akathisia Rating Scale (BARS), the Abnormal Involuntary Movement Scale (AIMS), and the Columbia-Suicide Severity Rating Scale (C-SSRS). These scales were chosen to specifically monitor EPS, since youths treated with antipsychotics are at greater risk for EPS side effects than adults (Findling et al., 2005). The Simpson-Angus Scale, BARS, and AIMS were utilized in Phase 2 studies and have been used in other clinical studies of atypical antipsychotics in children (Sikich et al., 2008; Stocks et al., 2012).

3.2 Imaging Acquisition and fMRI Set-up

This study is designed to use fMRI in conjunction with the PSAP aggression task. MR imaging parameters for the PSAP Task were optimized in the non-interventional 810P204a study that was conducted by the Sponsor in typically developing children 8-12 years of age.

3.2.1 *BOLD fMRI*

BOLD fMRI is a method used to investigate brain activity by measuring the change in blood oxygenation. When a brain area is active, the flow of oxygenated blood increases to that region in response to increased oxygen demand. Changes in the relative levels of oxyhemoglobin and deoxyhemoglobin can be detected due to their differences in magnetic susceptibility. Deoxygenated hemoglobin is paramagnetic while oxygenated hemoglobin is diamagnetic. An Echo-Planar Imaging (EPI) MRI sequence is sensitive to changes in magnetization (T2*) and can therefore be used to measure blood oxygenation as a proxy for brain activity.

This technique can be used during task-based fMRI, where the T2* contrast between a task and control condition can be used to identify regions of the brain that show a change in oxygenation as a result of the task. BOLD fMRI is therefore highly spatially selective, but less temporally specific (due to the slow time-course of blood flow). For instance, it can be used to see what regions are active during viewing of aggressive scenes, or what regions of the brain become active during a choice-inhibition task. Subsequently, the difference in the strength, location, or extent of brain activation between groups can be assessed.

Another approach to assessing brain function is resting-state BOLD fMRI (rs-fMRI), where BOLD fMRI is measured during rest (during which the participant looks at an image of a crosshair during an 8-minute scan). Rs-fMRI can be used to study brain networks by looking at correlations in the time-course of the spontaneous BOLD signal time-courses 'at rest' between

different regions of the brain. These networks are thought to have specific functions and are considered connected, and many have been identified (e.g., the default mode network, executive control network, praxis network). Studies of different disorders have shown differences in the functional connectivity in these networks in different populations and can be indicative of differences in brain function.

3.2.2 *Point Subtraction Aggression Paradigm (PSAP) Task*

The PSAP is a behavioral aggression paradigm in which each subject competes against a fictitious opponent (in reality, the computer) to earn points. At the start of the task, subjects will be instructed that they and another subject of the same age, who is located in a different building, will be competing to earn as many as points as possible. Subjects are told that they will win prizes for their participation and can win additional prizes (money) if they complete the task. The subjects can press 1 of 3 buttons on a keypad (Option 1, 2 or 3) a set number of times to achieve a specific outcome.

The PSAP Task will be presented using custom E-Prime 3.0 software (Psychology, Software Tools Pittsburgh, PA) developed by Dr. Todd Parrish's Lab at Northwestern University in Chicago. The program will be run from a laptop computer synchronized to the MRI scanner.

During each study visit at the Imaging Center, subjects will complete two PSAP-fMRI sessions, each lasting 12 minutes. For each run, the subject can remove points from his or her opponent (simulating aggressive behaviors) or have points stolen by the opponent (i.e., provocations). Options 1, 2 and 3 correspond to the index, middle, and ring finger of the dominant hand. The game status is presented on a screen, which includes the numbers of points earned and the current number of button presses.

By pressing the button for Option 1, 100 times, the subject will earn a point ($1.00); pressing the button for Option 2, 20 consecutive times is the aggression action that results in stealing a point ($1.00) from the opponent; pressing Option 3, 20 times protects the subject from the opponent's attempt to steal points (i.e., money) for a 60 second time frame. Once an option is selected, subjects are required to complete that option before choosing a new option. There will be a minimum of 170 ms between button presses to regulate how quickly they can choose the button to press. Provocations can occur at any time during the game and will be spaced at least 6-60s apart depending on the participant's use of the protection option.

When subjects reach 100 consecutive button presses, black flashing points ('+') are presented around the point total, which will then increase. When the subjects are provoked by having a point stolen, a red flashing '-' sign is displayed around the point total.

3.2.3 *Data Acquisition*

All scanning will be performed on a Siemens-Skyra 3T MRI scanner using a 32-channel head coil. Functional images for the PSAP Task will be collected at an angle of 30° from the anterior commissure-posterior commissure (AC-PC) axis, which reduces signal dropout in the

orbitofrontal cortex (Deichmann et al., 2003). Seventy-two slices will be acquired at a resolution of 2 mm x 2 mm x 2 mm, providing whole-brain coverage. A GRE EPI pulse sequence will be used (repetition time (TR) = 2000 ms, echo time (TE) = 25 ms, multiband factor of 2, field-of-view = 220 mm, flip angle = 80°).

Resting-state data will be collected using a similar sequence for a duration of 8 minutes.

Physiological measures of respiration and/or blood oxygen saturation will be measured during the scans to clean rs-fMRI data from physiological noise arising from these sources (Murphy et al., 2013).

3.2.4 *Magnetic Resonance Spectroscopy (MRS)*

MRS relies on the observation of hydrogen protons, which have a magnetic moment when placed in a magnetic field (such as the MRI scanner). Water is the most abundant hydrogen-containing compound in the brain, but when the water signal is suppressed, other H-proton-containing metabolites can be observed. MRS allows for the measurement and therefore quantification of different metabolites within the human brain. An MRS spectrum contains all metabolites from a predefined region of brain tissue plotted along a chemical shift axis.

3.2.4.1 GABA and Glutamate Brain Concentrations

GABA and Glu are the human brain's primary inhibitory and excitatory neurotransmitters, respectively, and play a key role in driving and regulating brain activity and function. While detectable using MRS, GABA and glutamate, though found at abundant concentrations in the human brain, have signals that overlap and are obscured by larger signals in conventional spectra. Therefore, use of conventional PRESS (Bottomley et al., 1987) sequence acquisition will be enhanced by dual echo time scheme, which allows additional information to be obtained on the spectral characteristics of the metabolites, lipids, and macromolecules. Furthermore, advanced numerical simulations that predict the exact pattern of the metabolites would be used during data fitting, which facilitates deconvolution of the spectral content (Kaiser et al., 2008; Veshtort et al., 2006). In this study, glutamate (Glu) concentrations will be measured using advanced fitting software on the spectra.

Due to the low sensitivity of MRS, these measurements are typically made from a large voxel in an approximately 8-minute scan duration to obtain sufficient signal to noise ratio to reliably estimate these neurotransmitters. There is no additional risk involved as this is a typical MRI scan protocol. Data will be acquired from the anterior cingulate cortex (ACC) region.

3.2.4.2 MRS Data Acquisition

MRS data will be acquired on a Siemens-Skyra 3T MRI scanner. Prior to MRS, a T1 Magnetization-Prepared Rapid Acquisition with Gradient Echo (MPRAGE) will be acquired for voxel localization. MRS will be acquired in the ACC (Ende et al., 2016).

A spatial localization in PRESS is performed using a 90° Hamming-filtered sync pulse (bandwidth time product = 8.75, duration = 2.12 msec, bandwidth [FWHM] = 4.2 kHz) and two 180° mao

pulses (duration = 5.25 msec, bandwidth = 1.2 kHz). All localization pulses are executed at 3 ppm. The sequence will utilize two echo times (TE=23 ms and TE=140 ms, with TR=4 s).

Variable power with optimized relaxation delays (VAPOR) and outer volume suppression are used to suppress water and to improve the localization of the volume of interest. The model spectra will be created using state-of-the art software Spinevolution, which employs advanced numerical simulation algorithms. Experimental parameters, such as echo time, pulse sequence delays, and RF pulse shapes will be utilized within the simulation to reproduce experimental conditions as close as possible (https://spinevolution.com). Other software packages may be used as needed to analyze the MRS data.

The analysis allows the calculation of the best fit of the experimental spectrum as a linear combination of model spectra. All metabolites (including GABA and Glu) will be calculated from the combined spectral information from dual echo time scheme.

The concentrations of the different metabolites of interest are expressed as ratios over creatine (Cr).

3.3 Duration of Study Treatment

The total subject duration on study: approximately 9 weeks.

- Pre-treatment Phase: Up to 30 days
  - Screening: 1 day
  - Baseline MRI: 1 day
- Treatment Phase: 28 days
  - Titration Period: 14 days
  - Maintenance Period: 14 days
- Taper/Conversion Phase: 7 days

Figure 1: Study Schematic: Conversion to Open-Label Extension Study

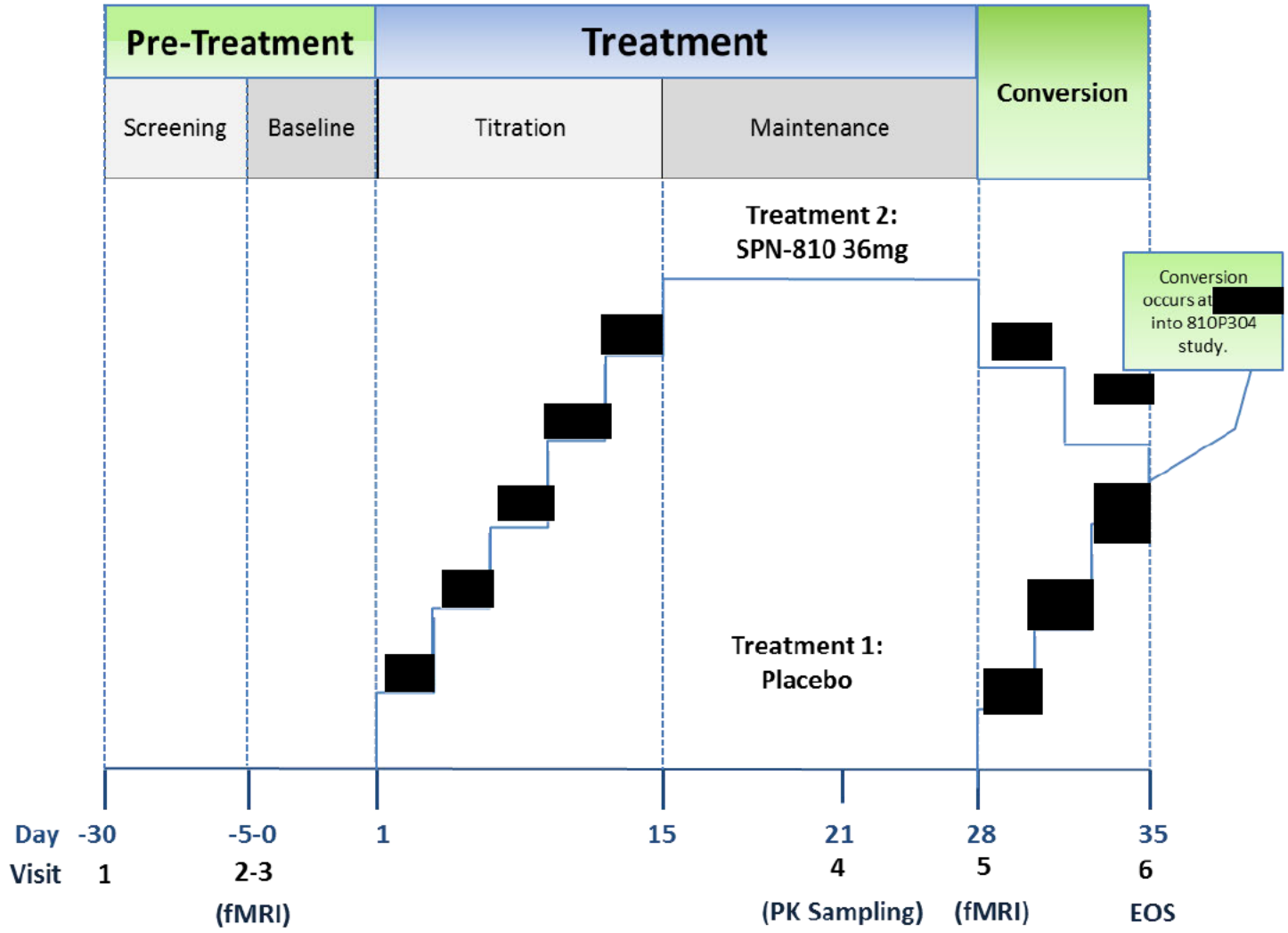
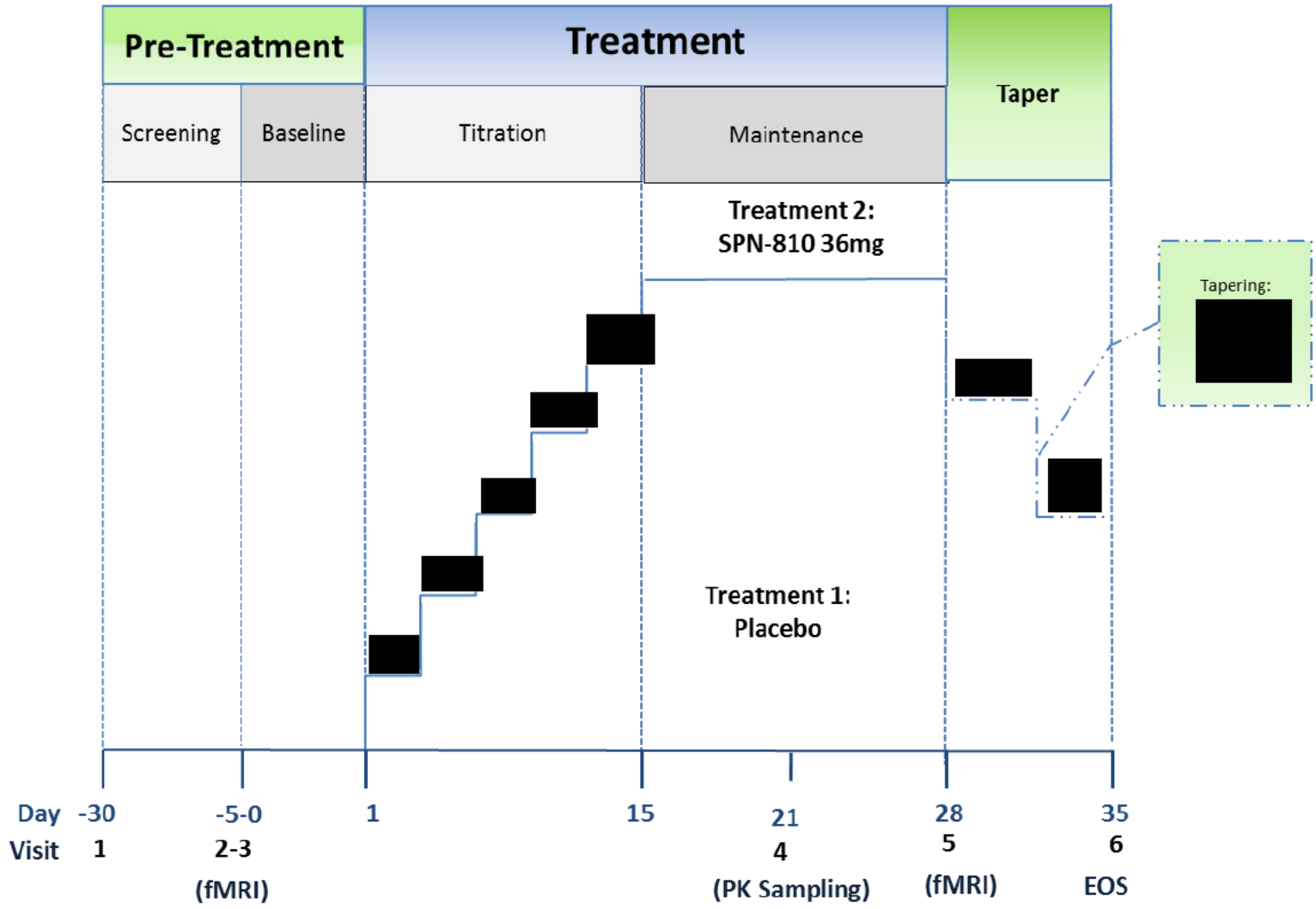


Figure 2: Study Schematic: Taper and Complete/Discontinue



3.4 Pre-Treatment Phase (Up to 30 days)

3.4.1 *Screening Period (Up to 30 days): Visit 1, Day -30*

Screening procedures will be conducted approximately 30 days before titration, and may be carried out over more than 1 visit if needed. Prior to conducting any study-related procedures, a written Informed Consent/Assent must be obtained from the subject's parent or legal representative, and the subject (when required). Abnormal results on screening laboratory tests may be repeated at the discretion of the Investigator and the Medical Monitor. Each screened subject will be assigned a subject number in a sequential order.

The population will be male and female subjects with IA and diagnosed with ADHD, currently being treated with an FDA-approved standard ADHD treatment. In addition, subjects who had qualified to participate in 1 of the ongoing double-blind Phase 3 studies (CHIME 1 and CHIME 2) but screen failed (i.e., non-compliance with the electronic diary or currently on ADHD treatment with more than one FDA-approved medication) may be eligible to participate in the 810P204 study if they meet the study criteria.

The diagnosis of ADHD will follow the definition found in the *Diagnostic and Statistical Manual of Mental Disorders-5* (DSM-5), as confirmed with the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). The MINI-KID instrument is designed to be used for children aged 6-17 years, and has been shown to have substantial to excellent concordance with the diagnosis of ADHD, among other Axis I psychiatric disorders (Sheehan et al., 2010; Leffler et al., 2015). The interview can take from 15 to 50 minutes, and can be given to parents or children, together or separately (Leffler et al., 2015).

The R-MOAS and the CGI-S scale will be administered to determine if the subject is eligible to participate in the study. Both of these scales measure severity of IA, and only those subjects with an R-MOAS score of ≥20 and a score of at least "moderately ill" on the CGI-S will be eligible for the study.

The Vitiello Aggression Scale will be used to evaluate the subtype of aggression (planned vs. impulsive); only those children who score between -2 and -5 and are considered predominantly impulsive will be included.

During the screening visit at the clinical site, subjects will have their head shape scanned (approximately 2 minutes) using a noninvasive handheld 3D scanning system from Caseforge.

3.4.2 *Baseline MRI (Visit 2) and Randomization (Visit 3): Day -5 to Day 0*

Baseline visits can be carried out in more than one day, within 30 days from screening. At Visit 2, subjects will receive the pre-treatment MRI scan at the Imaging Center. The subject's MRI eligibility will be re-confirmed using the MR Safety Questionnaire prior the MRI scan.
To be eligible for randomization at Visit 3, subjects must have minimally completed:

- two (2) sessions of the PSAP Task fMRI and
- the MPRAGE structural scan.

Subjects unable to finish these scans will not proceed to randomization.

At Visit 3 the study site will randomize (1:1 ratio) qualified subjects to receive placebo or 36 mg/day SPN-810. Subjects will be dispensed their study medication.

3.5 Treatment Phase (4 weeks)

3.5.1 *Titration Period, Day 1 to Day 14*

Subjects will be instructed to titrate to reach the maintenance dose over a period of 15 days, according to the dose titration schedule shown in Figure 1 and Figure 2. Dosing will begin at [redacted] SPN-810, and increase to [redacted] on Day 3, 9 mg/day on Day 5, [redacted] on Day 8, [redacted] on Day 11, and [redacted] on Day 15.

3.5.2 *Maintenance Period, (14 days) Day 15 to Day 28*

Following dose titration, treatment will be maintained for 2 weeks at 36 mg/day SPN-810 or placebo.

At Visit 4, before the end of the Maintenance period, blood will be drawn for quantitative PK analysis. The morning dose of study medication will be administered in the clinic. The following PK samples will be collected: pre-dose (-30 minutes), and 2, 3, 4 and 6 hours post-dose (± 15 minutes).

At Visit 4, all subjects will also have the option to participate in an OLE study (Protocol 810P304) in which all subjects will receive active treatment. At the visit, subjects will receive a blinded conversion medication card that will adjust the subject's total daily dose to 18 mg SPN-810 for initiation into the OLE (Figure 1). Those subjects who do not elect to participate in this extension study will be tapered down prior to discontinuation of the study medication and will receive a taper down card at Visit 4 (Figure 2).

At Visit 5, subjects will return to the Imaging Center for the post-treatment fMRI/PSAP Task and will use (when applicable) the same Caseforge helmet used at Visit 2.

At the completion of the MRI scans (Visit 2 and Visit 5), subjects will be administered the questionnaire to validate their understanding of the task and to describe the characteristics of their opponent. The results of the questionnaire will be provided to the study site.

3.6 Taper/Conversion Phase *(7 days),* Day 29 to Day 35

Subjects will complete the 1-week Taper or Conversion phase.

3.7 End of Study (EOS)/Early Termination, Visit 6 (Day 35)

Subjects will return to the study site for a final visit, after completing the 1-week Taper or Conversion phase. Those subjects who choose to continue into the OLE study will have procedures performed for that study; eligibility criteria will be confirmed at Visit 1 of study protocol 810P304. Only the subjects who discontinue from the study during the Maintenance

period or following Day 14 in the Titration period will be offered a Taper card at the study site one week prior the EOS. All subjects who discontinue early (i.e., during the Titration period, Day 1 to Day 14) will be instructed to return to the study site for a final visit (EOS), within 1 week after discontinuation.

4 STUDY METHODS

4.1 Study Population

Approximately 40 subjects aged 8-12 years (inclusive) will be screened to randomize 30 subjects; 15 in the SPN-810 arm and 15 in the placebo arm. The population will be male and female subjects with IA and diagnosed with ADHD, currently being treated with an FDA-approved standard ADHD treatment. In addition, subjects who had qualified to participate in one of the ongoing double-blind Phase 3 studies (CHIME 1 and CHIME 2) but screen failed (i.e., non-compliance with the electronic diary or currently on ADHD treatment with more than one FDA-approved medication) may be eligible to participate in the 810P204 study if they meet the study criteria.

4.1.1 *Inclusion Criteria*

1. Male or female subjects, aged 8-12 years (inclusive) at the time of screening.
2. Diagnosis of ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders-5* (DSM-5) confirmed by MINI-KID.
3. R-MOAS score of ≥20 at screening.
4. CGI-S score ≥4 at screening.
5. Vitiello Aggression Scale score from -2 to -5 at screening.
6. Treatment with FDA-approved optimized ADHD medication (i.e., psychostimulants) at an FDA-approved dose for at least 1 month prior to screening, and willing to maintain that dose throughout the Treatment phase.
7. Free of antipsychotic medication for at least 2 weeks prior to the treatment.
8. Medically healthy and with clinically normal laboratory profiles, vital signs, and ECGs.
9. Weight of at least 20 kg.
10. Able and willing to swallow tablets whole and not chewed, cut or crushed.
11. Written Informed Consent obtained from the subject's parent or legal representative, and written Informed Assent obtained from the subject, if appropriate.

4.1.2 *Exclusion Criteria*

1. Body mass index (BMI) ≥99th percentile.
2. Current or lifetime diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia or related disorder, personality disorder, Tourette's disorder, fetal alcohol syndrome, or psychosis not otherwise specified.

3. Currently meeting DSM-5 criteria for autism spectrum disorder, pervasive developmental disorder, obsessive-compulsive disorder, post-traumatic stress disorder, or intermittent explosive disorder.
4. Use of anticonvulsants including carbamazepine and valproic acid, antidepressants, mood stabilizers including lithium, benzodiazepines, cholinesterase inhibitors, or any drug known to inhibit or induce CYP2D6 activity within 2 weeks before the Treatment Period.
5. Use of herbal supplements within 1 week prior to Treatment Period.
6. Known or suspected IQ <70.
7. Unstable endocrine or neurologic conditions that confound the diagnosis or are a contraindication to treatment with antipsychotics.
8. Suicidality, defined as either active suicidal plan/intent or active suicidal thoughts in the 6 months before the Screening Visit or more than 1 lifetime suicide attempt.
9. Pregnancy, breastfeeding, or refusal to practice contraception during the study (for female subjects of childbearing potential and sexually active males).
10. Major visual impairment.
11. Documented hearing impairment ≥25 dB loss in either ear and or cochlear implants.
12. Known history of implanted brain stimulator, vagal nerve stimulator, ventriculoperitoneal shunt, cardiac pacemaker, orthodontic braces, or implanted medication port.
13. Pre-existing medical or psychological conditions that preclude being in the scanner (e.g., claustrophobia, morbid obesity, or marked anxiety about the procedure).
14. Substance or alcohol use during the last 3 months.
15. Urine drug test at screening that is positive for alcohol or drugs of abuse.
16. Known allergy or sensitivity to molindone hydrochloride.
17. Lack of IA symptoms due to current medication treatment.
18. Any condition that in the opinion of the Investigator or the Sponsor would prevent the subject or the subject's caregiver from participating in the study or complying with the study procedures.
19. Use of an investigational drug or participation in an investigational study within 30 days prior Visit 2.
20. Participation in a previous clinical trial with SPN-810 and received molindone hydrochloride (i.e., subjects who completed or discontinued from the CHIME studies or the OLE study 810P304).
21. Siblings of study participants.

4.2 Schedule of Visits and Procedures

All subjects who have consented are required to follow the protocol procedures, regardless of the number of doses of study medication taken. The Sponsor, or the Sponsor's designee, must be notified of all deviations from the Schedule of Events and Procedures (Table 1), and these

procedures, if applicable, should be performed at the nearest possible time to the original schedule. Subjects will be instructed to call study personnel to report any issues or abnormal reactions during the intervals between study visits and to return to the study site if medical evaluation is needed, especially when urgent. Unscheduled visits may be conducted at the discretion of the Investigator throughout all study periods. The Medical Monitor must be promptly contacted in the event that any clinically significant findings or information is obtained during the unscheduled visit. For emergency and other unscheduled visits to a medical facility other than the study site, medical records will be obtained by the Investigator or qualified designee as source data for study follow-up by the Investigator.

Table 1: Schedule of Events and Procedures

Phase	**Pre-treatment**			**Treatment**			**Taper/Conversion**
Period	**Screening**	**Baseline**		**Titration**	**Maintenance**		**EOS**
VISIT NUMBER	**1**	**2[a]**	**3**		**4[b]**	**5[a]**	**6[c]**
Day	-30	-5 to 0		1-14	21	28	35
Window (days)	≤30d prior to titration	≤5d prior to titration		0	- 2/+1 d from titration	-/+ 1d from titration	7d±2d from **Visit 5**
Informed Consent/Assent[d]	X						X
Inclusion/Exclusion Criteria	X						
R-MOAS, MINI-KID, CGI-S, and Vitiello Scales	X				X[e]		X[e]
CGI-I Scale					X		X
Medical History and Demographic Data	X		X				
Physical Examination	X				X		X
ECG (12-lead)	X				X		X
Vital Signs	X				X		X
Hematology/Chemistry/ Urinalysis	X						X
PK Blood Sampling					X		
Weight, Height, and BMI	X				X		X
Urine Drug Screen	X						
Urine Pregnancy Test[f]	X						X
Caseforge Scan	X						

Phase	**Pre-treatment**			**Treatment**			**Taper/Conversion**
Period	**Screening**	**Baseline**		**Titration**	**Maintenance**		**EOS**
VISIT NUMBER	**1**	**2[a]**	**3**		**4[b]**	**5[a]**	**6[c]**
Day	-30	-5 to 0		1-14	21	28	35
Window (days)	≤30d prior to titration	≤5d prior to titration		0	- 2/+1 d from titration	-/+ 1d from titration	7d±2d from **Visit 5**
Edinburgh Handedness Inventory		X					
MRI Safety Questionnaire		X				X	
Habituation Phase (Practice and Mock Scan)		X				X	
MRI Session		X				X	
PSAP Questionnaire		X				X	
Columbia-Suicide Severity Rating Scale (C-SSRS)	X				X		X
Safety Scales (Simpson-Angus, BARS, and AIMS)					X		X
Adverse Events			X		X	X[i]	X
Concomitant Medication	X		X		X	X[i]	X
Randomization			X[g]				
Drug Compliance					X		X
Drug Dispensation			X[j]		X[h]		
Drug Return					X		X

a. The fMRI for Visit 2 and Visit 5 will be performed at the Imaging Center. At Visit 5 the fMRI will be schedule preferably in the morning 3 hours +/- 1 hour from the time the study medication was taken in the maintenance period.
b. Subjects will decide if they will participate in the OLE
c. Subjects who choose to participate in the OLE will consent at Visit 6.
d. Written Informed Consent must be obtained prior to performing any study-related procedures.
e. Only R-MOAS and CGI-S scale will be administered.
f. To be performed for female subjects of childbearing potential
g. Randomization will be performed by the study site once eligibility from the two PSAP fMRI sessions and structural scan are completed at the Imaging Center.
h. Taper or Conversion kit will be dispensed.
i. AEs and Con Meds will be recorded through a follow up call from the site
j. Subjects will start their first dose the next day after dispensation (Day 1).

4.2.1 *Screening/Visit 1 (Day -30)*

Prior to conducting any procedures, written Informed Consent must be obtained from the parent or LAR, and, if appropriate, Informed Assent will be obtained from the subject. Subject screening procedures will be performed within 30 days prior to titration, and may be done on more than 1 day. At Visit 1, subjects will have their head shape scanned at the clinical site using a noninvasive handheld 3D scanning system from Caseforge system. A fitted and custom designed foam helmet will be ordered to be used inside the MRI scanner (Caseforge, California). The helmet has been shown to limit head motion in an fMRI scanner (Gao et al., 2015).

The following procedures will be performed at Visit 1:

1. Obtain written Informed Consent and Assent.
2. Confirm Inclusion/Exclusion criteria.
3. Administer MINI-KID for ADHD diagnosis.
4. Administer Vitiello Aggression Scale.
5. Administer R-MOAS.
6. Administer CGI-S.
7. Record Medical History.
8. Record Demographic Information.
9. Perform Physical Examination.
10. Perform 12-lead ECG.
11. Collect Urine for Urine Drug Screen and Urinalysis (all subjects) and Pregnancy Test (females of childbearing potential [FOCP] only).
12. Record Vital Signs (Heart Rate [HR], Blood Pressure [BP], Temperature, and Respiration Rate [RR]).
13. Record Weight, Height, and BMI.
14. Collect Blood Samples for Hematology and Chemistry.
15. Administer C-SSRS.
16. Record Concomitant Medications.
17. Access IWRS for subject number.
18. Scan head shape using the Caseforge system.

4.2.2 *Baseline MRI Scans/ Visit 2, (Day -5 to 0)*

Baseline may be carried out in more than one day but will occur within 5 days prior to the Titration period per the Schedule of Events and Procedures.

At Visit 2 the pre-treatment MRI session will be performed at the Imaging Center with the following activities:

1. Administer MRI Safety Questionnaire
2. Administer Edinburgh Handedness Inventory

3. Habituation Phase
4. MRI Session
5. Administer the PSAP Questionnaire

4.2.2.1 MR Safety Questionnaire and Edinburgh Handedness Inventory

Prior to any MRI procedures, subjects will complete the MR Safety Questionnaire to confirm their eligibility to proceed with the MRI scan.

The Edinburgh Handedness Inventory is a well-known short questionnaire used to objectively determine whether one is left or right handed (Oldfield, 1971),

The MR Safety Questionnaire and the Edinburgh Handedness Inventory will be recorded on a paper source and collected at the Imaging Center.

4.2.2.2 Habituation Phase

Eligible subjects will undergo a habituation phase, during which they will learn and practice the PSAP Task outside of the MRI environment. During this phase, subjects will perform a short, 3 to 5 minute version of the PSAP Task to habituate them to the task. In order to habituate to the horizontal position inside a head coil, subjects will undergo a 20-minute mock MRI acquisition. During the mock session, subjects will learn to keep their head still via feedback from the sensor based on the MoTrak head motion feedback system (Psychology Software Tools, Pennsylvania). The MoTrak system has been shown in multiple studies to be effective in training pediatric populations to limit their head motion inside an MRI scanner (Epstein et al., 2007; Greene et al., 2016). Subjects will also acclimate themselves to the MRI scanner sounds during this time.

4.2.2.3 MRI Session

After a short break, the subject will be placed on the MR scanner bed and positioned in the 32-channel head coil using the Caseforge customized helmet, such that the subject can see the projection screen at the back of the magnet via a mirror system. The subject will be given ear plugs, may have a respiratory belt placed around their chest, a pulse sensor placed on their toe, and given the button box for the PSAP Task and the emergency squeeze ball. Subjects will undergo approximately 1-hour MR imaging session with the following acquisitions:

1. 3-plane localizer scan
2. First 12-minute PSAP Task fMRI scan
3. Second 12-minute PSAP Task fMRI scan
4. A 6-minute 3D MPRAGE anatomical scan (subjects will be watching a short movie)
5. One 8-minute MRS acquisition
6. rs-fMRI scan to establish their resting-state BOLD signal (subjects will view a crosshair during 8 minutes)
7. A 3-minute T2 fluid-attenuated inversion recovery (FLAIR) clinical anatomical scan

Although breaks are not recommended during the imaging sessions, subjects may be allowed to take a short break (approximately 10 minutes) if they request it or once they complete the sessions up to the 3D MPRAGE scan.

Subjects who are not able to complete the aggression task session(s) and the structural scan (3D MPRAGE anatomical scan) will be considered early discontinued and not included in the analysis.

After the MRI session, subjects will be administered the PSAP Questionnaire to validate their understanding of the task and to describe their opponent. Subjects will be excluded from the analysis if they do not believe they played against a real person (e.g., they were thinking they were playing against a computer). The results of the questionnaire will be provided to the study site.

Once all the procedures are completed at the Imaging Center, eligible subjects will be instructed to return to the study site for Visit 3.

4.2.3 *Randomization/ Visit 3, (Day 0)*

The following procedures will be performed at the study site:

1. Randomization.
2. Record Concomitant Medications.
3. Record Adverse Events.
4. Assess for any clinical significant changes in Medical History.
5. Dispense Study Medication

4.2.4 *Maintenance/Visit 4 (Day 21)*

Visit 4 will occur 21 days after the start of the Titration period. Subjects will be instructed to take their morning dose at the site. The following procedures will be performed:

1. Administer CGI-I and CGI-S.
2. Administer R-MOAS.
3. Record Vital Signs (Heart Rate [HR], Blood Pressure [BP], Temperature, and Respiration Rate [RR]).
4. Perform Physical Examination.
5. Record Height, Weight, and BMI.
6. Perform 12-lead ECG.
7. Collect blood samples for PK.
8. Administer C-SSRS.

9. Administer Safety Scales (Simpson-Angus, Barnes Akathisia Rating, and AIMS).
10. Record Adverse Events.
11. Record Concomitant Medications.
12. Assess Drug Compliance.
13. Drug Return.
14. Dispense Study Medication (Either Conversion or Taper dose based on subject's decision to participate in OLE.

4.2.5 *Maintenance/Visit 5 (Day 28)*

Visit 5 will occur 28 days (± 1 day) after starting the Titration Period and no more than ***1 day*** after completion of Maintenance period per the Schedule of Events and Procedures. Subjects will take the morning dose of study medication and the ADHD medication before the visit.

The post-treatment MRI session will be scheduled preferably in the morning, within 3 hours +/- 1 hour from the time the study medication was taken during the maintenance period.

The following activities will be performed at the Imaging Center.

1. Administer MR Safety Questionnaire
2. Habituation Phase
3. MRI session
4. Administer the PSAP Questionnaire

Upon completion of the post-treatment MRI session, the study site will follow up with a call to collect the following activities:

1. Record Adverse Events.
2. Record Concomitant Medications.

4.2.6 *Taper/Conversion/Visit 6 (Day 35)/EOS*

Visit 6 will occur approximately 7 days (±2 days) following Visit 5 according to the Schedule of Events and Procedures. These procedures will be performed for all subjects who complete the Maintenance period and for those who discontinue early. Subjects who discontinue during the Maintenance period (between Day 15 and 28) will be offered a Taper card and return to the study site to complete Visit 6. Any subject who discontinues during the Titration period (Days 1-14), will be instructed to return to the study site for the final visit, within 1 week after discontinuation.

1. Administer R-MOAS.
2. Administer CGI-I and CGI-S.
3. Perform Physical Examination.
4. Perform 12-lead ECG.

5. Collect Urine for Pregnancy Test (FOCP only).
6. Record Vital Signs (Heart Rate [HR], Blood Pressure [BP], Temperature, and Respiration Rate [RR]).
7. Record Height, Weight, and BMI.
8. Collect Blood for Hematology and Chemistry.
9. Collect Urine for Urinalysis.
10. Administer C-SSRS.
11. Administer Safety Scales (Simpson-Angus, Barnes Akathisia Rating, AIMS).
12. Record Adverse Events.
13. Record Concomitant Medications.
14. Collect Study Medication and Assess Treatment Compliance.
15. Obtain written Informed Consent and Assent for OLE study.
16. Complete/Discontinue Subject.

4.2.7 *Pharmacokinetic Blood Sampling*

[redacted]

5 TREATMENTS

5.1 Treatments Administered

SPN-810

Subjects will take molindone hydrochloride extended-release tablet (SPN-810) or placebo twice each day (BID) with or without food, in the morning and in the evening, in addition to their stable dose of the optimized ADHD medication. Subjects should start the first dose the morning following Visit 3. Subjects will be randomized to one of the 2 treatments at the completion of Visit 3. Subjects will be titrated to the final randomized total daily dose (TDD).

Reference Treatment

- Treatment 1: Placebo (PBO) tablets (2 tablets), BID

Test Treatment

- Treatment 2: SPN-810, 36 mg (2 tablets) TDD, BID

ADHD Medication

The Investigator is not allowed to adjust the FDA-approved ADHD monotherapy medication and/or its dose at any time during the course of this study.

5.1.1 *Identity of Investigational Product(s)*

Study medication and reference (matching placebo) products are either purple (3 mg) or yellow (9 mg) round tablets which are printed with the appropriate dose strength in a black underscored font ("3" or "9").

A sufficient quantity of medication will be dispensed for the subject to take the designated dose every day until the next visit to the office, according to Table 1.

Each study medication blister card will contain combinations of SPN-810 and/or placebo tablets, which will supply a subject with 7 days of dosing with one additional dosing for lost product and/or to account for visit delays associated with patient schedules.

A single study medication kit contains a total of 6 pre-packaged blister cards (2 Titration blister cards, 2 Maintenance blister cards, 1 Taper blister card and 1 Conversion blister card) and is marked with a unique 4-digit study medication kit number.

5.1.2 *Study Medication Handling and Accountability*

All study medication is supplied to the Investigator by the Sponsor. Study medication must be kept in an appropriately secure area (e.g., locked cabinet) and stored according to the conditions specified on the study medication labels. Study medication must be stored between 59 – 86°F (15 – 30°C).

Following Sponsor instructions and in compliance with International Conference on Harmonization (ICH) E6 as well as local, state, and federal regulations, the Investigator and study staff will be responsible for the accountability of all clinical supplies (receiving, shipping, dispensing, maintaining inventory, and record-keeping) in a study medication accountability log, a copy of which will be collected by the Sponsor at the end of the study.

Under no circumstances will the Investigator allow the study medication to be used other than as directed by this protocol. Clinical supplies will not be dispensed to any individual who is not enrolled into the study.

An accurate and timely record of the receipt of all clinical supplies, the dispensing of study medication to the subject, the collection of unused supplies returned by the subject, and the return of unused study medication to the Sponsor must be maintained with dates. This study medication accountability log includes, but may not be limited to: (a) documentation of receipt of clinical supplies, (b) study medication inventory log, (c) study medication accountability log, and (d) all shipping notifications. All forms will be provided by the Sponsor. Any comparable forms that the study site wishes to use must be approved by the Sponsor.

Supplies and inventory records must be made available upon request for inspection by the designated representative of the Sponsor or a representative of the FDA. The assigned Clinical Research Associate (CRA) will review these documents along with all other study conduct

documents at each and every visit to the study site once study medication has been received by the study site. All used, partly used, and unused clinical supplies, including empty containers, are to be returned to the Investigator by the subjects and ultimately to the Sponsor at the conclusion of the study, unless provision is made by the Sponsor for destruction of supplies and containers at the study site. Upon completion of study medication accountability and reconciliation procedures by study site personnel and documentation procedures by Sponsor personnel, study medication is to be returned to the Sponsor with a copy of the completed study medication disposition form as outlined in the Study Medication Manual.

5.1.3 *Method of Assigning Subjects to Treatment Groups*

Allocation of the study medication will be completed centrally through the use of an interactive web response system (IWRS) that will determine which kit to assign to the subject. The final randomization schedules will be created by a designated unmasked statistician using SAS (SAS Institute, Cary, North Carolina, Version 9.2 or higher). Separate schedules for subject randomization and drug kit list will be created. The randomization scheme assigns treatment codes to each randomization number in a 1:1 ratio.

Upon enrollment to the study, subjects will be assigned site (01-99) and subject numbers in the sequence that they are entered. Subjects who minimally complete the two (2) PSAP sessions and the MPRAGE structural scan and meet all eligibility criteria will be assigned kit numbers, according to the randomization schedule, by using the IWRS.

5.1.4 *Treatment Replacement*

In the event that a subject's original kit is lost, damaged, or consumed prior to the end of treatment, the Investigator will consult the IWRS, which will specify a replacement kit number to be sent to the site. Separate reserve supplies will not be provided to the Investigators.

5.1.5 *Dosing Schedule*

At Visit 3, eligible subjects will be randomized to placebo or to SPN-810 in a 1:1 ratio and the study medication will be dispensed. Dosing will begin the following day after drug dispensation. Table 2 below presents the details of the dosing for each active treatment group throughout the 4-week Treatment Phase for this study. Dose reduction will not be permitted in the study.

Table 2: Titration Dosing Schedule

Treatment Arm	Final Dose	Study Days					
		1-2	3-4	5-7	8-10	11-14	15+
	Period*	T	T	T	T	T	M
1	Placebo	PBO	PBO	PBO	PBO	PBO	PBO
2	36 mg	[redacted]					

*T=Titration period; M=Maintenance period; PBO=Placebo

5.1.6 *Method of Administration*

The study medication must be swallowed whole. Study medication must not be crushed, chewed or cut. The study medication may be taken with or without food in the morning and in the evening, preferably every 12 hours.

5.1.7 *Blinding*

The subject and all study personnel involved with the conduct and interpretation of the study, including the Investigators, site personnel and the Sponsor will be blinded to the medication codes. A limited number of Supernus personnel will perform and interpret the plasma assays for the population PK analysis and will be aware of these PK data during the study. These personnel will not have access to the randomization schedule, are not associated with the clinical conduct of the study, and will not reveal to any clinical personnel involved in the study the treatment to which a subject is assigned. Randomization schedule data will be kept strictly confidential, filed securely by the IWRS vendor, and accessible only to authorized persons until the time of unblinding.

The study medication tablets have matching placebo tablets. Blinding is maintained through the IWRS, and will be maintained through the end of the Conversion/Taper phase.

The Investigator must try to avoid breaking the blind. The decoding information will not be viewed unless an actual medical or medication safety emergency occurs. The Investigator can access the subject's randomized treatment information via IWRS only if knowledge of the treatment regimen will influence or assist with medical management of the subject in an acute emergency. Before breaking the blind, every effort must be made to contact the Medical Monitor to ascertain the necessity of breaking the code. If the Investigator is unsuccessful in contacting the Medical Monitor, he/she will contact the backup Medical Monitor (or other appropriate designee if the backup Medical Monitor is unavailable). If it is not possible to contact the Medical Monitor or the backup Medical Monitor (or designee), and the situation is an emergency, the Investigator may break the blind and contact the Medical Monitor as soon as possible. The Investigator is to make a careful note of the date and time of decoding, the reason that necessitated breaking the code, and the signature of the person who broke the code. Upon breaking the randomization code, the subject should be withdrawn from the study but should be followed up for safety purposes.

5.1.8 *Allowed Medication*

The following medications are allowed during this study:

1. Current or other FDA-approved monotherapy ADHD medication (the ongoing medication will not be adjusted during the study).
2. EMLA (lidocaine 2.5% and prilocaine 2.5%) or other numbing cream for pharmacokinetic venipuncture.
3. Benztropine is permitted for the treatment of emerging EPS at a starting dose of 0.5 mg BID up to a range of 1 to 4 mg/day. Lorazepam (1 to 2 mg per dose not to exceed 3

times daily) and clonazepam (0.25 to 1 mg per dose not to exceed twice daily) is also permitted to treat EPS.

4. For the treatment of akathisia, propranolol is recommended, up to 90 mg/day in divided doses, 3 times per day, starting at 10 mg twice daily and up to 30 mg 3 times daily, as needed.
5. Common over-the-counter (OTC) therapies for minor transient ailments (e.g., acetaminophen for headache, ibuprofen for fever) will be allowed without exception.
6. Treatment for AEs other than EPS or minor transient ailments is permitted in consultation with the Medical Monitor and Sponsor.

All concomitant medications as well as the dosing of the FDA-approved ADHD medication will be recorded in the electronic case report form (eCRF).

5.1.9 *Study Restrictions*

Subjects may not be on any prohibited medication while on study as indicated in the Inclusion/Exclusion Criteria. These medications include:

- Anticonvulsants including carbamazepine and valproic acid, antidepressants, mood stabilizers including lithium, benzodiazepines, cholinesterase inhibitors, or any drug known to inhibit or induce CYP2D6 activity
- α_2-adrenergic agonists (e.g., clonidine and guanfacine) used for any other reason except for monotherapy treatment for ADHD
- Herbal and nutritional supplements

5.2 Completion of Study and Discontinuation of Subjects

Subjects will be considered to have completed the study if they complete all visits up to and including Visit 6. Any subject who discontinues from the study during the Maintenance period or following Day 14 in the Titration period will be offered a Taper card at the study site one week prior the EOS. Subjects who discontinue during the Titration period (i.e., Day 1 through Day 14) will be instructed to return 1 week after discontinuation to the study site for a final visit. All subjects who discontinue after Visit 2 will complete Visit 6, EOS procedures.

The Investigator(s) or subjects themselves may stop study medication treatment at any time for safety or personal reasons. A subject is free to withdraw from the study at any time for any reason without prejudice to their future medical care by the physician or at the institution. The Investigator or Sponsor may also withdraw the subject at any time in the interest of subject safety. The withdrawal of a subject from the study by the investigator should be discussed where possible with the Medical Monitor before the subject stops study medication. Subjects removed from the study for any reason will not be replaced.

Reasons for withdrawal may include but are not limited to subject withdrawal of consent, occurrence of unmanageable AEs, or if it is in the best interest of the subject as per Investigator's discretion.

The primary reason for withdrawal must be recorded in the subject's medical record and on the eCRF. If a subject is withdrawn for more than one reason, each reason should be documented in the source document and the most medically significant reason should be entered on the eCRF.

6 ANALYSIS VARIABLES

6.1 Primary Variable

The primary analysis variable will be the treatment effect of SPN-810 on the change in BOLD fMRI contrast associated with the aggressive response from Baseline (Visit 2) to Visit 5 measured in subjects with ADHD and IA participating in the PSAP aggression Task.

Briefly, the primary endpoint is the change in brain activity measured by a change in BOLD response in brain regions during provocation or during the aggressive response relative to the monetary response at baseline and following 4 weeks treatment with SPN-810, compared to placebo.

Behavioral data may allow calculation of the aggressive score, defined as the number of Option 2 presses (aggressive response) divided by the total number of button presses and the number of provocations received.

Details of the analyses will be provided in the statistical analysis plan (SAP).

6.2 Secondary Variables

6.2.1 *Functional Connectivity*

Resting-state data will be used to generate maps of functional connectivity within brain networks and/or ROI and will be stored in a correlation matrix. To investigate brain networks, a seed to whole brain correlation map may be used to investigate changes in network connectivity. All correlation coefficients will be converted to a z-score using Fisher's Z-transformation to normalize values.

To look at connectivity between ROIs, seed to seed correlation values will be calculated. All correlation coefficients will be converted to a z-score using Fisher's Z-transformation to normalize values. In addition, the relevant variables for the correlation matrices will be calculated by Northwestern University.

6.2.2 *GABA and Glutamate Brain Concentrations*

The concentrations of neurotransmitters Glu and GABA will be achieved during the MRS scan and evaluated in the anterior cingulate cortex (ACC).

6.3 Safety Assessments

6.3.1 *Adverse Events*

Although adverse events (AEs) for MRI scans are very rare, any medical occurrence during and after the study procedures will be recorded as an AE.

As defined by the ICH Guideline for Good Clinical Practice (GCP), an **adverse event (AE)** is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with treatment.

An AE can be:

1. Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
2. Any new disease, intercurrent injuries, or exacerbation of an existing disease.
3. Any deterioration in a laboratory value or other clinical test (e.g., ECG) that results in symptoms, a change in treatment, or discontinuation from study medication.
4. Recurrence of an intermittent medical condition (e.g., headache) not present at the beginning of the study.

Surgical procedures are not AEs; they are therapeutic measures for conditions that require surgery. The condition for which the surgery is required is an AE if it occurs or is detected during the study period.

6.3.1.1 Causality

AEs may be categorized as either adverse drug reactions or suspected adverse drug reactions (SADRs) based on their relationship to the study medication or procedure and the degree of certainty about causality.

SADRs are a subset of AEs for which there is evidence to suggest a causal relationship between the drug and the AE; i.e., there is a reasonable possibility that the drug caused the AE.

Adverse drug reactions (ADRs) are a subset of all AEs for which there is reason to conclude that the drug or procedure caused the event.

6.3.1.2 Recording and Evaluation of Adverse Events

All subjects who provided written Informed Consent (starting at Visit 1) will be questioned regarding the occurrence of AEs. Treatment emergent adverse events (TEAE) are undesirable events not present prior to study treatment/procedures, or an already present event that worsens either in intensity or frequency following the study treatment/procedure. A treatment emergent adverse event (TEAE) is an adverse event that occurs after study treatment/procedures has started. Adverse events occurring prior to the administration of the study medication/procedures (Day 1) will become part of the subject's

medical history including the severity of the event. At each visit, the Investigator must seek information on AEs by specific questioning and, as appropriate, by examination. Information on all AEs should be recorded immediately in the source document and also in the appropriate AE module of the eCRF. All clearly related signs, symptoms, and abnormal diagnostic procedures/laboratory results should be recorded in the source document, though they may be assessed as one diagnosis. For example fever, elevated white blood cells, cough, abnormal chest X-ray, etc., may all be reported as pneumonia.

6.3.1.3 Criteria for Assessing Severity

The Investigator will evaluate the comments of the subject and the response to treatment in order that he or she may judge the true nature and severity of the AE. Severity refers to the accumulated intensity of discomfort/impairment of health since the last recording of AEs and will be assessed according to the following criteria:

- **Mild:** Awareness of sign, symptom, or event, but easily tolerated
- **Moderate:** Discomfort enough to interfere with usual activity and may warrant intervention
- **Severe:** Incapacitating with inability to do usual activities or significantly affects clinical status and warrants intervention

The criteria for assessing severity are different from those used for seriousness.

6.3.1.4 Criteria for Assessing Causality

The Investigator is responsible for determining the relationship between the administration of study medication and the occurrence of an AE as **not suspected** or as a **suspected** reaction to study medication. These are defined as follows:

Not suspected: The temporal relationship of the AE to study medication administration makes a **causal relationship unlikely**, or other drugs, therapeutic interventions, or underlying conditions provide a sufficient explanation for the observed event.

- **Not related:** Temporal relationship to study medication administration is missing or implausible, or there is an evident other cause.
- **Unlikely related**: Temporal relationship to study medication administration makes a causal relationship improbable; and other drugs, chemicals, or underlying disease provide plausible explanations.

Suspected: The temporal relationship of the AE to study medication administration makes a **causal relationship possible**, and other drugs, therapeutic interventions, or underlying conditions do not provide a sufficient explanation for the observed event.

- **Possibly related:** Temporal relationship to study medication administration is plausible, but concurrent disease or other drugs or chemicals could also explain the event.

Information on medication withdrawal may be lacking or unclear. This will be reported as a **SADR**.

- **Definitely related:** Temporal relationship to study medication administration is plausible, and concurrent disease or other drugs or chemicals cannot explain the event. The response to withdrawal of the medication (de-challenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory re-challenge procedure if necessary. This will be reported as an **adverse drug reaction (ADR).**

6.3.2 *Serious Adverse Events (SAEs)*

AEs are classified as serious or non-serious. An AE or ADR is considered "**serious**" if, in the view of either the Investigator or Sponsor, it results in one of the following outcomes:

- Death
- Life-threatening AE (I.e., the subject was at immediate risk of death from the AE as it occurred. This does not include an event that, had it occurred in a more severe form or was allowed to continue, might have caused death.)
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability or incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly or birth defect
- An important medical event

Important medical events are those that may not be immediately life-threatening or result in death or hospitalization, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug dependence or abuse, blood dyscrasias, a seizure that did not result in inpatient hospitalization, or intensive treatment for allergic bronchospasm in an emergency department would typically be considered serious.

6.3.2.1 Investigator Responsibilities for Reporting SAEs

The Investigator must immediately report to the Sponsor all SAEs, regardless of whether the Investigator believes they are drug related.

The Investigator must report all SAEs to the Drug Safety Contact person(s) within 24 hours of first becoming aware of the SAE. The Investigator must complete an SAE Form and include a detailed description of the SAE, as well as other available information pertinent to the case (e.g., hospital records, autopsy reports, and other relevant documents). The Investigator will keep a copy of this SAE Report Form on file at the study site.

The Investigator or study physician, after thorough consideration of all facts that are available, must include an assessment of causality of an AE to study medication in the report to the Sponsor.

Follow-up information, or new information available after the initial report, should be actively sought and reported to the Sponsor as it becomes available using the SAE Report Form.

The Drug Safety Contact for SAE reporting is:

[redacted]

6.3.2.2 Other Events Requiring Immediate Reporting

The Investigator must report a **pregnancy** that occurs in a subject during a clinical study to the Drug Safety Contact within 24 hours of first becoming aware of the event. Pregnancy should be reported on a Pregnancy Report Form. The Investigator should discuss the case with the Sponsor Medical Monitor; the Investigator must also follow any pregnant subject for 3 months after the child is born. Any AEs concerning the health of the subject during pregnancy or the child after birth must be documented and reported to the Sponsor.

Treatment-emergent **EPS** (e.g., akathisia, dystonia, parkinsonism, tardive dyskinesia), and neuroleptic malignant syndrome should in addition to documenting in the CRF, be reported to the Drug Safety Contact by faxing or scanning the appropriate completed form/source documentation within 24 hours of first becoming aware of the event. EPS incidence will be summarized and shared with study Investigators throughout the clinical trial.

Overdosage of molindone presumably may be manifested by severe EPS and sedation. Coma with respiratory depression and severe hypotension resulting in a shock-like syndrome could occur. In the event of a suspected overdose, the parent or legal representative should be instructed to call 911 or their local poison control center at[redacted]

Symptomatic, supportive therapy should be the rule. Gastric lavage is indicated for the reduction of absorption of SPN-810, which is freely soluble in water. Since the adsorption of SPN-810 by activated charcoal has not been determined, the use of this antidote must be considered of theoretical value.

Emesis in a comatose patient is contraindicated. Additionally, while the emetic effect of apomorphine is blocked by SPN-810 in animals, this blocking effect has not been determined in humans.

6.3.2.3 Sponsor Responsibilities for Expedited Reporting of SAEs

The Sponsor will inform Investigators and regulatory authorities of ADRs that are both serious and unexpected, in compliance with applicable regulatory requirements, on an expedited basis (i.e., within specific time frames). For this reason, it is imperative that study sites submit SAE information to the Sponsor in the manner described above.

6.3.3 *Management of Treatment-Emergent Extrapyramidal Symptoms*

If a subject experiences treatment-emergent EPS (including akathisia, dystonia, parkinsonism, or tardive dyskinesia), benztropine will be permitted at a starting dose of 0.5 mg BID up to a range of 1 to 4 mg/day. Lorazepam (1 to 2 mg per dose not to exceed 3 times daily) and clonazepam (0.25 to 1 mg per dose not to exceed twice daily) will also be permitted to treat the occurrence of EPS. For the treatment of akathisia, propranolol is recommended up to 90 mg/day in divided doses, 3 times per day, starting at 10 mg twice daily and up to 30 mg three times daily, as needed.

A positive finding on an EPS safety assessment scale (Barnes Akathisia Rating, Simpson-Angus, or AIMS) does not necessarily equate to an EPS event. Investigators should evaluate positive findings on the EPS safety assessment scales and integrate them into a global clinical observation to determine if an AE of EPS should be recorded.

6.3.4 *Laboratory Measurements*

With the exception of urine pregnancy tests, clinical laboratory tests will be performed by a central laboratory as specified in the reference binder.

Details for collecting, handling, and shipping samples (including shipment addresses) will be described in a separate laboratory manual. The Schedule of Visits and Procedures (Table 1) shows the time points at which urine samples will be collected for urinalysis and blood samples will be collected for clinical laboratory tests and plasma concentration levels.

Table 3 presents the clinical laboratory tests to be performed. Metabolic parameters (including insulin, glucose, triglycerides, and cholesterol) and prolactin will be measured.

All laboratory tests will be reviewed in a timely manner by qualified site personnel to ensure safety. Abnormal lab findings may be confirmed if necessary by one repeated test at the discretion of the Investigator. Any laboratory abnormality may qualify as an AE in the Investigator's judgment.

A total of approximately 42 mL of blood per subject will be drawn during the study: 22 mL is for clinical laboratory tests and 20 mL is for PK sampling.

Table 3: Clinical Laboratory Tests

Category	Parameters
Hematology	WBC with differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils, large unstained cells), Hgb, HCT, RBC, MCH, MCHC, MCV, and platelet count

Chemistry	**Electrolytes:** Na^+, K^+, chloride, bicarbonate
	Liver function tests: alkaline phosphatase, AST, ALT, total bilirubin, direct bilirubin, indirect bilirubin
	Renal function parameters: BUN, creatinine
	Other: glucose, Ca^{2+}, albumin, phosphorus, lactate dehydrogenase, total protein, CK/CPK, globulin, uric acid, triglycerides, insulin, prolactin, cholesterol (total, HDL, and LDL), amylase, GGT, iron, lipase, and magnesium
Urinalysis	Glucose, protein (total), ketones, bilirubin, urobilinogen, hemoglobin, leukocyte esterase, nitrite
Urine drug test	Cocaine, amphetamines, barbiturates, benzodiazepines, cannabinoids, opioids, phencyclidine, propoxyphene, methadone and alcohol
Urine pregnancy test (FOCP only)	hCG

ALT: alanine transaminase; AST: aspartate transaminase; BUN: blood urea nitrogen; CK/CPK: creatinine kinase/creatinine phosphokinase; FOCP: females of childbearing potential; GGT: gamma glutamyl-transferase; hCG: human chorionic gonadotropin; HCT: hematocrit; HDL: high-density lipoprotein; Hgb: hemoglobin; LDL: low-density lipoprotein; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; MCV: mean corpuscular volume; RBC: red blood cells; WBC: white blood cells.

6.3.5 *Vital Signs and Height/Weight Measurements*

Vital signs' measurements (e.g., blood pressure, heart rate, temperature, and respiratory rate) and height, weight, and BMI will be obtained at visits designated on the Schedule of Visits and Procedures (Table 1). Blood pressure and heart rate will be measured after the subject has been sitting for 5 minutes. Vital signs may be taken at any other time, as deemed necessary by the Investigator.

6.3.6 *Medical History*

Medical history will be collected at visits designated on the Schedule of Visits and Procedures (Table 1).

6.3.7 *Physical Examinations and Electrocardiograms (ECGs)*

A complete physical examination will be conducted at visits designated on the Schedule of Visits and Procedures (Table 1). This will include assessments of the head, eye, ears, nose, throat, skin, thyroid, abdomen (liver and spleen), lymph nodes, and extremities and the cardiovascular and nervous systems (motor strength, cranial nerves, deep tendon reflexes, coordination, balance, and gait).

6.3.8 *Electrocardiograms*

A 12-lead ECG will be obtained at visits designated on the Schedule of Visits and Procedures (Table 1). Additional ECGs may be performed at other times if deemed necessary by the Investigator. The ECG will be recorded while the subject is resting in a supine position. The ECG will electronically calculate the heart rate and will measure the PR, QRS, QT, and QTc intervals.

All ECG tracings will be reviewed within 24 hours by the Investigator or qualified Sub-Investigator. PR intervals will be determined for each of these ECGs from a single reading. Invalid measurements will be repeated. QTc will be reported as QTcF (QT corrected using Fridericia's method).

6.3.9 *Special Safety Assessments*

The following special scales will be administered in the clinic at visits designated in the Schedule of Visits and Procedures (Table 1):

6.3.9.1 Simpson-Angus Scale (Section 12.3)

The Simpson-Angus Scale is a 10-item rating scale that is widely used for assessment of neuroleptic-induced parkinsonism (Simpson & Angus, 1970). It consists of 1 item measuring gait, 6 items measuring rigidity, and 3 items measuring glabella tap, tremor, and salivation, respectively. This assessment will be administered at Visit 1, Visit 4, and Visit 6.

6.3.9.2 Barnes Akathisia Rating Scale (BARS) (Section 12.4)

The BARS is a rating scale for drug-induced akathisia and includes components for rating the observable, restless movements characteristic of akathisia, the awareness of restlessness, and any distress associated with the condition (Barnes, 1989). This assessment will be administered at Visit 1, Visit 4, and Visit 6.

6.3.9.3 Abnormal Involuntary Movement Scale (AIMS) (Section 12.5)

The AIMS test is a rating scale used to measure tardive dyskinesia (Munetz & Benjamin, 1988). There are 12 items that rate involuntary movements of various areas of the subject's body. This assessment will be administered at Visit 1, Visit 4, and Visit 6.

6.3.9.4 Columbia-Suicide Severity Rating Scale (C-SSRS) (Section 12.6)

The C-SSRS is a questionnaire that prospectively assesses suicidal ideation and behavior using a semi-structured interview to probe patient responses (Posner et al., 2011). The C-SSRS versions applicable to the current study are the Baseline version and the Since Last Visit version (Visit 1, Visit 4 and Visit 6).

The Baseline version of the scale assesses lifetime suicidal ideation and behavior. This version is suitable as part of a subject's first interview and will be used at Visit 1 to identify volunteers who must not participate in the trial due to their suicidal tendencies.

The Since Last Visit version of the scale assesses any suicidal thoughts or behaviors the subjects may have had since the last administration of the C-SSRS. This version will be used for the other study visits.

6.4 Tertiary Variables

6.4.1 *Pharmacokinetic Measurements*

[redacted].

6.4.1.1 Pharmacokinetic Variables

The pharmacokinetic variables of interest will be (but not limited to) the following:

1. Apparent clearance (CL/F),
2. Apparent volume of distribution (V/F) of molindone in the study population

6.4.2 *Clinical Global Impression Scale (Section 12.1)*

The Clinical Global Impression scale was developed to provide a brief, stand-alone assessment of the clinician's view of a subject's global functioning prior to and after administration of a study medication (Guy, 1976). Severity of illness (CGI-S) and global improvement (CGI-I) are both rated on a scale of 1 to 7, with 7 being "extremely ill" or "very much worse," respectively. Successful therapy is indicated by a lower overall score in subsequent testing. Investigators should consider their total clinical experience with children who have ADHD and associated feature of IA and rate how severe the subject's condition is at the time.

- CGI-S will be evaluated by the Investigator on a 7-point scale with 1=Normal, 2=Borderline ill, 3=Mildly ill, 4=Moderately ill, 5=Markedly ill, 6=Severely ill, and 7=Extremely ill.

CGI-S will be administered by the Investigator at Visit 1, Visit 4, and Visit 6.

- CGI-I will be evaluated by the Investigator on a 7-point scale with 1=Very much improved, 2=Much improved, 3=Minimally improved, 4=No change, 5=Minimally worse, 6=Much worse, and 7=Very much worse.

CGI-I will be administered by the Investigator at Visit 4 and Visit 6.

6.4.3 *Retrospective-Modified Overt Aggression Scale (R-MOAS) (Section 12.2)*

The R-MOAS was developed to gauge the severity of aggressive behavior (Blader et al., 2009). Parents rate the frequency over the past week of 16 aggressive behaviors in 4 areas: verbal aggression; physical aggression toward others; aggression toward oneself; and destruction or hostile misuse of property. Numeric weighting amplifies the seriousness of more harmful behaviors in the total score. The R-MOAS will be administered at Visit 1, Visit 4, and Visit 6.

6.5 Other Special Tests

The following special tests will be administered in the clinic as per Schedule of Events during the Screening Period:

6.5.1 *MINI-KID (Section 12.7)*

The MINI-KID is designed to be used for children aged 6 to 17 years old, and has been shown to have substantial to excellent concordance with the diagnosis of ADHD, among other Axis I psychiatric disorders (Sheehan et al., 2010; Leffler et al., 2015). The interview can take from 15 to 50 minutes, and can be given to parents or children, together or separately (Leffler et al., 2015). All the modules will be administered except for modules R, S, T, U, V and W. This assessment will be administered at Visit 1.

6.5.2 *Vitiello Aggression Scale (Section 12.8)*

The Vitiello Aggression Scale is a 10-item rating scale that uses a cluster analysis to categorize aggression into 2 subtypes, predatory (or planned) and affective (or impulsive) (Vitiello et al., 1990). This assessment will be administered at Visit 1.

6.5.3 *Edinburgh Handedness Inventory (Section 12.9)*

The Edinburgh Handedness Inventory is a measurement scale designed to establish hand dominance. The shorter version, 10-item inventory is a self-report questionnaire on everyday common activities such as writing, drawing, throwing and using utensils. Subjects place 1 or 2 "+" marks under "left" or "right," indicating strength of preference for each activity; 2 "++" are to be used if the individual "would never try to use the other hand unless absolutely forced to" for the given function (Oldfield, 1971). This assessment will be administered at Visit 2.

7 STATISTICAL METHODS

7.1 General Notions

Tabular summaries of the data collected during the study will provide a general description of the subjects studied and an overview of the treatment effect on brain functioning, GABA and Glu levels, PK, and safety results. Data from all sites will be combined in the computation of these summaries. Correlations between changes in neuronal activation and neurotransmitter concentrations will be analyzed. Continuous variables will be summarized using descriptive statistics (number of subjects, mean, standard deviation [SD], median, and minimum and maximum). Categorical (nominal) variables will be summarized by reporting the frequency and percentage of subjects in each category.

In addition to tabular summaries, subject data listings, as specified in Sections 16.2 and 16.4 of ICH Guidance E3, will be provided. Analysis processing will be performed before the database is released. Statistical programming and analyses will be performed.

Complete details of the statistical analysis will be provided in a separate Statistical Analysis Plan (SAP), which will be written, finalized, and approved prior to the database lock and will be

included in the Clinical Study Report (CSR) for this protocol. Any deviation from the statistical plan will be documented and described in the final report. If changes to principal features stated in the protocol are required, these will be documented in a protocol amendment. The final SAP will take into account any amendment to the protocol.

7.2 Handling of Dropout or Missing Data

No imputation will be implemented.

7.3 Analysis Populations

The population of "all enrolled subjects" consists of all those screened subjects who meet the requirements for study participation and have completed the imaging procedures prior to randomization. The population of "all randomized subjects" consists of all those enrolled subjects who complete the Baseline Period including imaging scans, meet the inclusion/exclusion criteria and are randomized. The following populations will be analyzed:

Safety Population: includes all subjects randomized and who received at least 1 dose of study drug.

Completed Population: includes all subjects randomized, who have baseline imaging scans (including the anatomical scan) and post-treatment imaging scans.

PK population: includes all subjects in the safety population who had at least 1 PK sample drawn which had a quantifiable concentration of molindone.

7.4 Demographics

Demographic variables include age, sex, ethnicity, race, height, weight, and medical history at Screening. Tabular summaries of the demographic/baseline variables will be presented for the completed and safety populations, except for medical history, which will be summarized for the safety population.

7.5 Subject Disposition

The number and percentage of subjects who completed and discontinued from the study will be summarized in each of the following categories:

- Subjects in the randomized population
- Subjects treated (safety population)
- Subjects in the completed population

The reasons for study discontinuation may include one of the following:

- Subject withdrew consent
- Lost to follow-up
- Lack of efficacy
- Administrative reason
- Adverse event

- Investigator decision
- Failure to follow required study procedures
- Other

Only one reason for study discontinuation will be recorded for each subject.

7.6 Protocol Deviations

Protocol deviations will be presented in listings. If applicable, the number and percent of subjects within each type of protocol deviation will be presented using discrete summary statistics. Protocol deviations may include, but are not limited to:

- Non-compliance with any scheduled study visit
- Compliance with study treatment <80%
- Disallowed concomitant medications
- Non-compliance with study inclusion or exclusion criteria
- Non-compliance with study assessment procedures

7.7 Study Medication Exposure and Compliance

Duration of treatment exposure is defined as the total number of days a subject is exposed to study treatment. This will be calculated for each subject by taking the difference between the date of last dose *minus* the date of the first dose, *plus* 1 (date of last dose – date of first dose +1).

Duration of treatment exposure will also be summarized using descriptive statistics (n, mean, SD, median, minimum, and maximum).

Percent of study drug compliance will be calculated as:

> {(D-R)/ 4*(D_L- D_F)}*100, where D=number of tablets dispensed, R=number of tablets returned, D_L=date of last visit (dose) and D_F=date of first visit (dose)

The study medication compliance will be summarized by compliance category (<80%, 80-120%, and >120%) and number of subjects in each compliance category. Study medication compliance will also be summarized as a continuous variable using descriptive statistics (n, mean, standard deviation, median, minimum, and maximum).

Summaries of treatment compliance and exposure will be presented separately for the Titration period, Maintenance period, and combined Titration and Maintenance periods.

8 STATISTICAL ANALYSIS

Both primary and secondary analyses will be based on the completed population.

8.1 Primary Endpoint Analysis

The primary endpoint will be analyzed by assessing the difference in the change in BOLD fMRI contrast related to the aggressive response in the PSAP Task from baseline (Visit 2) to the end of treatment (Visit 5) in each treatment group.

8.1.1 *Imaging Analysis*

All functional imaging data will be analyzed using statistical parametric mapping software SPM12 package (Wellcome Trust Centre for Neuroimaging, Institute of Neurology; London, UK), Analysis of Functional Neuroimages (AFNI, NIH, USA) and software developed in-house at Dr. Parrish's lab, by Dr. Lana Kaiser, and at Supernus. Additional software that may be used includes FSL (Oxford, Cambridge, UK), Freesurfer (MGH, USA), and Matlab (MathWorks, USA). While performing the PSAP Task, neuronal activation is anticipated in the ACC, ventromedial PFC, amygdala, insular regions, and ventral striatum including nucleus accumbens, etc. Therefore these ROIs will be emphasized during the imaging analysis.

8.1.1.1 PSAP Task

For the PSAP Task data, the analyses will be mainly descriptive and will be assessed as the change in BOLD fMRI contrast associated with the aggressive response at baseline and post-treatment. The primary endpoint may be analyzed by assessing the mean, standard deviation, median, minimum and maximum of the BOLD signal change related to aggression for each treatment group (SPN-810 36 mg group and placebo) and study visit (baseline and Visit 5).

Additional analysis details will be described in the SAP.

8.2 Secondary Endpoint Analyses

8.2.1 *Functional Connectivity (Resting State fMRI)*

The secondary endpoints for functional connectivity will be the actual z-score, converted from the Fisher's Z-transformation of correlation coefficients, acquired during the rs-fMRI at Baseline (Visit 2) and Visit 5.

The analyses of the resting state data will be exploratory and informative of the connectivity between ROIs of the aggression network. Correlation matrices representing functional connectivity in the aggression network for each resting state scan will be generated at Visit 2 (baseline) and at Visit 5. The correlation values will be converted to a z-score (Fisher's Z-transformation). The descriptive analyses will be performed to assess the z-scores by treatment group (SPN-810 36 mg group and placebo) and visit (baseline and Visit 5).

The mean difference, of the z-scores between two treatment groups (SPN-810 36 mg group minus placebo) and pre- and post-treatment (post- minus pre-treatment) and the associated 2-sided 95% CI of the differences will be reported.

Additional analysis details will be provided in the SAP.

8.2.2 *GABA and Glutamate Concentrations*

The concentrations of GABA and Glu in the ACC will be obtained during MRS acquisition. The analyses will be descriptive by assessing the statistics for the concentrations of GABA and Glu by treatment group and visit (pre-treatment: Visit 2 fMRI scan and post-treatment: Visit 5). The change from baseline will be defined as the difference in concentration of GABA and Glu between Visit 2 and Visit 5 for each treatment group. The 2-sided 95% CI for the mean difference between treatment group and pre- and post-treatment will be also examined.

8.3 Safety Analysis

Evaluation of safety will be performed for the safety population. Safety data that will be evaluated include concomitant medications, AEs, clinical laboratory results, vital signs, ECGs, and findings from the physical examinations. The occurrence of neurological side effects will be assessed by looking at any worsening in scores from Visit 1 to the end of the study visit for each of the Simpson-Angus Scale, Barnes Akathisia Rating Scale, and AIMS. Suicidal ideation and suicidal behavior will be measured by the C-SSRS.

All summary tables related to safety analyses will use the safety population.

8.3.1 *Adverse Events*

AEs will be classified into standardized medical terminology from the verbatim description (Investigator term) using the Medical Dictionary for Regulatory Activities (MedDRA). AEs will be summarized using discrete summaries at the subject and event level by system organ class and preferred term for each group of doses. Similarly, treatment-emergent AEs will be summarized by severity and relationship separately. Verbatim description and all MedDRA level terms, including the lower-level terms, for all AEs will be contained in the subject data listings.

All AEs occurring throughout the study period will be recorded. Treatment-emergent AEs (TEAEs) will be collected starting after the baseline fMRI scan and after the first dose of study medication (after Visit 3) to the end of the study. These AEs include those that emerge after the fMRI procedures and during treatment or worsen in severity during treatment. These AEs will be tabulated, listed, and analyzed.

Separate TEAE incidence tables will be presented for the 2 treatment groups. The incidence rates for all SADRs will also be summarized as described for all TEAEs.

In addition, these same tables will be presented by treatment period (Titration, Maintenance, and combined Titration and Maintenance periods). For the combined Titration and Maintenance periods, the incidence of TEAEs will also be presented by highest severity reported and the dose of study medication at first occurrence. Listings (and tabular summaries, if warranted) of deaths, other SAEs, and other significant TEAEs, including TEAEs resulting in treatment discontinuation, will be provided.

8.3.2 *Laboratory Values*

Clinical laboratory values will be summarized by visit and by treatment group using descriptive statistics for hematology, chemistry, and urinalysis. For quantitative laboratory parameters, both actual values and change from Baseline values will be summarized.

Laboratory test results will be assigned a low, normal, high (LNH) classification according to whether the values were below (L), within (N), or above (H) the laboratory parameters' reference ranges provided by the central laboratory. Within-treatment comparisons will be based on 3 x 3 tables (shift tables) that, for a particular laboratory test, compare the LNH classification at baseline to the LNH classification at visit. Listings of all abnormal laboratory values by subject (i.e., those with L or H classification) will be provided.

8.3.3 *Vital Signs, Height, Weight, and BMI*

Vital signs will be summarized by the visit and by treatment group using descriptive statistics. Both actual values and changes from the baseline to final visit will be summarized. Descriptive summary statistics (mean, SD, median, and range) for vital sign data, height, weight, and BMI will be evaluated.

8.3.4 *ECG Results*

Tabular summaries of the quantitative ECG parameters and the overall ECG findings (normal, abnormal not clinically significant, or abnormal clinically significant) will be presented. The QT will be corrected using Fridericia's method.

ECG results will be summarized by visit and by treatment group using descriptive statistics (for quantitative ECG parameters) and frequency tables (for qualitative ECG parameters, including the overall ECG finding). For quantitative ECG parameters, both actual values and change from Baseline values will be summarized.

8.3.5 *Physical Examinations*

Findings from the physical examinations will be listed for each system or area examined.

8.3.6 *Concomitant Medications*

Concomitant medications will be assigned an 11-digit code using the World Health Organization Drug Dictionary (WHO DD) drug codes. Concomitant medications will be further coded to the appropriate Anatomical-Therapeutic-Chemical (ATC) code indicating therapeutic classification. A tabular summary of concomitant medications by drug class will be presented.

8.3.7 *C-SSRS*

C-SSRS outcomes will be summarized using number and percent of subjects by categories for suicidal ideation only, suicidal behavior only, and suicidality (ideation and behavior combined). The summary will be presented by treatment group. The proportion of subjects in each treatment group will be compared with the proportion of subjects in the placebo group using Fisher's exact test or chi-square test as appropriate.

8.3.8 *Extrapyramidal Symptoms*

The occurrence of neurological side effects will be assessed by looking at the changes in scores from Baseline to Visit 4 and Visit 6 for each of the Simpson-Angus Scale, Barnes Akathisia Rating Scale, and AIMS. For each item on each of these scales, the number (and percentage) of subjects with a worse score at any post-Baseline visit, compared to Baseline, will be presented. A listing of these subjects will also be provided.

8.4 Tertiary Variable Analysis

8.4.1 *Pharmacokinetic Analysis*

[redacted]

8.4.2 *Behavioral Scales*

Each of 3 variables (R-MOAS, CGI-I, and CGI-S) will be analyzed using two-sample t-test (or nonparametric analysis as appropriate) for the completed population. The means of each treatment group, the difference in means (36-mg dose minus placebo), and the 2-sided 95% CI for the difference will be obtained. The descriptive statistics will be reported for absolute value and change from baseline for each measurement (as appropriate) at each visit for both study treatment groups.

9 DOCUMENTATION

9.1 Adherence to the Protocol

The Investigator agrees, when signing the study protocol, to adhere to the instructions and procedures described within and to the principles of ICH GCP as well as all governing local regulations and principles for medical research.

The protocol, ICF, and appropriate related documents must be reviewed and approved by an Institutional Review Board (IRB) constituted and functioning in accordance with ICH E6, Section 4, “Investigator Guideline for GCP”, and any local regulations. Documentation of IRB compliance with the ICH and any local regulations regarding constitution and review conduct will be provided to the Sponsor.

A signed letter of study approval from the IRB must be sent to the Investigator, and a copy must be sent to the Sponsor prior to study start and the release of study medication to the site by the Sponsor or its designee. If the IRB decides to suspend or terminate the study, the Investigator will immediately send notice of study suspension or termination by the IRB to the Sponsor.

Study progress is to be reported to the IRB annually (or as required) by the Investigator or Sponsor, depending on local regulatory obligations. If the Investigator is required to report to the IRB, he/she will forward a copy to the Sponsor at the time of each periodic report.

9.2 Changes to the Protocol

There are to be no changes to the protocol without written approval from the Sponsor. Any change to the protocol requires a written protocol amendment or administrative change that must be approved by the Sponsor before implementation. Amendments specifically affecting the safety of subjects, the scope of the investigation, or the scientific quality of the study require additional approval by the applicable IRBs and, in some countries, by the regulatory authority. These requirements should in no way prevent any immediate action from being taken by the Investigator, or by the Sponsor, in the interest of preserving the safety of all subjects included in the study. If an immediate change to the protocol is felt by the Investigator to be necessary for safety reasons, the Medical Monitor and IRB must be notified promptly.

Changes to the protocol that are administrative in nature do not require formal protocol amendments or IRB approval, but the IRB must be kept informed of such changes. In these cases, the Sponsor will send a letter to the IRB detailing such changes.

9.3 Protocol Deviations

There are to be no Investigator-initiated deviations from the protocol. Any subject whose treatment deviates from the protocol or who is not qualified for study participation may be ineligible for analysis and may compromise the study. The date of and reason for deviations must be documented in all cases. Significant or major protocol deviations impacting the safety of the subject or the integrity of the study must be reported by the Investigator to the IRB immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB. Protocol assessments will continue until the end of the study, unless the protocol deviations put the subject at risk or the subject's condition requires that he/she be discontinued from the study. The Sponsor will make the determination as to whether the subject will continue in the study. The Sponsor also has the right to discontinue the subject for protocol violations. The IRB may also have to be contacted if safety to the subject or if the scientific soundness of the study is involved. All protocol deviations must be documented in the eCRFs.

9.4 Data Quality Assurance

This study will be organized, performed, and reported in compliance with the protocol, standard operating procedures (SOPs), working practice documents, and applicable regulations and guidelines. Site audits may be made periodically by the Sponsor's Quality Assurance team or qualified designee, as an independent function from the study conduct team.

9.4.1 *Data Collection*

The primary source document will be the subject's medical record. If separate research records are maintained by the Investigator(s), both the medical record and the research record will be considered the source documents for the purposes of monitoring and auditing the study.

Electronic data collection techniques will be used to collect data directly from the study sites using eCRFs. The electronic data will be stored centrally in a fully validated clinical database.

Data recorded on source documents will be transcribed into the eCRFs in accordance with the eCRF Completion Instructions provided to the study sites. The Investigator is responsible for ensuring that all sections of each eCRF are completed correctly, and that entries can be verified against source documents. The eCRFs will be monitored for completeness and accuracy against the source documents by the CRA(s) on a regular basis. Inconsistencies between the eCRFs and source documents will be resolved in accordance with the principles of GCP.

The Investigator will permit representatives of the Sponsor to inspect all Case Report Forms (CRFs) and corresponding study subject original medical records (source documents) at regular intervals throughout the study. Subjects' original medical records and other relevant data must be available to support all data recorded in the eCRFs. In addition to the original medical records, these data may include but are not limited to study, laboratory reports, etc.

In accordance with federal regulations, site inspections will serve to verify strict adherence to the protocol and the accuracy of the data that are being entered on the CRFs. A Monitoring Log will be maintained at each study site, which will be signed by the Medical Monitor, stating the type and date of visit. The Investigator should be aware that the study site and subject records may be inspected by the Sponsor and the FDA, or other regional regulatory authority. At the conclusion of the clinical study, each site's eCRF data will be extracted from the clinical database, stored on a CD-ROM and sent to the respective clinical study site for archiving. A CD-ROM containing all eCRFs will be kept by the Sponsor in the Sponsor's Trial Master File.

9.4.2 *Clinical Data Management*

Data from eCRFs and other external data sources (e.g., laboratory data) will be entered into and/or merged within a single clinical database as specified in the data management plan. Quality control and data validation procedures will be applied to ensure the validity and accuracy of the data in the clinical database.

9.4.3 *Database Quality Assurance*

In accordance with the vendor's procedures, the clinical database will be reviewed and checked for omissions, apparent errors, and values requiring further clarification using computerized and manual procedures. Data queries requiring clarification will be documented and returned to the study site for resolution. Only authorized personnel will make corrections to the clinical database, and all corrections will be documented in an audit trail.

9.5 Retention of Records

The Investigator has the responsibility to retain all study "essential documents", as described in ICH E6. Essential documents include but are not limited to the protocol, copies of paper CRFs or eCRFs, source documents, laboratory test results, study medication inventory records, Investigator's Brochure, and regulatory agency registration documents (e.g., FDA form 1572, ICFs, and IRB/ Independent Ethics Committee [IEC] correspondence). The investigator should take measures to prevent accidental or premature destruction of these documents. Study-essential documents should be retained until at least 2 years after the last approval of a marketing application or after formal discontinuation of clinical development of the

investigational product. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the Sponsor. The Investigator must obtain written permission from the Sponsor prior to the destruction of any study document.

It is requested that at the completion of the required retention period, or should the Investigator retire or relocate, the Investigator contact the Sponsor, allowing the Sponsor the option of permanently retaining the study records.

These records must be made available at reasonable times for inspection and duplication, if required, by a properly authorized representative of the FDA in accordance with the US 21 CFR 312.68 or other national or foreign regulatory authorities in accordance with regulatory requirements.

9.6 Auditing Procedures

In addition to the routine monitoring procedures, the Sponsor's Corporate Quality Assurance department or qualified designee may conduct audits of clinical research activities in accordance with the Sponsor's written SOPs to evaluate compliance with the principles of ICH GCP and all applicable local regulations. A government regulatory authority may also wish to conduct an inspection (during the study or after its completion). Any inspections requested by a regulatory authority must be communicated immediately by the Investigator to the Sponsor.

9.7 Publication of Results

Any presentation or publication of data collected as a direct or indirect result of this trial will be considered as a joint publication by the Investigator(s) and the appropriate personnel at the Sponsor. Authorship will be determined by mutual agreement. All manuscripts, abstracts, or other modes of presentation arising from the results of the study must be reviewed and approved in writing by the Sponsor, prior to submission for publication or presentation. No publication or presentation with respect to the study shall be made until any Sponsor comments on the proposed publication or presentation have been addressed to the Sponsor's satisfaction.

The detailed obligations regarding the publication of any data, material results, or other information, generated or created in relation to the study shall be outlined in the agreement between each Investigator and the Sponsor or designee.

9.8 Financing and Insurance

Financing and Insurance information will be set forth in a separate document between the Investigator and Sponsor (provided by the Sponsor or designee).

9.9 Disclosure and Confidentiality

The contents of this protocol, any amendments, and results obtained during the course of this study will be kept confidential by the Investigator, the Investigator's staff, and the IRB and will not be disclosed in whole or in part to others or used for any purpose other than reviewing or performing the study without the written consent of the Sponsor. No data collected as part of

this study will appear in any written work, including publications, without the written consent of Sponsor.

All persons assisting in the performance of this study must be bound by the obligations of confidentiality and non-use set forth in the Confidentiality Agreement between the Investigator and Sponsor.

9.10 Discontinuation of Study

The Sponsor reserves the right to discontinue the study for medical or administrative reasons at any time. The Investigator will be reimbursed for reasonable expenses covering subjects, use of live-in facilities, laboratory tests, and other professional fees. The Investigator will refund the excess of payments made in advance.

The Investigator reserves the right to discontinue the study should his/her judgment so dictate. The Investigator will notify the IRB in case of study discontinuation. Study records must be retained as noted above.

10 ETHICS

10.1 Institutional Review Boards / Independent Ethics Committees

A list of the IRB(s) and/or IEC(s) that approved this study and the approval letters will be included in the clinical study report for this protocol.

The protocol, any protocol amendments, and the Informed Consent form (ICF) will be reviewed and approved by the appropriate IRB/IEC before subjects are enrolled. IRB/IEC approval is required and will be acquired prior to the distributing study medication to investigational sites. The Investigators or Sponsor will submit, depending on local regulations, periodic reports and inform the IRB/IEC of any reportable AEs per ICH guidelines and local IRB/IEC standards of practice.

10.2 Ethical Conduct of the Study

This study will be conducted in accordance with SOPs from the Sponsor. These SOPs are designed to ensure adherence to GCP guidelines as required by the following:

- Declaration of Helsinki, 1964 (“Recommendations Guiding Physicians in Biomedical Research Involving Human Patients”), and all its accepted amendments to date concerning medical research in humans.
- ICH Guideline for GCP (Committee for Proprietary Medicinal Products/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, ICH of Pharmaceuticals for Human Use.
- United States (US) Code of Federal Regulations (CFR) dealing with clinical studies (21 CFR, including parts 50 and 56 concerning Patient Informed Consent and IRB regulations).
- Local and national legal guidelines.

10.3 Investigators and Study Personnel

This study will be conducted by qualified Investigators under the sponsorship of Supernus Pharmaceuticals, Inc. (Sponsor) at United States study sites.

Contact persons at the Sponsor are listed in the reference binder provided to each investigational site. The study will be monitored by qualified personnel from the Sponsor. The Sponsor will oversee and review the monitoring activities of the CRA monitor. Medical writing, data management, and statistical analyses will be performed by qualified service partners. Laboratory tests will be conducted by a central laboratory as designated in the reference binder.

10.4 Subject Information and Consent/Assent

The Investigator (or designee) will inform the subject and their parent(s), or legal representative, of all aspects pertaining to the subject's participation in the study and will provide oral and written information describing the nature and duration of the study, the procedures involved, the expected duration, the potential risks and benefits involved, and any potential discomfort.

The process for obtaining Informed Consent/assent will be in accordance with all applicable regulatory requirements. The Investigator (or designee) and the parent (or legal representative) must sign and date the Informed Consent Form (ICF)/Informed Assent Form (IAF) before the subject can participate in the study. The parent or legal representative and the subject will be given a copy of the signed and dated ICF/IAF and the original will be retained in the investigational site study records.

The decision regarding subject participation in the study is voluntary. The Investigator (or designee) must emphasize to the subject and their parent(s) or legal representative that consent regarding study participation may be withdrawn at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The ICF/IAF should be given by means of a standard written statement, written in non-technical language. The subject should understand the statement before signing and dating it. If written consent is not possible, oral consent may be obtained if witnessed by at least one person not involved in the study. The verbal consent will be documented and signed by the Investigator and the witness(es). No subject can enter the study before his/her ICF has been obtained.

If the ICF/IAF is amended during the study, the Investigator must follow all applicable regulatory requirements pertaining to approval of the amended ICF by the IRB and use the amended ICF (including ongoing subjects).

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12 APPENDICES

12.1 Clinical Global Impression (CGI) Scale

☐ **(1) NOT DONE**

INSTRUCTIONS: Indicate only one response for the question by placing a cross (X) in the appropriate numbered box.

SEVERITY OF ILLNESS:
Considering your total clinical experience with this particular population (*impulsive aggression comorbid with ADHD*), how severe is the subject's condition at this time?

☐ (0) NOT ASSESSED
☐ (1) Normal, not at all ill
☐ (2) Borderline mentally ill
☐ (3) Mildly ill
☐ (4) Moderately ill
☐ (5) Markedly ill
☐ (6) Severely ill
☐ (7) Among the most extremely ill patients

GLOBAL IMPROVEMENT: Rate total improvement whether or not, in your judgment, it is due entirely to drug treatment. Compared to his/her condition at Visit 1/Baseline, how much has the subject's *impulsive aggression* changed?

☐ (0) NOT ASSESSED
☐ (1) Very much improved
☐ (2) Much improved
☐ (3) Minimally improved
☐ (4) No change
☐ (5) Minimally worse
☐ (6) Much worse
☐ (7) Very much worse

12.2 Retrospective-Modified Overt Aggression Scale (R-MOAS)

A. Child's First Name: B. Child's Last Name:

C. Your First Name: D. Your Last Name:

E. Your Relationship to Child:

○ Mother ○ Father ○ Grandmother ○ Grandfather ○ Other

Staff Entries

Site Project Participant

Visit Type Visit #

Month Day Year

Retrospective Modified Overt Aggression Scale (R-MOAS)

Instructions: These questions focus on difficulties with emotions and behavior. Please indicate how many times each of these behaviors occurred in the PAST WEEK.

Verbal Incidents:	0 - 1 times	2 - 4 times	5 or more times
1. How many times did your child *shout angrily, curse,* or *insult people* but then stopped quickly?	○	○	○
2. How many times did your child *shout angrily, curse,* or *insult people* in a repetitive, out-of-control way during episodes that lasted less than five minutes?	○	○	○
3. How many times did your child *shout angrily, curse,* or *insult people* in a repetitive, out-of-control way during episodes that lasted more than five minutes?	○	○	○
4. How many times did your child *threaten to hurt someone*?	○	○	○

5. Other verbal incidents (Please describe):

Incidents Toward Other People:	None	1 - 2 times	3 - 4 times	5 or more times
1. How many times did your child act like he/she was *about to hit* somebody or *took a swing at someone* without actually hitting another person?	○	○	○	○
2. How many times did your child *hit someone* with hands or an object, *kick*, *push, scratch* or *pull hair*, without causing real injury?	○	○	○	○
3. How many times did your child do any of the things in Item 2 and caused some mild injury (bruises, sprains, welts, etc.)?	○	○	○	○
4. How many times did your child do any of the things in Item 2 and caused serious injury (fracture, lost tooth, loss of consciousness, etc.)?	○	○	○	○

5. Other incidents toward other people (Please describe):

RMOAS-P -- Page 2 of 2

Site ___ ___ Project ___ ___ | Visit Type ___ Visit # ___ ___ | Month ___ ___ / Day ___ ___ / Year ___ ___ | Subject # ___ ___ ___ ___ Initials ___ ___

Incidents Involving Property:

	None	1 - 2 times	3 - 4 times	5 or more times
1. How many times did your child *slam a door or cabinet*, *rip clothing*, or *knock something over* in anger?	○	○	○	○
2. How many times did your child *throw things down, kick furniture,* or otherwise *misuse things angrily* but did not break them?	○	○	○	○
3. How many times did your child *break things*, *smash windows*, or *damage or deface property* on purpose?	○	○	○	○
4. How many times did your child *set a fire* or *throw things at people* in order to hurt them?	○	○	○	○

5. Other incidents involving property (Please describe):

Incidents Directed Toward Self:

	None	1 - 2 times	3 - 4 times	5 or more times
1. How many times did your child *pick at or scratch* his or her skin, *pull out hair*, or *hit himself or herself* while upset or angry?	○	○	○	○
2. How many times did your child *bang his or her head, hit his or her fists into the wall*, or *throw* himself or herself on the floor?	○	○	○	○
3. How many times did your child *cut*, *bruise*, or *burn* himself or herself on purpose?	○	○	○	○
4. How many times did your child *severely injure* himself or herself, or *try to kill* himself or herself?	○	○	○	○

5. Other incidents in which your child acted harmfully toward himself or herself (Please describe):

Staff Use:
VE.....
PH....
PR.....
SE.....
Total.....

12.3 Simpson-Angus Scale

1. GAIT:
The patient is examined as he walks into the examining room, his gait, the swing of his arms, his general posture, all form the basis for an overall score for this item. This is rated as follows:

0 = Normal

1 = Diminution in swing while the patient is walking

2 = Marked diminution in swing with obvious rigidity in the arm

3 = Stiff gait with arms held rigidly before the abdomen

4 = Stopped shuffling gait with propulsion and retropulsion

2. ARM DROPPING:
The patient and the examiner both raise their arms to shoulder height and let them fall to their sides. In a normal subject, a stout slap is heard as the arms hit the sides. In the patient with extreme Parkinson's syndrome, the arms fall very slowly:

0 = Normal, free fall with loud slap and rebound

1 = Fall slowed slightly with less audible contact and little rebound

2 = Fall slowed, no rebound

3 = Marked slowing, no slap at all

4 = Arms fall as though against resistance; as though through glue

3. SHOULDER SHAKING:
The subject's arms are bent at a right angle at the elbow and are taken one at a time by the examiner who grasps one hand and also clasps the other around the patient's elbow. The subject's upper arm is pushed to and fro and the humerus is externally rotated. The degree of resistance from normal to extreme rigidity is scored as follows.

0 = Normal

1 = Slight stiffness and resistance

2 = Moderate stiffness and resistance

3 = Marked rigidity with difficulty in passive movement

4 = Extreme stiffness and rigidity with almost a frozen shoulder

4. ELBOW RIGIDITY:
The elbow joints are separately bent at right angles and passively extended and flexed, with the subject's biceps observed and simultaneously palpated. The resistance to this procedure is rated. (The presence of cogwheel rigidity is noted separately.)

0 = Normal

1 = Slight stiffness and resistance

2 = Moderate stiffness and resistance

3 = Marked rigidity with difficulty in passive movement

4 = Extreme stiffness and rigidity with almost a frozen shoulder

5. WRIST RIGIDITY or Fixation of position:
The wrist is held in one hand and the fingers held by the examiner's other hand, with the wrist n1oved to extension, flexion and ulner and radial deviation:

0 = Normal

1 = Slight stiffness and resistance

2 = Moderate stiffness and resistance

3 = Marked rigidity with difficulty in passive movement

4 = Extreme stiffness and rigidity with almost a frozen shoulder

6. LEG PENDULOUSNESS:
The patient sits on a table with his legs hanging down and swinging free. The ankle is grasped by the examiner and raised until the knee is partially extended. It is then allowed to fall. The resistance to falling and the Jack of swinging form the basis for the score on this item:

0 = The legs swing freely

1 = Slight diminution in the swing of the legs

2 = Moderate resistance to swing

3 = Marked resistance and damping of swing

4 = Complete absence of swing

7. HEAD DROPPING:
The patient lies on a well-padded examining table and his head is raised by the examiner's hand. The hand is then withdrawn and the head allowed to drop. In the normal subject the head will fall upon the table. The movement is delayed in extrapyramidal system disorder and in extreme parkinsonism it is absent. The neck muscles are rigid and the head docs not reach the examining table. Scoring is as follows:

0 = The head falls completely with a good thump as it hits the table

1 = Slight slowing in fall, mainly noted by lack of slap as head meets the table

2 = Moderate slowing in the fall quite noticeable to the eye

3 = Head falls stiffly and slowly

4 = Head does not reach the examining table

8. GLABELLA TAP:
Subject is told to open eyes wide and not to blink. The glabella region is tapped at a steady, rapid speed. The number of times patient blinks in succession is noted:

0 = 0 - 5 blinks

1 = 6 – 10 blinks

2 = 11 – 15 blinks

3 = 16 - 20 blinks

4 = 21 and more blinks

9. TREMOR:
Patient is observed walking into examining room and is then reexamined for this item:

0 = Normal

1 = Mild finger tremor, obvious to sight and touch

2 = Tremor of hand or arm occurring spasmodically

3 = Persistent tremor of one or more limbs

4 = Whole body tremor

10. SALIVATION:
Patient is observed while talking and then asked to open his mouth and elevate his tongue. The following ratings are given:

0 = Normal

1 = Excess salivation to the extent that pooling takes place if the mouth is open and the tongue raised.

2 = When excess salivation is present and might occasionally result in difficulty in speaking

3 = Speaking with difficulty because of excess salivation

4 = Frank drooling

12.4 Barnes Akathisia Rating Scale (BARS)

Name:_____ **Date:**_____

Barnes Akathisia Rating Scale (BARS)

Instructions: Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Objective

0 Normal, occasional fidgety movements of the limbs
1 Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, *and/or* rocking from foot to foot or "walking on the spot" when standing, but movements present for less than half the time observed
2 Observed phenomena, as described in (1) above, which are present for at least half the observation period
3 Patient is constantly engaged in characteristic restless movements, *and/or* has the inability to remain seated or standing without walking or pacing, during the time observed

Subjective

Awareness of restlessness
0 Absence of inner restlessness
1 Non-specific sense of inner restlessness
2 The patient is aware of an inability to keep the legs still, or a desire to move the legs, *and/or* complains of inner restlessness aggravated specifically by being required to stand still
3 Awareness of intense compulsion to move most of the time *and/or* reports strong desire to walk or pace most of the time

Distress related to restlessness
0 No distress
1 Mild
2 Moderate
3 Severe

Global Clinical Assessment of Akathisia

0 *Absent.* No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia
1 *Questionable.* Non-specific inner tension and fidgety movements
2 *Mild akathisia.* Awareness of restlessness in the legs *and/or* inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.
3 *Moderate akathisia.* Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing
4 *Marked akathisia.* Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.
5 *Severe akathisia.* The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.

Scoring the Barnes Akathisia Rating Scale (BARS)

The Barnes Akathisia Rating Scale is scored as follows:

Objective Akathisia, Subjective Awareness of Restlessness and Subjective Distress Related to Restlessness are rated on a 4-point scale from 0 – 3 and are summed yielding a total score ranging from 0 to 9.

The Global Clinical Assessment of Akathisia uses a 5-point scale ranging from 0 – 4.

Citation: Barnes TR: A Rating Scale for Drug-Induced Akathisia. British Journal of Psychiatry 154:672-676, 1989.

12.5 Abnormal Involuntary Movement Scale (AIMS)

Abnormal Involuntary Movement Scale (AIMS)

Abnormal Involuntary Movement Scale

(AIMS)

Abnormal Involuntary Movement Scale (AIMS)

Examination Procedure

Either before or after completing the examination procedure, observe the patient unobtrusively at rest (e.g., in the waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask the patient whether there is anything in his or her mouth (such as gum or candy) and, if so, to remove it.
2. Ask about the *current* condition of the patient's teeth. Ask if he or she wears dentures. Ask whether teeth or dentures bother the patient *now*.
3. Ask whether the patient notices any movements in his or her mouth, face, hands, or feet. If yes, ask the patient to describe them and to indicate to what extent they *currently* bother the patient or interfere with activities.
4. Have the patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at the entire body for movements while the patient is in this position.)
5. Ask the patient to sit with hands hanging unsupported -- if male, between his legs, if female and wearing a dress, hanging over her knees. (Observe hands and other body areas).
6. Ask the patient to open his or her mouth. (Observe the tongue at rest within the mouth.) Do this twice.
7. Ask the patient to protrude his or her tongue. (Observe abnormalities of tongue movement.) Do this twice.
8. Ask the patient to tap his or her thumb with each finger as rapidly as possible for 10 to 15 seconds, first with right hand, then with left hand. (Observe facial and leg movements.)
9. Flex and extend the patient's left and right arms, one at a time.
10. Ask the patient to stand up. (Observe the patient in profile. Observe all body areas again, hips included.)
11. Ask the patient to extend both arms out in front, palms down. (Observe trunk, legs, and mouth.)
12. Have the patient walk a few paces, turn, and walk back to the chair. (Observe hands and gait.) Do this twice.

Abnormal Involuntary Movement Scale (AIMS)

Patient Information									
Patient		Date	Day	Mth.	Year	Time	Hour	Min	
Personal notes									

Scoring Procedure

Complete the examination procedure before making ratings.
For the movement ratings (the first three categories below), rate the highest severity observed.
0 = none, 1 = minimal (may be extreme normal), 2 = mild, 3 = moderate, 4 = severe.
According to the original AIMS instructions, one point is subtracted if movements are seen **only on activation**, but not all investigators follow that convention.

Facial and Oral Movements	
1. Muscles of facial expression, e.g., movements of forehead, eyebrows, periorbital area, cheeks. Include frowning, blinking, grimacing of upper face.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4
2. Lips and perioral area, e.g., puckering, pouting, smacking.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4
3. Jaw, e.g., biting, clenching, chewing, mouth opening, lateral movement.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4
4. Tongue. Rate only increase in movement both in and out of mouth, not inability to sustain movement.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4

Abnormal Involuntary Movement Scale (AIMS)

Extremity Movements	
5. Upper (arms, wrists, hands, fingers). Include movements that are choreic (rapid, objectively purposeless, irregular, spontaneous) or athetoid (slow, irregular, complex, serpentine). Do not include tremor (repetitive, regular, rhythmic movements).	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4
6. Lower (legs, knees, ankles, toes), e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4

Trunk Movements	
7. Neck, shoulders, hips, e.g., rocking, twisting, squirming, pelvic gyrations. Include diaphragmatic movements.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4

Global Judgements	
8. Severity of abnormal movements. Based on the highest single score on the above items.	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4
9. Incapacitation due to abnormal movements.	☐ none, normal ☐ minimal ☐ mild ☐ moderate ☐ severe
10. Patient's awareness of abnormal movements.	☐ no awareness ☐ aware, no distress ☐ aware, mild distress ☐ aware, moderate distress ☐ aware, severe distress

Abnormal Involuntary Movement Scale (AIMS)

Dental status	
11. Current problems with teeth and/or dentures.	☐ no ☐ yes
12. Does patient usually wear dentures?	☐ no ☐ yes

12.6 Columbia-Suicide Severity Rating Scale (C-SSRS)

12.6.1 *C-SSRS, Children's Baseline/Screening*

COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Children's Baseline/Screening

Version 6/23/10

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

Disclaimer:

This scale is intended to be used by individuals who have received training in its administration. The questions contained in the Columbia-Suicide Severity Rating Scale are suggested probes. Ultimately, the determination of the presence of suicidal ideation or behavior depends on the judgment of the individual administering the scale.

Definitions of behavioral suicidal events in this scale are based on those used in ***The Columbia Suicide History Form****, developed by John Mann, MD and Maria Oquendo, MD, Conte Center for the Neuroscience of Mental Disorders (CCNMD), New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY, 10032. (Oquendo M. A., Halberstam B. & Mann J. J., Risk factors for suicidal behavior: utility and limitations of research instruments. In M.B. First [Ed.]* Standardized Evaluation in Clinical Practice*, pp. 103-130, 2003.)*

For reprints of the C-SSRS contact Kelly Posner, Ph.D., New York State Psychiatric Institute, 1051 Riverside Drive, New York, New York, 10032; inquiries and training requirements contact posnerk@nyspi.columbia.edu

SUICIDAL IDEATION		
Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.	**Lifetime**	**Past 6 Months**
1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. ***Have you thought about being dead or what it would be like to be dead?*** ***Have you wished you were dead or wished you could go to sleep and never wake up?*** ***Do you ever wish you weren't alive anymore?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
2. Non-Specific Active Suicidal Thoughts General, non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period. ***Have you thought about doing something to make yourself not alive anymore?*** ***Have you had any thoughts about killing yourself?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g., thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it…and I would never go through with it."* ***Have you thought about how you would do that or how you would make yourself not alive anymore (kill yourself)? What did you think about?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them."* ***When you thought about making yourself not alive anymore (or killing yourself), did you think that this was something you might actually do?*** ***This is different from (as opposed to) having the thoughts but knowing you wouldn't do anything about it.*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
5. Active Suicidal Ideation with Specific Plan and Intent Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. ***Have you ever decided how or when you would make yourself not alive anymore/kill yourself? Have you ever planned out (worked out the details of) how you would do it?*** ***What was your plan?*** ***When you made this plan (or worked out these details), was any part of you thinking about actually doing it?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
INTENSITY OF IDEATION		
The following feature should be rated with respect to the most severe type of ideation (i.e., 1-5 from above, with 1 being the least severe and 5 being the most severe). ***Most Severe Ideation:*** _____ _____ ***Type # (1-5)*** ***Description of Ideation***	Most Severe	Most Severe
Frequency ***How many times have you had these thoughts?*** ***Write response***_____ (1) Only one time (2) A few times (3) A lot (4) All the time (0) Don't know/Not applicable	____	____

 C-SSRS—Children's Baseline/Screening (Version 6/23/10) Page 1 of 2

SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	**Lifetime**
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act.* Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Did you ever do anything to try to kill yourself or make yourself not alive anymore? What did you do?*** ***Did you ever hurt yourself on purpose? Why did you do that?*** ***Did you_____ as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to make yourself not alive anymore when you _____?*** ***Or did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons, not at all to end your life or kill yourself (like to make yourself feel better, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe:	Yes ☐ No ☐ Total # of Attempts _____
Has subject engaged in Non-Suicidal Self-Injurious Behavior?	Yes ☐ No ☐
Has subject engaged in Self-Injurious Behavior, intent unknown?	Yes ☐ No ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred).* Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to make yourself not alive anymore (end your life or kill yourself) but someone or something stopped you before you actually did anything? What did you do?*** If yes, describe:	Yes ☐ No ☐ Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to make yourself not alive anymore (end your life or kill yourself) but you changed your mind (stopped yourself) before you actually did anything? What did you do?*** If yes, describe:	Yes ☐ No ☐ Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you done anything to get ready to make yourself not alive anymore (to end your life or kill yourself)- like giving things away, writing a goodbye note, getting things you need to kill yourself?*** If yes, describe:	Yes ☐ No ☐
Suicidal Behavior: Suicidal behavior was present during the assessment period?	Yes ☐ No ☐

Answer for Actual Attempts Only	Most Recent Attempt Date:	Most Lethal Attempt Date:	Initial/First Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____

 C-SSRS—Children's Baseline/Screening (Version 6/23/10) Page 2 of 2

12.6.2 *C-SSRS, Since Last Visit*

COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Since Last Visit - Clinical

Version 1/14/09

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

Disclaimer:

This scale is intended to be used by individuals who have received training in its administration. The questions contained in the Columbia-Suicide Severity Rating Scale are suggested probes. Ultimately, the determination of the presence of suicidal ideation or behavior depends on the judgment of the individual administering the scale.

Definitions of behavioral suicidal events in this scale are based on those used in ***The Columbia Suicide History Form****, developed by John Mann, MD and Maria Oquendo, MD, Conte Center for the Neuroscience of Mental Disorders (CCNMD), New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY, 10032. (Oquendo M. A., Halberstam B. & Mann J. J., Risk factors for suicidal behavior: utility and limitations of research instruments. In M.B. First [Ed.]* Standardized Evaluation in Clinical Practice*, pp. 103 -130, 2003.)*

For reprints of the C-SSRS contact Kelly Posner, Ph.D., New York State Psychiatric Institute, 1051 Riverside Drive, New York, New York, 10032; inquiries and training requirements contact posnerk@nyspi.columbia.edu

SUICIDAL IDEATION

Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.

Since Last Visit

1. Wish to be Dead
Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up.
Have you wished you were dead or wished you could go to sleep and not wake up?
If yes, describe:
Yes ☐ **No** ☐

2. Non-Specific Active Suicidal Thoughts
General, non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period.
Have you actually had any thoughts of killing yourself?
If yes, describe:
Yes ☐ **No** ☐

3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act
Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g., thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it…and I would never go through with it."*
Have you been thinking about how you might do this?
If yes, describe:
Yes ☐ **No** ☐

4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan
Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them."*
Have you had these thoughts and had some intention of acting on them?
If yes, describe:
Yes ☐ **No** ☐

5. Active Suicidal Ideation with Specific Plan and Intent
Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out.
Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?
If yes, describe:
Yes ☐ **No** ☐

INTENSITY OF IDEATION

The following features should be rated with respect to the most severe type of ideation (i.e., 1-5 from above, with 1 being the least severe and 5 being the most severe).

Most Severe Ideation: _____ _____
Type # (1-5) ***Description of Ideation***

Most Severe

Frequency
How many times have you had these thoughts?
(1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day
____

Duration
When you have the thoughts, how long do they last?
(1) Fleeting - few seconds or minutes
(2) Less than 1 hour/some of the time
(3) 1-4 hours/a lot of time
(4) 4-8 hours/most of day
(5) More than 8 hours/persistent or continuous
____

Controllability
Could/can you stop thinking about killing yourself or wanting to die if you want to?
(1) Easily able to control thoughts
(2) Can control thoughts with little difficulty
(3) Can control thoughts with some difficulty
(4) Can control thoughts with a lot of difficulty
(5) Unable to control thoughts
(0) Does not attempt to control thoughts
____

Deterrents
Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?
(1) Deterrents definitely stopped you from attempting suicide
(2) Deterrents probably stopped you
(3) Uncertain that deterrents stopped you
(4) Deterrents most likely did not stop you
(5) Deterrents definitely did not stop you
(0) Does not apply
____

Reasons for Ideation
What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?
(1) Completely to get attention, revenge or a reaction from others
(2) Mostly to get attention, revenge or a reaction from others
(3) Equally to get attention, revenge or a reaction from others and to end/stop the pain
(4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling)
(5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling)
(0) Does not apply
____

SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	Since Last Visit
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act*. Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Have you made a suicide attempt?*** ***Have you done anything to harm yourself?*** ***Have you done anything dangerous where you could have died?*** ***What did you do?*** ***Did you_____ as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to end your life when you _____?*** ***Or did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe: **Has subject engaged in Non-Suicidal Self-Injurious Behavior?**	**Yes** **No** ☐ ☐ Total # of Attempts _____ **Yes** **No** ☐ ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred)*. Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything?*** If yes, describe:	**Yes** **No** ☐ ☐ Total # of interrupted _____
Aborted or Self-Interrupted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything?*** If yes, describe:	**Yes** **No** ☐ ☐ Total # of aborted or self-interrupted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?*** If yes, describe:	**Yes** **No** ☐ ☐ Total # of preparatory acts _____
Suicide: Death by suicide occurred since last assessment.	**Yes** **No** ☐ ☐
	Most Lethal Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____

 C-SSRS—Since Last Visit - Clinical (Version 1/14/09) Page 2 of 2

12.7 Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)

M.I.N.I. KID

MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW
FOR **CHILDREN** AND **ADOLESCENTS**

English Version 7.0.2

For

DSM-5

DISCLAIMER

Our aim is to assist in the assessment and tracking of patients with greater efficiency and accuracy. Before action is taken on any data collected and processed by this program, it should be reviewed and interpreted by a licensed clinician.

This program is not designed or intended to be used in the place of a full medical and psychiatric evaluation by a qualified licensed physician – psychiatrist. It is intended only as a tool to facilitate accurate data collection and processing of symptoms elicited by trained personnel. It is not a diagnostic test.

M.I.N.I. *Kid* 7.0.2 for Children and Adolescents (August 8, 2016) (8/8/16)

Patient Name:		***Patient Number:***	
Date of Birth:		***Time Interview Began:***	
Interviewer's Name:		***Time Interview Ended:***	
Date of Interview:		***Total Time:***	

	MODULES	TIME FRAME	MEETS CRITERIA	ICD-10-CM	PRIMARY DIAGNOSIS
A	MAJOR DEPRESSIVE EPISODE	Current (2 weeks)	☐		
		Past	☐		
		Recurrent	☐		
	MAJOR DEPRESSIVE DISORDER	Current (2 weeks)	☐	F32.x	☐
		Past	☐	F32.x	☐
		Recurrent	☐	F33.x	☐
B	SUICIDALITY	Current (Past Month)	☐		☐
		Lifetime attempt	☐	☐ Low ☐ Moderate ☐ High	☐
	SUICIDE BEHAVIOR DISORDER	Current	☐	(In Past Year)	☐
		In early remission	☐	(1 - 2 Years Ago)	☐
C	MANIC EPISODE	Current	☐		
		Past	☐		
	HYPOMANIC EPISODE	Current	☐		
		Past	☐	☐ Not Explored	
	BIPOLAR I DISORDER	Current	☐	F31.0 - F31.76	☐
		Past	☐	F31.0 - F31.76	☐
	BIPOLAR II DISORDER	Current	☐	F31.81	☐
		Past	☐	F31.81	☐
	OTHER SPECIFIED BIPOLAR AND RELATED DISORDER	Current	☐	F31.89	☐
		Past	☐	F31.89	☐
D	PANIC DISORDER	Current (Past Month)	☐	F41.0	☐
		Lifetime	☐	F40.0	☐
E	AGORAPHOBIA	Current	☐	F40.00	☐
F	SEPARATION ANXIETY DISORDER	Current (Past Month)	☐	F93.0	☐
G	SOCIAL ANXIETY DISORDER (Social Phobia)	Current (Past Month)	☐	F40.10	☐
H	SPECIFIC PHOBIA	Current (Past Month)	☐	F40.218 – F40.298	☐
I	OBSESSIVE-COMPULSIVE DISORDER	Current (Past Month)	☐	F42.2	☐
J	POSTTRAUMATIC STRESS DISORDER	Current (Past Month)	☐	F43.10	☐
K	ALCOHOL USE DISORDER	Past 12 Months	☐	F10.10 - F10.21	☐
L	SUBSTANCE USE DISORDER (Non-alcohol)	Past 12 Months	☐	F11.10 - F19.21	☐

M	TOURETTE'S DISORDER	Current	☐	F95.2		☐
	PERSISTENT (CHRONIC) MOTOR TIC DISORDER	Current	☐	F95.1		☐
	PERSISTENT (CHRONIC) VOCAL TIC DISORDER	Current	☐	F95.1		☐
	PROVISIONAL TIC DISORDER	Current	☐	F95.0		☐
N	ADHD COMBINED PRESENTATION	Past 6 Months	☐	F90.2		☐
	ADHD PREDOMINANTLY INATTENTIVE PRESENTATION	Past 6 Months	☐	F90.0		☐
	ADHD PREDOMINANTLY HYPERACTIVE TYPE PRESENTATION	Past 6 Months	☐	F90.1		☐
O	CONDUCT DISORDER	Past 12 Months	☐	F91.1/F91.2/F91.9		☐
P	OPPOSITIONAL DEFIANT DISORDER	Past 6 Months	☐	F91.3		☐
Q	ANY PSYCHOTIC DISORDER	Current Lifetime	☐ ☐	F20.xx-F29 F20.xx-F29		☐ ☐
	MAJOR DEPRESSIVE DISORDER WITH PSYCHOTIC FEATURES	Current Past	☐ ☐	F32.3/F33.3 F32.3/F33.3		☐ ☐
	BIPOLAR I DISORDER WITH PSYCHOTIC FEATURES	Current Past	☐ ☐	F31.2/F31.5/F31.64 F31.2/F31.5/F31.64		☐ ☐
R	ANOREXIA NERVOSA	Current (Past 3 Months)	☐	F50.01/F50.02		☐
S	BULIMIA NERVOSA	Current (Past 3 Months)	☐	F50.2		☐
T	BINGE-EATING DISORDER	Current (Past 3 Months)	☐	F50.81		☐
U	GENERALIZED ANXIETY DISORDER	Current (Past 6 Months)	☐	F41.1		☐
V	ADJUSTMENT DISORDERS	Current	☐	F43.20 – 43.25		☐
W	MEDICAL, ORGANIC, DRUG CAUSE RULED OUT			☐ No ☐ Yes ☐ Uncertain		
X	AUTISM SPECTRUM DISORDER	Cannot be ruled out	☐	F84.0		☐

IDENTIFY THE PRIMARY DIAGNOSIS BY CHECKING THE APPROPRIATE CHECK BOX.
(Which problem troubles you the most or dominates the others or came first in the natural history?)

INTERVIEWER INSTRUCTIONS

INTRODUCING THE INTERVIEW

The nature and purpose of the interview should be explained to the child or adolescent prior to the interview. A sample introduction is provided below:

"I'm going to ask you a lot of questions about yourself. This is so that I can get to know more about you and figure out how to help you. Most of the questions can be answered either 'yes' or 'no'. If you don't understand a word or a question, ask me, and I'll explain it. If you are not sure how to answer a question, don't guess - just tell me you are not sure. Some of the questions may seem weird to you, but try to answer them anyway. It is important that you answer the questions as honestly as you can so that I can help you. Do you have any questions before we start?"

For children under 13, we recommend interviewing the parent and the child together. Questions should be directed to the child, but the parent should be encouraged to interject if s/he feels that the child's answers are unclear or inaccurate. The interviewer makes the final decision based on his/her best clinical judgment, whether the child's answers meet the diagnostic criterion in question. With children you will need to use more examples than with adolescents and adults.

GENERAL FORMAT:

The MINI is divided into **modules** identified by letters, each corresponding to a diagnostic category.
- At the beginning of each diagnostic module (except for psychotic disorders module), screening question(s) corresponding to the main criteria of the disorder are presented in a **gray box**.
- At the end of each module, diagnostic box(es) permit the clinician to indicate whether diagnostic criteria are met.

CONVENTIONS:

Sentences written in «normal font» should be read exactly as written to the patient in order to standardize the assessment of diagnostic criteria.

Sentences written in «CAPITALS» should not be read to the patient. They are instructions for the interviewer to assist in the scoring of the diagnostic algorithms.

Sentences written in «**bold**» indicate the time frame being investigated. The interviewer should read them as often as necessary. Only symptoms occurring during the time frame indicated should be considered in scoring the responses.

Answers with an arrow above them (➡) indicate that one of the criteria necessary for the diagnosis or the diagnoses is not met. In this case, the interviewer should go to the end of the module and circle «**NO**» in all the diagnostic boxes and move to the next module.

When terms are separated by a *slash (/)* the interviewer should read only those symptoms known to be present in the patient (for example, question L2b).

Phrases in (parentheses) are clinical examples of the symptom. These may be read to the patient to clarify the question.

FORMAT OF THE INTERVIEW

The interview questions are designed to elicit specific diagnostic criteria. The questions should be read verbatim. If the child or adolescent does not understand a particular word or concept, you may explain what it means or give examples that capture its essence. If a child or adolescent is unsure if s/he has a particular symptom, you may ask him/her provide an explanation or example to determine if it matches the criterion being investigated. If an interview item has more than 1 question, the interviewer should pause between questions to allow the child or adolescent time to respond.

Questions about the duration of symptoms are included for diagnoses when the time frame of symptoms is a critical element. Because children may have difficulty estimating time, you may assist them by helping them connect times to

significant events in their lives. For example, the starting point for "past year" might relate to a birthday, the end or beginning of a school year, a particular holiday or another annual event.

RATING INSTRUCTIONS:

All questions must be rated. The rating is done at the right of each question by circling either YES or NO. Clinical judgment by the rater should be used in coding the responses. The rater should ask for examples when necessary, to ensure accurate coding. The child or adolescent should be encouraged to ask for clarification on any question that is not absolutely clear.

The clinician should take each dimension of the question into account (for example, time frame, frequency, severity, and/or alternatives).

Symptoms better accounted for by an organic cause or by the use of alcohol or drugs should not be coded positive in the MINI KID. The MINI Kid has questions that investigate these issues (Module W).

For any questions, suggestions, need for a training session or information about updates of the MINI Kid, please contact:
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A. MAJOR DEPRESSIVE EPISODE

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** IN THE DIAGNOSTIC BOX, AND MOVE TO THE NEXT MODULE)

A1	a	At any time in your life, did you feel sad or depressed? Felt down or empty or hopeless? Felt grouchy or annoyed? Did you feel this way most of the time, for at least 2 weeks? **IF YES** TO **ANY**, CONTINUE. **IF NO** TO **ALL**, CODE **NO TO A1a AND A1b**.	NO	YES
	b	For the past 2 weeks, did you feel this way, most of the day, nearly every day?	NO	YES
A2	a	At any time in your life, were you bored a lot or much less interested in things (like playing your favorite games)? Have you felt that you couldn't enjoy things? Did you feel this way most of the time, for at least 2 weeks? **IF YES** TO **ANY**, CONTINUE. **IF NO** TO **ALL**, CODE **NO TO A2a AND A2b**.	NO	YES
	b	For the past 2 weeks, did you feel this way, most of the day, nearly every day?	NO	YES
		IS **A1**a OR **A2**a CODED **YES**? ➡	NO	YES

A3 IF **A1b** OR **A2b** = **YES**: EXPLORE THE **CURRENT** AND THE MOST SYMPTOMATIC **PAST** EPISODE, OTHERWISE
IF **A1b** AND **A2b** = **NO**: EXPLORE **ONLY** THE MOST SYMPTOMATIC **PAST** EPISODE

	In the past two weeks, when you felt depressed / grouchy / uninterested:	Past 2 Weeks		Past Episode	
a	Were you less hungry or more hungry most days? Did you lose or gain weight without trying? [i.e., by ± 5% of body weight in the past month]? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	NO	YES
b	Did you have trouble sleeping almost every night ("trouble sleeping" means trouble falling asleep, waking up in the middle of the night, waking up too early or sleeping too much)?	NO	YES	NO	YES
c	Did you talk or move slower than usual? Were you fidgety, restless or couldn't sit still almost every day? Did anyone notice this? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	NO	YES
d	Did you feel tired most of the time?	NO	YES	NO	YES
e	Did you feel bad about yourself most of the time? Did you feel guilty most of the time? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	NO	YES
	IF **YES**, ASK FOR EXAMPLES. LOOK FOR DELUSIONS OF FAILURE, OF INADEQUACY, OF RUIN OR OF GUILT, OR OF NEEDING PUNISHMENT OR DELUSIONS OF DISEASE OR DEATH OR NIHILISTIC OR SOMATIC DELUSIONS. THE EXAMPLES ARE CONSISTENT WITH A DELUSIONAL IDEA. Current Episode ☐ No ☐ Yes Past Episode ☐ No ☐ Yes				
f	Did you have trouble concentrating or thinking or did you have trouble making up your mind almost every day? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	NO	YES
g	Did you feel so bad that you wished that you were dead? Did you think about hurting yourself? Did you have thoughts of death? Did you think about killing yourself? **IF YES** TO **ANY**, CODE **YES**. (FEAR OF DYING DOES NOT COUNT HERE).	NO	YES	NO	YES

		Past 2 Weeks		Past Episode	
		NO	YES	NO	YES
A4	Did these sad, depressed feelings cause a lot of problems at home? At school? With friends? With other people? Or in some other important way?				

		N/A	NO	YES
A5	In between your times of depression, were you free of depression or sadness for of at least 2 months?			

ARE **5** OR MORE ANSWERS (**A1-A3**) CODED **YES** AND IS **A4** CODED **YES** FOR THAT TIME FRAME?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY IF THE EPISODE IS CURRENT AND / OR PAST.

IF **A5** IS CODED **YES,** CODE **YES** FOR RECURRENT.

NO	**YES**

MAJOR DEPRESSIVE EPISODE

CURRENT	☐
PAST	☐
RECURRENT	☐

A6 a How many episodes of depression did you have in your lifetime? _____

Between each episode there must be at least 2 months without any significant depression.

B. SUICIDALITY (for ages 13 through 17)

				Points
	In the past month did you:			
B1	Have any accident? This includes taking too much of your medication by accident. **IF NO** TO **B1**, SKIP TO **B2**. **IF YES**, ASK **B1a**:	NO	YES	0
B1a	Plan or expect to hurt yourself on purpose in any accident, or put yourself in a position where you could be hurt? **IF NO** TO **B1a**, SKIP TO **B2**. **IF YES**, ASK **B1b**:	NO	YES	0
B1b	Want to die as a result of any accident?	NO	YES	0
B2	Think that you would be better off dead or wish you were dead or need to be dead?	NO	YES	1
B3	Think about hurting yourself, with the possibility that you might die? Or did you think about killing yourself? **IF YES** TO **EITHER**, CODE **YES**. **IF NO** TO **B2 + B3**, SKIP TO **B4**. OTHERWISE ASK: How often? How strong were the thoughts? ☐ Occasionally ☐ Often ☐ Very often ☐ Mild ☐ Moderate ☐ Severe	NO	YES	6
B4	Hear a voice or voices telling you to kill yourself or have a dream or a nightmare about killing yourself? IF YES, mark either or both: ☐ was it a voice or voices? ☐ was it a dream or a nightmare?	NO	YES	4
B5	Have a way or a method in mind to kill yourself (i.e. **how**)?	NO	YES	8
B6	Think about **what you would use** to kill yourself?	NO	YES	8
B7	Think about **where you would go** to kill yourself?	NO	YES	8
B8	Think about **when** you could kill yourself?	NO	YES	8
B9	Think about anything **you would like to finish before** trying to kill yourself? (e.g. writing a suicide note)	NO	YES	8
B10	Expect to **go through with a plan to** kill yourself? IF YES, mark either or both: ☐ did you intend to act at the time? ☐ did you intend to act at some time in the future?	NO	YES	8
B11	**Expect to die** as a result of trying to hurt yourself? IF YES, mark either or both: ☐ did you intend to die by suicide at the time? ☐ did you intend to die by suicide at some time in the future?	NO	YES	8
B12	Feel the **need or impulse** to kill yourself or to plan to kill yourself **sooner** rather than later? IF YES, mark either or both: ☐ was it to kill yourself? ☐ was it to plan to kill yourself? IF YES, mark either or both: ☐ was it for no good reason? ☐ was it for some good reason? IN ASSESSING WHETHER THIS WAS LARGELY UNPROVOKED ("FOR NO GOOD REASON") OR PROVOKED ASK: "5 minutes before this impulse to kill yourself, could you have predicted it would occur at that time?" IF NO TO **B12**, SKIP TO **B14**.	NO	YES	8

B13	Have difficulty **resisting** these impulses to kill yourself?	NO	YES	8
B14	Do things to **prepare** to kill yourself, but were interrupted or stopped yourself, before harming yourself? **IF NO** TO **B14**, SKIP TO **B15**. OTHERWISE GO TO **B14a**.	NO	YES	
B14a	Do things to **get ready** to kill yourself, but you did not start to kill yourself?	NO	YES	9
B14b	Do things to **get ready** to kill yourself, but then **you stopped yourself** just before you hurt yourself ("aborted")?	NO	YES	10
B14c	Do things to **get ready** to kill yourself, but then **someone or something stopped you just before** you hurt yourself ("interrupted")?	NO	YES	11
B15	Hurt yourself on purpose **without** trying to kill yourself? (B15 IS NOT COUNTED AS SUICIDAL BEHAVIOR)	NO	YES	0
B16	Try to kill yourself? **IF NO** TO **B16**, SKIP TO **B17**.	NO	YES	
B16a	Start to kill yourself, but then **you decided to stop** and you did not finish the attempt?	NO	YES	12
B16b	Start to kill yourself, but then **someone or something stopped you** and you did not finish the attempt?	NO	YES	13
B16c	Do **everything you could** to try to kill yourself **completely,** as you meant to? A suicide attempt means you did something where you could possibly be injured, with at least a slight intent to die. **IF NO**, SKIP TO **B17**. Hope to be rescued / survive ☐ Expected / intended to die ☐	NO	YES	14

B17 **TIME SPENT PER DAY WITH ANY SUICIDAL IMPULSES, THOUGHTS OR ACTIONS:**
Usual time spent per day: ____ hours ____ minutes.
Least amount of time spent per day: ____ hours ____ minutes.
Most amount of time spent per day: ____ hours ____ minutes.

In your lifetime:

B18	Did you ever try to kill yourself? **IF YES**, how many times? _____ **IF YES**, when was the last suicide attempt? Current: within the past 12 months ☐ In early remission: between 12 and 24 months ago ☐ In remission: more than 24 months ago ☐	NO	YES	4

"A suicide attempt is any self-injurious behavior, with at least some intent (> 0) to die as a result of the act. Evidence that the individual intended to kill him-or herself, at least to some degree, can be explicit or inferred from the behavior or circumstance. For example, it is defined as a suicide attempt if it is clearly not an accident or if the individual thinks the act could be lethal, even though denying intent." (FDA Guidance for Industry Suicidal Ideation and Behavior Document 2012 and C-CASA definition). Posner K et al. Am J Psychiatry 2007; 164 (7): 1035-1043 & http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm/

B19	How likely are you to try to kill yourself within the next 3 months on a scale of 0-100% _____% ANY LIKELIHOOD **> 0%** ON **B19** SHOULD BE CODED **YES**.	NO	YES	13

IS AT LEAST **1** OF THE ABOVE (EXCEPT B1) CODED **YES**?

IF **YES,** ADD THE TOTAL POINTS FOR THE ANSWERS (B1-B19) CHECKED 'YES' AND SPECIFY THE SUICIDALITY SCORE CATEGORY AS INDICATED IN THE DIAGNOSTIC BOX:

INDICATE WHETHER THE SUICIDALITY IS CURRENT (PAST MONTH) OR A LIFETIME SUICIDE ATTEMPT OR BOTH BY MARKING THE APPROPRIATE BOXES OR BY LEAVING EITHER OR BOTH OF THEM UNMARKED.

CURRENT = ANY POSITIVE RESPONSE IN **B1a** THROUGH **B16c** (EXCEPT B15) OR ANY TIME SPENT IN **B17**.
LIFETIME ATTEMPT = **B18** CODED **YES.**
LIKELY IN THE NEAR FUTURE = **B19** CODED **YES.**

MAKE ANY ADDITIONAL COMMENTS ABOUT YOUR ASSESSMENT OF THIS PATIENT'S CURRENT AND NEAR FUTURE SUICIDALITY IN THE SPACE BELOW:

NO	YES

SUICIDALITY

1-8 points	Low	☐
9-16 points	Moderate	☐
≥ 17 points	High	☐
CURRENT		☐
LIFETIME ATTEMPT		☐
LIKELY IN NEAR FUTURE		☐

IS **B18** CODED **YES**?

AND A YES RESPONSE TO

WAS THE SUICIDAL ACT STARTED WHEN THE SUBJECT *WAS NOT* IN A STATE OF CONFUSION OR DELIRIUM?

AND A YES RESPONSE TO

Was the suicidal act done without a political or religious purpose?
IF **YES,** SPECIFY WHETHER THE DISORDER IS CURRENT, IN EARLY REMISSION OR IN REMISSION.

NO	YES

SUICIDAL BEHAVIOR DISORDER

Current	☐
In early remission	☐
In remission	☐

B. SUICIDALITY (for ages 9 through 12)

				Points
	In the past month did you:			
B1	Have an accident? This includes taking too much of your medication by accident. **IF NO** TO **B1**, SKIP TO **B2**. **IF YES**, ASK **B1a**:	NO	YES	0
B1a	Plan or expect to hurt yourself on purpose in an accident? **IF NO** TO **B1a**, SKIP TO **B2**. **IF YES**, ASK **B1b**:	NO	YES	0
B1b	Try to die as a result of an accident?	NO	YES	0
B2	Think (even momentarily) that you would be better off dead or wish you were dead?	NO	YES	1
B3	Think about hurting yourself, with the possibility that you might die? Or did you think about killing yourself? **IF YES** TO **EITHER**, CODE **YES**. **IF NO** TO **B2 + B3**, SKIP TO **B4**. OTHERWISE ASK: How often? How strong were the thoughts? Occasionally ☐ Mild ☐ Often ☐ Moderate ☐ Very often ☐ Severe ☐	NO	YES	6
B4	Hear a voice or voices telling you to kill yourself or have a dream or a nightmare about killing yourself? IF YES, mark either or both: ☐ was it a voice or voices? ☐ was it a dream or a nightmare?	NO	YES	4
B5	Think about **how** to kill yourself?	NO	YES	8
B6	Think about **what you would use** to kill yourself?	NO	YES	8
B7	Think about **where you would go** to kill yourself?	NO	YES	8
B8	Think about **when** to kill yourself?	NO	YES	8
B9	Think about anything **you would like to finish before** you tried to kill yourself? (e.g. writing a suicide note)	NO	YES	8
B10	**Want** to **go through with a plan** to kill yourself?	NO	YES	8
B11	**Want to die** by hurting yourself?	NO	YES	8
B12	Think all of a **sudden** about killing yourself sooner rather than later? IF YES, mark either or both: ☐ was this to kill yourself? ☐ was this to plan to kill yourself? IF YES, mark either or both: ☐ was it for no good reason? ☐ was it for some good reason? IN ASSESSING WHETHER THIS WAS LARGELY UNPROVOKED ("FOR NO GOOD REASON") OR PROVOKED ASK: "5 minutes before this impulse to kill yourself, could you have predicted it would occur at that time?" IF NO TO **B12**, SKIP TO **B14**.	NO	YES	8
B13	Have difficulty resisting (or fighting against) these impulses to kill yourself?	NO	YES	8
B14	Do things to prepare to kill yourself? **IF NO** TO **B14**, SKIP TO **B15**. OTHERWISE GO TO **B14a**.	NO	YES	

B14a	Do things to **get ready** to kill yourself, but you did not start to kill yourself?	NO	YES	9
B14b	Do things to **get ready** to kill yourself, but then **you stopped yourself** just before you hurt yourself ("aborted")?	NO	YES	10
B14c	Do things to **get ready** to kill yourself, but then **someone or something stopped you** just before you hurt yourself ("interrupted")?	NO	YES	11
B15	Hurt yourself on purpose **without** trying to kill yourself? (B15 IS NOT COUNTED AS SUICIDAL BEHAVIOR)	NO	YES	0
B16	Try to kill yourself? **IF NO** TO **B16**, SKIP TO **B17**.	NO	YES	
B16a	Start to kill yourself, but then **you decided to stop** and did not finish trying?	NO	YES	12
B16b	Start to kill yourself, but then **someone or something stopped you** and did not finish the attempt?	NO	YES	13
B16c	Do **everything you could** to try to kill yourself? A suicide attempt means you did something where you could possibly be injured, with at least a slight intent to die. **IF NO**, SKIP TO **B17**.	NO	YES	14

Hope to be rescued / survive ☐
Expected / intended to die ☐

B17 **TIME SPENT PER DAY WITH ANY SUICIDAL IMPULSES, THOUGHTS OR ACTIONS:**
Usual time spent per day: ____ hours ____ minutes.
Least amount of time spent per day: ____ hours ____ minutes.
Most amount of time spent per day: ____ hours ____ minutes.

In your lifetime:

B18 Did you ever try to kill yourself? NO YES 4
IF YES, how many times? _____
IF YES, when was the last suicide attempt?
Current: within the past 12 months ☐
In early remission: between 12 and 24 months ago ☐
In remission: more than 24 months ago ☐

"A suicide attempt is any self-injurious behavior, with at least some intent (> 0) to die as a result of the act. Evidence that the individual intended to kill him-or herself, at least to some degree, can be explicit or inferred from the behavior or circumstance. For example, it is defined as a suicide attempt if it is clearly not an accident or if the individual thinks the act could be lethal, even though denying intent." (FDA Guidance for Industry Suicidal Ideation and Behavior Document 2012 and C-CASA definition). Posner K et al. Am J Psychiatry 2007; 164 (7): 1035-1043 & http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm/

B19	How likely are you to try to kill yourself within the next 3 months on a scale of 0-100% _____% ANY LIKELIHOOD **> 0%** ON **B19** SHOULD BE CODED **YES**.	NO	YES	13

IS AT LEAST **1** OF THE ABOVE (EXCEPT B1) CODED **YES**?

IF **YES,** ADD THE TOTAL POINTS FOR THE ANSWERS (B1-B19) CHECKED 'YES' AND SPECIFY THE SUICIDALITY SCORE CATEGORY AS INDICATED IN THE DIAGNOSTIC BOX:

INDICATE WHETHER THE SUICIDALITY IS CURRENT (PAST MONTH) OR A LIFETIME SUICIDE ATTEMPT OR BOTH BY MARKING THE APPROPRIATE BOXES OR BY LEAVING EITHER OR BOTH OF THEM UNMARKED.

CURRENT = ANY POSITIVE RESPONSE IN **B1a** THROUGH **B16c** (EXCEPT B15) OR ANY TIME SPENT IN **B17**.
LIFETIME ATTEMPT = **B18** CODED **YES.**
LIKELY IN THE NEAR FUTURE = **B19** CODED **YES.**

MAKE ANY ADDITIONAL COMMENTS ABOUT YOUR ASSESSMENT OF THIS PATIENT'S CURRENT AND NEAR FUTURE SUICIDALITY IN THE SPACE BELOW:

NO	YES

SUICIDALITY

1-8 points	Low	☐
9-16 points	Moderate	☐
≥ 17 points	High	☐
CURRENT		☐
LIFETIME ATTEMPT		☐
LIKELY IN NEAR FUTURE		☐

IS **B18** CODED **YES**?

AND A YES RESPONSE TO

WAS THE SUICIDAL ACT STARTED WHEN THE SUBJECT *WAS NOT* IN A STATE OF CONFUSION OR DELIRIUM?

AND A YES RESPONSE TO

WAS THE SUICIDAL ACT DONE WITHOUT A POLITICAL OR RELIGIOUS PURPOSE?
IF **YES,** SPECIFY WHETHER THE DISORDER IS CURRENT, IN EARLY REMISSION OR IN REMISSION.

NO	YES

SUICIDAL BEHAVIOR DISORDER

Current	☐
In early remission	☐
In remission	☐

B. SUICIDALITY (for ages 6 through 8)

				Points
	In the past month did you:			
B1	Have an accident? This includes taking too much of your medication by accident. **IF NO** TO **B1**, SKIP TO **B2**. **IF YES**, ASK **B1a**:	NO	YES	0
B1a	Plan or expect to try **to get hurt** or to **hurt yourself** in an accident? **IF NO** TO **B1a**, SKIP TO **B2**. **IF YES**, ASK **B1b**:	NO	YES	0
B1b	Try to die or to make yourself dead in an accident?	NO	YES	0
B2	Wish you were dead?	NO	YES	1
B3	Think about hurting yourself, **knowing** you could die, or how much did you think about making yourself dead or killing yourself? **IF YES** TO **EITHER**, CODE **YES**. **IF NO** TO **B2 + B3**, SKIP TO **B4**. OTHERWISE ASK: How often? How strong were the thoughts? ☐ Occasionally ☐ Often ☐ Very often ☐ Mild ☐ Moderate ☐ Severe	NO	YES	6
B4	Hear a voice telling you to make yourself dead or to kill yourself or have a dream or a nightmare about killing yourself? IF YES, mark either or both: ☐ was it a voice or voices? ☐ was it a dream or a nightmare?	NO	YES	4
B5	Think about **how** to kill yourself or how to make yourself dead?	NO	YES	8
B6	Think about **what you would use** to kill yourself or to make yourself dead?	NO	YES	8
B7	Think about **where you would go** to kill yourself or to make yourself dead?	NO	YES	8
B8	Think about **when you would** kill yourself or to make yourself dead?	NO	YES	8
B9	Think about **anything you would like to finish before** you tried to kill yourself? (e.g. writing a suicide note)	NO	YES	8
B10	Mean to **go ahead and to do something** to make yourself dead?	NO	YES	8
B11	Mean **to die** (or make yourself dead) by hurting yourself?	NO	YES	8
B12	Feel all of a **sudden** that you needed to kill yourself (or to make yourself dead)? IF YES, mark either or both: ☐ was it for no good reason? ☐ was it for some good reason? IF NO TO **B12**, SKIP TO **B14**.	NO	YES	8
B13	Have difficulty **resisting** (or fighting against) the sudden need (or impulse) to kill yourself?	NO	YES	8
B14	Do things to **get ready** to kill yourself? **IF NO** TO **B14**, SKIP TO **B15**. OTHERWISE GO TO **B14a**.	NO	YES	
B14a	Do things to **get ready** to kill yourself, but you **did not start** to kill yourself?	NO	YES	9
B14b	Do things to **get ready** to kill yourself, but then **you stopped yourself just before** harming yourself ("aborted")?	NO	YES	10

B14c	Do things to **get ready** to kill yourself, but then **someone or something stopped you just before** harming yourself ("interrupted")?	NO	YES	11
B15	Hurt yourself on purpose **without** trying to kill yourself? (B15 IS NOT COUNTED AS SUICIDAL BEHAVIOR)	NO	YES	0
B16	Try to kill yourself (or to make yourself dead)? **IF NO** TO **B16**, SKIP TO **B17**.	NO	YES	
B16a	Start to try to kill yourself, but then **you decided to stop** and did not finish the attempt?	NO	YES	12
B16b	Start to try to kill yourself, but then **you were interrupted** and did not finish the attempt?	NO	YES	13
B16c	Do **everything you could** to kill yourself **completely** (or to make yourself dead)? **IF NO** to **B16c**, SKIP TO **B17**.	NO	YES	14

Hope to be rescued / survive ☐
Expected / intended to die ☐

B17 **TIME SPENT PER DAY WITH ANY SUICIDAL IMPULSES, THOUGHTS OR ACTIONS:**
Usual time spent per day: ____ hours ____ minutes.
Least amount of time spent per day: ____ hours ____ minutes.
Most amount of time spent per day: ____ hours ____ minutes.

In your lifetime:

B18 Did you ever try to kill yourself or to make yourself dead? NO YES 4
IF YES, how many times? _____
IF YES, when was the last suicide attempt?
Current: within the past 12 months ☐
In early remission: between 12 and 24 months ago ☐
In remission: more than 24 months ago ☐

"A suicide attempt is any self-injurious behavior, with at least some intent (> 0) to die as a result of the act. Evidence that the individual intended to kill him-or herself, at least to some degree, can be explicit or inferred from the behavior or circumstance. For example, it is defined as a suicide attempt if it is clearly not an accident or if the individual thinks the act could be lethal, even though denying intent." (FDA Guidance for Industry Suicidal Ideation and Behavior Document 2012 and C-CASA definition). Posner K et al. Am J Psychiatry 2007; 164 (7): 1035-1043 & http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm/

B19	How likely are you to try to kill yourself within the next 3 months on a scale of 0-100% _____% ANY LIKELIHOOD **> 0%** ON **B19** SHOULD BE CODED **YES**.	NO	YES	13

IS AT LEAST **1** OF THE ABOVE (EXCEPT B1) CODED **YES**?

IF **YES,** ADD THE TOTAL POINTS FOR THE ANSWERS (B1-B19) CHECKED 'YES' AND SPECIFY THE SUICIDALITY SCORE CATEGORY AS INDICATED IN THE DIAGNOSTIC BOX:

INDICATE WHETHER THE SUICIDALITY IS CURRENT (PAST MONTH) OR A LIFETIME SUICIDE ATTEMPT OR BOTH BY MARKING THE APPROPRIATE BOXES OR BY LEAVING EITHER OR BOTH OF THEM UNMARKED.

CURRENT = ANY POSITIVE RESPONSE IN **B1a** THROUGH **B16c** (EXCEPT B15) OR ANY TIME SPENT IN **B17**.
LIFETIME ATTEMPT = **B18** CODED **YES.**
LIKELY IN THE NEAR FUTURE = **B19** CODED **YES.**

MAKE ANY ADDITIONAL COMMENTS ABOUT YOUR ASSESSMENT OF THIS PATIENT'S CURRENT AND NEAR FUTURE SUICIDALITY IN THE SPACE BELOW:

NO	YES

SUICIDALITY

1-8 points Low	☐
9-16 points Moderate	☐
≥ 17 points High	☐
CURRENT	☐
LIFETIME ATTEMPT	☐
LIKELY IN NEAR FUTURE	☐

IS **B18** CODED **YES**?

AND A YES RESPONSE TO

WAS THE SUICIDAL ACT STARTED WHEN THE SUBJECT *WAS NOT* IN A STATE OF CONFUSION OR DELIRIUM?

AND A YES RESPONSE TO

WAS THE SUICIDAL ACT DONE WITHOUT A POLITICAL OR RELIGIOUS PURPOSE?
IF **YES,** SPECIFY WHETHER THE DISORDER IS CURRENT, IN EARLY REMISSION OR IN REMISSION.

NO	YES

SUICIDAL BEHAVIOR DISORDER

Current	☐
In early remission	☐
In remission	☐

C. MANIC AND HYPOMANIC EPISODES

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** TO THE RELEVANT TIME FRAME IN THE DIAGNOSTIC BOXES AND THEN MOVE TO THE NEXT MODULE)

Do you have anyone in your family who had manic-depressive illness or bipolar disorder, or a family member who had mood swings treated with a medication like lithium, sodium valproate (Depakote or Valproate), lamotrigine (Lamictal)? NO YES
THIS QUESTION IS NOT A CRITERION FOR BIPOLAR DISORDER, BUT IS ASKED TO INCREASE THE CLINICIAN'S VIGILANCE ABOUT RISK FOR BIPOLAR DISORDER.

IF **YES**, PLEASE SPECIFY WHO:_____

C1	a	Has there **ever** been a time when you were so happy that you felt 'up' or 'high' or 'hyper' and full of energy? By 'up' or 'high' or 'hyper' I mean feeling really good; full of energy; needing less sleep; your thoughts going very fast or being full of ideas. Did you feel very active or full of energy? **CODE YES** ONLY IF **BOTH** QUESTIONS ARE ANSWERED **YES**. DO NOT CONSIDER TIMES WHEN THE PATIENT WAS INTOXICATED ON DRUGS OR ALCOHOL OR DURING SITUATIONS THAT NORMALLY OVER STIMULATE AND MAKE CHILDREN VERY EXCITED LIKE CHRISTMAS, BIRTHDAYS, ETC. IF PATIENT IS PUZZLED OR UNCLEAR ABOUT WHAT YOU MEAN BY 'UP' OR 'HIGH' OR 'HYPER' CLARIFY AS FOLLOWS: By 'up' or 'high' or 'hyper' I mean: having elated mood; increased energy or increased activity; needing less sleep; your thoughts going very fast; being full of ideas; having an increase in productivity, motivation, creativity or impulsive behavior; phoning or working excessively or spending more money. IF **NO** TO **ALL**, CODE **NO** TO **C1b**. IF **YES** TO **ANY**, ASK:	NO	YES
	b	Are you currently feeling full of energy or 'up' or 'high' or 'hyper' and more active than usual?	NO	YES
C2	a	Has there **ever** been a time when you were so grouchy or annoyed for several days, that you yelled or started fights with people outside your family? Have you or others noticed that you have been more grouchy than other kids, even when you thought you were right to act this way? DO NOT CONSIDER TIMES WHEN THE PATIENT WAS INTOXICATED ON DRUGS OR ALCOHOL. IF **NO** TO **ALL**, CODE **NO** TO **C2b**. IF **YES** TO **ANY**, ASK:	NO	YES
	b	Are you currently feeling grouchy or annoyed most of the time?	NO	YES
			➡	
		IS **C1a** OR **C2a** CODED **YES**?	NO	YES

C3 IF **C1b** OR **C2b** = **YES**: EXPLORE THE **CURRENT** EPISODE FIRST AND THEN THE MOST SYMPTOMATIC **PAST** EPISODE, OTHERWISE
IF **C1b** AND **C2b** = **NO**: EXPLORE **ONLY** THE MOST SYMPTOMATIC **PAST** EPISODE

WHEN EXPLORING THE CURRENT EPISODE, PREFACE EACH QUESTION AS FOLLOWS:
Over the past few days including today, when you felt high and full of energy or irritable, did you:

WHEN EXPLORING THE PAST EPISODE, PREFACE EACH QUESTION AS FOLLOWS:
Over a period of a few days in the past, when you felt most high and most full of energy or most irritable, did you:

		Current Episode		Past Episode	
a	Feel that you could do things others couldn't do? Feel that you are a very important person? IF **YES** TO EITHER, CODE **YES**. IF **YES**, ASK FOR EXAMPLES. THE EXAMPLES ARE CONSISTENT WITH A DELUSIONAL IDEA. Current Episode ☐ No ☐ Yes Past Episode ☐ No ☐ Yes	NO	YES	NO	YES
b	Need less sleep (Did you feel rested after only a few hours of sleep)?	NO	YES	NO	YES
c	Talk too much without stopping? Talk so fast that people couldn't understand or follow what you were saying? Did you feel a pressure to keep talking?	NO	YES	NO	YES
d	Notice your thoughts going very fast or running together or racing or moving very quickly from one subject to another?	NO	YES	NO	YES
e	Get distracted very easily by little things?	NO	YES	NO	YES
f	Get much more involved in things at school, at home or socially than others, or did you feel much more fidgety or restless? THIS INCREASE IN ACTIVITY MAY BE WITH OR WITHOUT A PURPOSE.	NO	YES	NO	YES
g	Want to do fun things even if you could get hurt doing them? Want to do things even though it could get you into trouble? (Like staying out late, skipping school, driving dangerously or spending too much money)? IF **YES** TO **ANY**, CODE **YES**.	NO	YES	NO	YES
C3 SUMMARY:	WHEN RATING CURRENT EPISODE: IF **C1b** IS **NO,** ARE **4** OR MORE **C3** ANSWERS **INCLUDING C3f** CODED **YES**? IF **C1b** IS **YES**, ARE **3** OR MORE **C3** ANSWERS **INCLUDING C3f** CODED **YES**? WHEN RATING PAST EPISODE: IF **C1a** IS **NO**, ARE **4** OR MORE **C3** ANSWERS **INCLUDING C3f** CODED **YES**? IF **C1a** IS **YES**, ARE **3** OR MORE **C3** ANSWERS **INCLUDING C3f** CODED **YES**?	NO	YES	NO	YES
	CODE YES ONLY IF THE ABOVE **3** OR **4** SYMPTOMS OCCURRED DURING THE SAME TIME PERIOD. RULE: ELATION/EXPANSIVENESS REQUIRES ONLY **3 C3** SYMPTOMS, WHILE IRRITABLE MOOD ALONE REQUIRES **4** OF THE **C3** SYMPTOMS.				
C4	What is the longest time these symptoms lasted? ASSESS THIS DURATION FROM THE VERY START TO THE VERY END OF SYMPTOMS, NOT JUST THE PEAK.				
	a) 3 consecutive days or less		☐		☐
	b) 4, 5 or 6 consecutive days or more		☐		☐
	c) 7 consecutive days or more		☐		☐
C5	Were you put in the hospital for these problems? **IF YES**, CIRCLE **YES** IN MANIC EPISODE FOR THAT TIME FRAME AND GO TO **C7**.	NO	YES	NO	YES
C6	Did these symptoms cause a lot of problems at home? At school? With friends? With other people? Or in some other important way? IF **YES** TO **ANY**, CODE **YES**.	NO	YES	NO	YES
C7	Were these problems different from the way you were before? Was it different from the way that you usually are? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	NO	YES

ARE **C3 SUMMARY** AND **C7** AND (**C4c** OR **C5** OR **C6** OR **ANY** PSYCHOTIC FEATURE IN **Q1** THROUGH **Q8**) CODED **YES**?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY IF THE EPISODE IS CURRENT AND / OR PAST.

NO **YES**

MANIC EPISODE

CURRENT ☐
PAST ☐

IS **C3 SUMMARY** CODED **YES** AND ARE **C5** AND **C6** CODED **NO** AND **C7** CODED **YES**, AND IS EITHER **C4b** OR **C4c** CODED **YES**?
AND
IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?
AND
ARE **ALL** PSYCHOTIC FEATURES IN **Q1** THROUGH **Q8** CODED **NO**?

SPECIFY IF THE EPISODE IS CURRENT AND / OR PAST.

IF **YES** TO CURRENT MANIC EPISODE, THEN CODE CURRENT HYPOMANIC EPISODE AS **NO**.

IF **YES** TO PAST MANIC EPISODE, THEN CODE PAST HYPOMANIC EPISODE AS **NOT EXPLORED**.

HYPOMANIC EPISODE

CURRENT ☐ **NO**
☐ **YES**

PAST ☐ **NO**
☐ **YES**
☐ **NOT EXPLORED**

ARE **C3 SUMMARY** AND **C4a** CODED **YES** AND IS **C5** CODED **NO**?

SPECIFY IF THE EPISODE IS CURRENT AND / OR PAST.

IF **YES** TO CURRENT MANIC EPISODE OR HYPOMANIC EPISODE, THEN CODE CURRENT HYPOMANIC SYMPTOMS AS **NO**.

IF **YES** TO PAST MANIC EPISODE OR **YES** TO PAST HYPOMANIC EPISODE, THEN CODE PAST HYPOMANIC SYMPTOMS AS **NOT EXPLORED**.

HYPOMANIC SYMPTOMS

CURRENT ☐ **NO**
☐ **YES**

PAST ☐ **NO**
☐ **YES**
☐ **NOT EXPLORED**

C8 a) IF MANIC EPISODE IS POSITIVE FOR EITHER CURRENT OR PAST ASK:
Did you have 2 or more of these (manic) episodes lasting 7 days or more (**C4c**) in your lifetime (including the current episode if present)? NO YES

b) IF MANIC OR HYPOMANIC EPISODE IS POSITIVE FOR EITHER CURRENT OR PAST ASK:
Did you have 2 or more of these (hypomanic) episodes lasting 4 days or more (**C4b**) in your lifetime (including the current episode)? NO YES

c) IF THE PAST "HYPOMANIC SYMPTOMS" CATEGORY IS CODED POSITIVE ASK:
Did you have (hypomanic) symptoms like these lasting only 1 to 3 days (**C4a**) 2 or more times in your lifetime, (including the current episode, if present)? NO YES

D. PANIC DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

D1	a	Have you ever been really frightened or nervous for no reason; or have you ever been really frightened or nervous in a situation where most kids would not feel that way? IF **YES** TO EITHER, CODE **YES**. IF **NO** TO **ALL**, CODE **NO**.	➡ NO	YES
	b	Did this happen more than one time?	➡ NO	YES
	c	Did this nervous feeling increase quickly over the first few minutes?	➡ NO	YES
D2		Has this ever happened when you didn't expect it?	➡ NO	YES
D3	a	After this happened, were you afraid it would happen again or that something bad would happen as a result of these attacks? Did you change what you did because of these attacks? (e.g., going out only with someone, not wanting to leave your house, going to the doctor more frequently or doing things to avoid a panic attack)?	NO	YES
	b	Did you have these worries for a month or more?	NO	YES
		D3 SUMMARY: IF YES TO BOTH **D3a** AND **D3b** QUESTIONS, CODE **YES**.	NO	YES
D4		**Think about the time you were the most frightened or nervous for no good reason:**		
	a	Did your heart beat fast or loud?	NO	YES
	b	Did you sweat? Did your hands sweat a lot? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	c	Did your hands or body shake?	NO	YES
	d	Did you have trouble breathing or feel like you were running out of air?	NO	YES
	e	Did you feel like you were choking? Did you feel you couldn't swallow? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	f	Did you have pain or pressure in your chest?	NO	YES
	g	Did you feel like throwing up? Did you have an upset stomach? Did you have diarrhea? **IF YES** TO **ANY**, CODE **YES**.	NO	YES
	h	Did you feel dizzy or faint?	NO	YES
	i	Did you feel hot or cold?	NO	YES
	j	Did parts of your body tingle or go numb?	NO	YES

k Did things around you feel strange or like they weren't real? Did you feel or see things as if they were far away? Did you feel outside of or cut off from your body?
IF YES TO **ANY**, CODE **YES**. NO YES

l Were you afraid that you were losing control of yourself? Were you afraid that you were going crazy?
IF YES TO **EITHER**, CODE **YES**. NO YES

m Were you afraid that you were dying? NO YES

➡

D5 ARE **BOTH D3 SUMMARY,** AND **4** OR MORE **D4** ANSWERS, CODED **YES**? NO YES
PANIC DISORDER LIFETIME

D6 a **In the past month**, did you have these problems more than one time? NO YES

IF NO, CIRCLE **NO** TO **D6 SUMMARY**, COMPLETE THE DIAGNOSTIC BOX AND MOVE TO **E1**.

For the past month:

b Did you worry that it would happen again? NO YES

c Did you worry that something bad would happen because of the attack? NO YES

d Did anything change for you because of the attack? (e.g., going out only with someone, not wanting to leave your house, going to the doctor more frequently)? NO YES

D6 SUMMARY: **IF YES** TO **D6b**, or **D6c**, or **D6d**, CODE **YES**. NO YES
PANIC DISORDER CURRENT

IS EITHER **D5** OR **D6** CODED **YES**?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY IF THE EPISODE IS CURRENT AND / OR LIFETIME.

NO	**YES**
PANIC DISORDER	
LIFETIME	☐
CURRENT	☐

E. AGORAPHOBIA

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

E1	Do you feel anxious, scared, or uneasy in places or situations where you might become really frightened; like being in a crowd or in a closed place, standing in a line (queue), when you are all alone, or when crossing a bridge or when you are in an open space, or when traveling in a bus, train, car or on a subway? **IF YES** TO **ANY**, CODE **YES**.	➡ NO	YES
	ARE **2** OR MORE OF THE ABOVE SITUATIONS CODED **YES**?	➡ NO	YES
E2	Do these situations almost always make you anxious or scared?	➡ NO	YES
E3	Are you so afraid of these things that you try to stay away from them? Or you can only do them if someone is with you? Or you do them, but it's really hard for you? **IF YES** TO **ANY**, CODE **YES**.	➡ NO	YES
E4	Are you much more scared than other kids your age in these situations?	➡ NO	YES
E5	Have you been scared of and avoiding these situations for at least 6 months?	➡ NO	YES
E6	Did these symptoms cause significant problems at home, at school, at work, with your friends, or upset you in some other important way?	➡ NO	YES

IS **E6** CODED **YES**?

NO	YES
	AGORAPHOBIA CURRENT

F. SEPARATION ANXIETY DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

F1	a	**In the past month,** were you really afraid about being away from someone close to you; or have you been really afraid that you would lose somebody you are close to? (Like getting lost from your parents or having something bad happen to them). **IF YES TO EITHER, CODE YES.**	➡ NO	YES
	b	Who are you afraid of losing or being away from _____?		
F2	a	Did it happen several times that you got upset a lot when you were away from _____? Did you get upset a lot when you thought you would be away from _____? **IF YES TO EITHER, CODE YES.**	NO	YES
	b	Did you get really worried that you would lose _____? Did you get really worried that something bad would happen to _____? (like having a car accident or dying). **IF YES TO EITHER, CODE YES.**	NO	YES
	c	Did you get really worried that you would be separated from _____? (Like getting lost or being kidnapped?	NO	YES
	d	Did you refuse to go to school or other places because you were afraid to be away from _____?	NO	YES
	e	Did you get really afraid being at home or anywhere else if _____ wasn't there?	NO	YES
	f	Did you not want to go to sleep unless _____ was there?	NO	YES
	g	Did you have nightmares about being away from _____? Did this happen more than once? **IF NO TO EITHER, CODE NO.**	NO	YES
	h	Did you feel sick a lot (like headaches, stomach aches, nausea or vomiting, heart beating fast or feeling dizzy) when you were away from _____? Did you feel sick a lot when you thought you were going to be away from _____? **IF YES TO EITHER, CODE YES.**	NO	YES
		F2 SUMMARY: ARE AT LEAST **3** OF **F2a-h** CODED **YES**?	➡ NO	YES
F3		Did this last for at least 4 weeks?	➡ NO	YES
F4		Did your fears of being away from _____ really bother you a lot? Cause you a lot of problems at home? At school? With friends? In any other way? **IF YES TO ANY, CODE YES.**	➡ NO	YES

ARE **F1, F2 SUMMARY, F3** AND **F4** CODED **YES**?

NO	YES
	SEPARATION ANXIETY DISORDER

G. SOCIAL ANXIETY DISORDER (Social Phobia)

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

G1	**In the past month,** were you afraid or embarrassed when others your age were watching you? Were you afraid of being teased? Like talking in front of the class? Or eating or writing or doing things in front of others? **IF YES TO ANY**, CODE **YES**.	➡ NO	YES
G2	Do these social situations almost always make you anxious or scared?	➡ NO	YES
G3	Are you so afraid of these things that you try to stay away from them? Or you can only do them if someone is with you? Or you do them, but it's really hard for you? **IF YES TO ANY**, CODE **YES**.	➡ NO	YES
G4	Are you much more scared of these situations than other kids your age?	➡ NO	YES
G5	Have you been scared of and avoiding these situations for at least 6 months?	➡ NO	YES
G6	Did these social fears cause significant problems at home, at school, at work, with your friends, or upset you in some other important way?	➡ NO	YES

IS **G6** CODED YES?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED YES?

NOTE TO INTERVIEWER: PLEASE SPECIFY IF THE SUBJECT'S FEARS ARE RESTRICTED TO SPEAKING OR PERFORMING IN PUBLIC.

NO **YES**

SOCIAL ANXIETY DISORDER
(Social Phobia)
CURRENT

RESTRICTED TO PERFORMANCE SAD ONLY ☐

H. SPECIFIC PHOBIA

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

H1	**In the past month,** have you been really afraid of something like: snakes or bugs? Dogs or other animals? High places? Flying? Storms? The dark? Or seeing blood or needles?	➡ NO	YES
H2	List any specific phobia(s): _____		
	CLINICIAN: MAKE SURE THIS PHOBIA IS NOT BETTER EXPLAINED BY A FEAR, ANXIETY OR AVOIDANCE ASSOCIATED WITH PANIC DISORDER, AGORAPHOBIA, SEPARATION ANXIETY OCD, PTSD, OR SOCIAL ANXIETY DISORDER.		
H3	Does being near or around (NAME SPECIFIC PHOBIA) make you afraid immediately?	➡ NO	YES
H4	Are you so afraid of (NAME SPECIFIC PHOBIA) that you try to stay away from it / them? Or you can only be around it / them if someone is with you? Or can you be around it / them but it's really hard for you? **IF YES TO ANY, CODE YES.**	➡ NO	YES
H5	Are you more afraid of (NAME SPECIFIC PHOBIA) than other kids your age?	➡ NO	YES
H6	Have you been afraid of (NAME SPECIFIC PHOBIA) for 6 months or more?	➡ NO	YES
H7	Does this fear really bother you a lot? Does it cause you problems at home or at school or at work or with your friends? Does it keep you from doing things you want to do? **IF YES TO ANY, CODE YES.**	➡ NO	YES

IS H7 CODED YES?

NO	**YES**
SPECIFIC PHOBIA CURRENT	

I. OBSESSIVE-COMPULSIVE DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

I1a	**In the past month**, have you been bothered by bad things that come into your mind that you couldn't get rid of? Like bad thoughts or urges? Or nasty pictures? For example, did you think about hurting somebody even though it disturbs or distresses you? Were you afraid you or someone would get hurt because of some little thing you did or didn't do? Did you worry a lot about having dirt or germs on you? Did you worry a lot that you would give someone else germs or make them sick somehow? Or were you afraid that you would do something really shocking? **IF YES** TO **ANY**, CODE **YES**.	NO YES ↓ SKIP TO **I3a**
I1b	In the past month, did you try to make these thoughts, impulses, or images go away or try to push them away with some other thought or action? DO NOT INCLUDE SIMPLY EXCESSIVE WORRIES ABOUT REAL LIFE PROBLEMS. DO NOT INCLUDE OBSESSIONS DIRECTLY RELATED TO HOARDING, HAIR PULLING, SKIN PICKING, BODY DYSMORPHIC DISORDER, TO EATING DISORDERS, SEXUAL BEHAVIOR, PATHOLOGICAL GAMBLING, OR ALCOHOL OR DRUG ABUSE BECAUSE THE PATIENT MAY DERIVE PLEASURE FROM THE ACTIVITY AND MAY WANT TO RESIST IT ONLY BECAUSE OF ITS NEGATIVE CONSEQUENCES.	NO YES ↓ SKIP TO **I3a**
I2	Did they keep coming back into your mind even when you tried to ignore or get rid of them?	NO YES obsessions
I3a	**In the past month,** did you do something over and over without being able to stop doing it, like washing over and over? Straightening things up over and over? Counting something or checking on something over and over? Saying or doing something over and over? **IF YES** TO **ANY**, CODE **YES**.	NO YES
I3b	Did you do these rituals to make the anxiety less or to prevent something bad from happening? Do they happen to you more than to other kids your age? CODE **YES** ONLY IF **YES** TO BOTH PARTS OF **I3b.** CHILDREN MAY NOT BE ABLE TO EXPLAIN THE PURPOSE OF THE RITUALS.	NO YES compulsions

ARE (**I1a** AND **I1b** AND **I2**) OR (**I3a** AND **I3b**) CODED YES? ➡ NO YES

I4 In the past month, did these thoughts or actions cause you to miss out on things at home? At school? With friends? Did they cause a lot of problems with other people? Did these things take more than one hour a day?
IF YES TO **ANY**, CODE **YES**.

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED YES?
(CHECK FOR ANY OBSESSIVE-COMPULSIVE SYMPTOMS STARTING WITHIN 3 WEEKS OF AN INFECTION)

SPECIFY THE LEVEL OF INSIGHT AND IF THE EPISODE IS TIC-RELATED.

NO **YES**

O.C.D. CURRENT

INSIGHT:
- GOOD OR FAIR ☐
- POOR ☐
- ABSENT ☐
- DELUSIONAL ☐

TIC - RELATED ☐

M.I.N.I. *Kid* 7.0.2 (August 8, 2016) (8/8/16). 26

J. POSTTRAUMATIC STRESS DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

J1	Has anything really awful ever happened to you? Like being in a flood, tornado or earthquake? Like being in a fire or a really bad accident? Like seeing someone being killed or badly hurt. Have you ever been attacked by someone? EXAMPLES OF TRAUMATIC EVENTS INCLUDE: SERIOUS ACCIDENTS, SEXUAL OR PHYSICAL ASSAULT, A TERRORIST ATTACK, BEING HELD HOSTAGE, KIDNAPPING, FIRE, DISCOVERING A BODY, WAR, OR NATURAL DISASTER, WITNESSING THE VIOLENT OR SUDDEN DEATH OF SOMEONE CLOSE TO YOU, OR A LIFE THREATENING ILLNESS.	➡ NO	YES
J2	**In the past month**, has this awful thing come back to you in some way? Like dreaming about it or having a strong memory of it or feeling it in your body? IN CHILDREN THE TRAUMA MAY BE EXPRESSED IN REPETITIVE PLAY, AND THE DREAMS MAY BE FRIGHTENING WITHOUT OBVIOUS CONTENT.	➡ NO	YES
J3	**In the past month**:		
a	Have you tried not to think about or talk about this awful thing?	NO	YES
b	Have you tried to stay away from people or things that might remind you of it?	NO	YES
	J3 SUMMARY: ARE **1** OR MORE **J3** ANSWERS CODED **YES**?	➡ NO	YES
J4	**In the past month**:		
a	Have you had trouble remembering some important part of what happened?	NO	YES
b	Were you down on yourself or others too much?	NO	YES
c	Did you frequently blame yourself or others for the bad things that happened?	NO	YES
d	Did you feel more down on yourself, like feeling guilty, ashamed, angry or frightened?	NO	YES
e	Have you been much less interested in your hobbies or your friends?	NO	YES
f	Have you felt cut off from other people?	NO	YES
g	Have you not been able to feel any good feelings, (like being happy)?	NO	YES
	J4 SUMMARY: ARE **3** OR MORE **J4** ANSWERS CODED **YES**?	➡ NO	YES
J5	**In the past month**:		
a	Were you been moody or angry for no reason?	NO	YES
b	Did you do more risky things or do things that could harm you?	NO	YES
c	Were you nervous or watching out in case something bad might happen?	NO	YES

	d	Would you jump when you heard noises? Or when you saw something out of the corner of your eye? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	e	Did you have trouble paying attention?	NO	YES
	f	Did you have trouble sleeping?	NO	YES
		J5 SUMMARY: ARE **2** OR MORE **J5** ANSWERS CODED **YES**?	NO	YES
J6		Did all these problems start after the traumatic event and last for more than one month?	NO	YES

J7 **In the past month,** have these problems upset you a lot? Have they caused you to have problems at school? At home? At work? With your friends? With your family? Or in some other important way?
IF YES TO **ANY**, CODE **YES**.

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY IF THE CONDITION IS ASSOCIATED WITH DEPERSONALIZATION, DEREALIZATION OR WITH DELAYED EXPRESSION.

NO **YES**

POSTTRAUMATIC STRESS DISORDER CURRENT

WITH
DEPERSONALIZATION ☐
DEREALIZATION ☐
DELAYED EXPRESSION ☐

K. ALCOHOL USE DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

			➡ NO	YES
K1	**In the past year**, have you had 3 or more drinks of alcohol in a day? At those times, did you have 3 or more drinks in 3 hours? Did you do this 3 or more times in the past year? **IF NO** TO **ANY**, CODE **NO**.			
K2	**In the past year**:			
	a	During the times when you drank alcohol, did you end up drinking more than you planned to?	NO	YES
	b	Did you repeatedly want to reduce or control your alcohol use? Did you try to cut down or stop your alcohol use, but were not able to? IF YES TO EITHER, CODE YES.	NO	YES
	c	On days when you drank, did you spend more than three hours doing it? Count the time it took you to get the alcohol, drink it, and get over it.	NO	YES
	d	Did you crave or have a strong desire or urge to use alcohol?	NO	YES
	e	Did you spend less time doing things you were supposed to do at school, at work, or at home, because of your repeated drinking?	NO	YES
	f	Did you keep on drinking even if it caused problems with your family or with other people?	NO	YES
	g	Were you drunk more than once while doing something risky (like riding a bike, driving a car or boat, or using machines)?	NO	YES
	h	Did your drinking cause problems with your health or your mind? Did you keep on drinking even though you knew that it caused these problems or made them worse? IF YES TO **BOTH**, CODE YES.	NO	YES
	i	Did you reduce or give up important work, school, social or other activities because of your drinking?	NO	YES
	j	Did you need to drink a lot more alcohol to get the same feeling you got when you first started drinking? Did the same amount of alcohol have less effect over time? IF YES TO EITHER, CODE YES.	NO	YES
	k1	When you cut down on drinking did you have any of the following:	NO	YES

1. increased sweating or increased heart rate, ☐
2. hand tremor or "the shakes" ☐
3. trouble sleeping ☐
4. nausea or vomiting ☐
5. hearing or seeing things other people could not see or hear or having sensations in your skin for no apparent reason ☐
6. agitation ☐
7. anxiety ☐
8. seizures ☐

IF YES TO **2** OR MORE OF THE ABOVE 8, CODE **k1** AS YES.

k2 Did you drink alcohol to reduce or avoid these withdrawal symptoms or to avoid being hung-over? NO YES

K2K SUMMARY: IF YES TO **K2k1** OR **K2k2**, CODE **YES.** NO YES

ARE **2** OR MORE **K2** ANSWERS FROM **K2a** THROUGH **K2K SUMMARY** CODED **YES**?
(**K2k1** AND **K2k2** TOGETHER COUNT AS ONE AMONG THESE CHOICES.)

NO **YES**

ALCOHOL USE DISORDER

PAST 12 MONTHS

SPECIFIERS FOR ALCOHOL USE DISORDER:

MILD = **2-3** OF THE **K2** SYMPTOMS
MODERATE = **4-5** OF THE **K2** SYMPTOMS
SEVERE = **6** OR MORE OF THE **K2** SYMPTOMS

IN EARLY REMISSION = CRITERIA NOT MET FOR BETWEEN 3 & 12 MONTHS.
IN SUSTAINED REMISSION = CRITERIA NOT MET FOR 12 MONTHS OR MORE.
(BOTH WITH THE EXCEPTION OF **CRITERION d** [CRAVING] ABOVE).

IN A CONTROLLED ENVIRONMENT = WHERE ALCOHOL ACCESS IS RESTRICTED.

SPECIFY IF:

MILD ☐
MODERATE ☐
SEVERE ☐

IN EARLY REMISSION ☐
IN SUSTAINED REMISSION ☐

IN A CONTROLLED ENVIRONMENT ☐

L. SUBSTANCE USE DISORDER (Non-Alcohol)

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

			➡ NO	YES
L1	a	Now I am going to read you a list of street drugs or medicines. Stop me if, **in the past year,** you have taken any of them more than one time to get high? To feel better or to change your mood?		

CIRCLE EACH DRUG TAKEN:

Stimulants: amphetamines, "speed", crystal meth, "crank", Dexedrine, Ritalin, diet pills.

Cocaine: snorting, IV, freebase, crack, "speedball".

Opiates: heroin, morphine, Dilaudid, opium, Demerol, methadone, Darvon, codeine, Percodan, Vicodin, OxyContin.

Hallucinogens: LSD ("acid"), mescaline, peyote, psilocybin, STP, "mushrooms", "ecstasy", MDA, MDMA.

Dissociative Drugs: PCP (Phencyclidine,"Angel Dust", "Peace Pill", "Hog"), or ketamine ("Special K").

Inhalants: "glue", ethyl chloride, "rush", nitrous oxide ("laughing gas"), amyl or butyl nitrate ("poppers").

Cannabis: marijuana, hashish ("hash"), THC, "pot", "grass", "weed", "reefer".

Tranquilizers: Quaalude, Seconal ("reds"), Valium, Xanax, Librium, Ativan, Dalmane, Halcion, barbiturates, Miltown, GHB, Roofinol, "Roofies".

Miscellaneous: steroids, nonprescription sleep or diet pills. Cough Medicine? Any others?

SPECIFY THE MOST USED DRUG(S): _____

WHICH DRUG(S) CAUSE THE BIGGEST PROBLEMS? _____

FIRST EXPLORE THE CRITERIA BELOW FOR THE DRUG CLASS CAUSING THE BIGGEST PROBLEMS AND THE ONE MOST LIKELY TO MEET CRITERIA FOR SUBSTANCE USE DISORDER. IF SEVERAL DRUG CLASSES HAVE BEEN MISUSED, EXPLORE AS MANY OR AS FEW AS REQUIRED BY THE PROTOCOL.

L2		Think about your use of (NAME THE DRUG/DRUG CLASS SELECTED) **over the past year:**		
	a	During the times when you used (NAME THE DRUG/DRUG CLASS SELECTED), did you end up using more than you planned to?	NO	YES
	b	Did you repeatedly want to reduce or control your (NAME THE DRUG/DRUG CLASS SELECTED) use? Did you try to cut down or stop your (NAME THE DRUG/DRUG CLASS SELECTED) use, but were not able to? IF YES TO EITHER, CODE YES.	NO	YES
	c	On days when you used (NAME THE DRUG/DRUG CLASS SELECTED), did you spend more than three hours doing it? Count the time it took you to get the drug, use it, and recover from it.	NO	YES
	d	Did you crave or have a strong desire or urge to use (NAME THE DRUG/DRUG CLASS SELECTED)?	NO	YES
	e	Did you spend less time doing things you were supposed to do at school, at work, or at home, because of your repeated (NAME THE DRUG/DRUG CLASS SELECTED) use?	NO	YES
	f	Did you keep on using (NAME THE DRUG/DRUG CLASS SELECTED), even if it caused problems with your family or with other people?	NO	YES

g Were you using (NAME THE DRUG/DRUG CLASS SELECTED), more than once while doing something risky (like riding a bike, driving a car or boat, or using machines)? NO YES

h Did your use of (NAME THE DRUG/DRUG CLASS SELECTED), cause problems with your health or your mind? Did you keep on using (NAME THE DRUG/DRUG CLASS SELECTED) even though you knew that it caused these problems or made them worse?
IF YES TO **BOTH**, CODE **YES**. NO YES

i Did you reduce or give up important work, school, social or other activities because of your use of (NAME THE DRUG/DRUG CLASS SELECTED)? NO YES

j Did you need to use a lot more (NAME THE DRUG/DRUG CLASS SELECTED) to get the same feeling you got when you first started using it? Did the same amount of drug have less effect over time?
IF YES TO **EITHER**, CODE **YES**.
THIS CRITERION IS CODED NO IF THE MEDICATION IS PRESCRIBED AND USED UNDER MEDICAL SUPERVISION. NO YES

k1 When you cut down on heavy or prolonged use of the drug did you have any of the following withdrawal symptoms:
IF **YES** TO THE REQUIRED NUMBER OF WITHDRAWAL SYMPTOMS FOR EACH CLASS, CODE **L2k1** AS **YES**.
THIS CRITERION IS CODED **NO** IF THE MEDICATION IS PRESCRIBED AND USED UNDER MEDICAL SUPERVISION. NO YES

Sedative, Hypnotic or Anxiolytic (2 or more withdrawal symptoms)
1. increased sweating or increased heart rate ☐
2. hand tremor or "the shakes" ☐
3. trouble sleeping ☐
4. nausea or vomiting ☐
5. hearing or seeing things other people could not see or hear or having sensations in your skin for no apparent reason ☐
6. agitation ☐
7. anxiety ☐
8. seizures ☐

Opiates (3 or more withdrawal symptoms)
1. feeling depressed ☐
2. nausea or vomiting ☐
3. muscle aches ☐
4. runny nose or teary eyes ☐
5. dilated pupils, goose bumps or hair standing on end or sweating ☐
6. diarrhea ☐
7. yawning ☐
8. hot flashes ☐
9. trouble sleeping ☐

Stimulants (2 or more withdrawal symptoms)
1. fatigue ☐
2. vivid or unpleasant dreams ☐
3. difficulty sleeping or sleeping too much ☐
4. increased appetite ☐
5. feeling or looking physically or mentally slowed down ☐

Cannabis (3 or more withdrawal symptoms)

1. irritability, anger or aggression ☐
2. nervousness or anxiety ☐
3. trouble sleeping ☐
4. appetite or weight loss ☐
5. restlessness ☐
6. feeling depressed ☐
7. significant discomfort from one of the following: "stomach pain", tremors or "shakes", sweating, hot flashes, chills, headaches. ☐

k2 Did you use (NAME OF DRUG / DRUG CLASS SELECTED) to reduce or avoid withdrawal symptoms? NO YES

L2k SUMMARY: IF **YES** TO **L2k1** OR **L2k2**, CODE **YES**. NO YES

ARE **2** OR MORE **L2** ANSWERS FROM **L2a** THROUGH **L2k SUMMARY** CODED **YES**?
(**L2k1** AND **L2k2** TOGETHER COUNT AS ONE AMONG THESE CHOICES.)

NO **YES**

SUBSTANCE (Drug or Drug Class Name) USE DISORDER

PAST 12 MONTHS

SPECIFIERS FOR SUBSTANCE USE DISORDER:

MILD = **2-3** OF THE **L2** SYMPTOMS
MODERATE = **4-5** OF THE **L2** SYMPTOMS
SEVERE = **6** OR MORE OF THE **L2** SYMPTOMS

IN EARLY REMISSION = CRITERIA NOT MET FOR BETWEEN 3 & 12 MONTHS
IN SUSTAINED REMISSION = CRITERIA NOT MET FOR 12 MONTHS OR MORE
(BOTH WITH THE EXCEPTION OF **CRITERION d** [CRAVING] ABOVE).

IN A CONTROLLED ENVIRONMENT = WHERE SUBSTANCE / DRUG ACCESS IS RESTRICTED.

SPECIFY IF:

MILD ☐
MODERATE ☐
SEVERE ☐

IN EARLY REMISSION ☐
IN SUSTAINED REMISSION ☐

IN A CONTROLLED ENVIRONMENT ☐

M. TIC DISORDERS

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

M1	a	Did you ever have movements of your body called "Tics"? "Tics" are sudden, quick movements of some part of your body that are hard to control. A tic might be blinking your eyes over and over, twitches of your face, jerking your head, making a movement with your hand over and over, or squatting, or shrugging your shoulders over and over. IF NO, CODE NO TO **M1b**: IF YES ASK:	NO	YES
M1	b	In the past month, did you have these movements of your body called "Tics"?	NO	YES
M2	a	Did you ever had a tic that made you say something or make a sound over and over and was hard to stop? Like coughing or sniffling or clearing your throat over and over when you did not have a cold; or grunting or snorting or barking; having to say certain words over and over, having to say bad words, or having to repeat sounds you hear or words that other people say? IF NO, CODE NO TO **M2b**: IF YES ASK:	NO	YES
M2	b	In the past month, did you have any tics that made you say something or make a sound over and was hard to stop? IF **BOTH M1a** AND **M2a** ARE BOTH CODED **NO**, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES AND SKIP TO **N1**.	NO	YES
M3		Did they keep happening for a year or more after the first tic, even if they came and went during this time?	NO	YES
M4		Did the tics only occur when you are taking a medicine or drug, like Ritalin, Adderal, Cylert, Dexedrine, Provigil, Concerta or other medications for ADHD or after using cocaine?	NO	➡ YES
M5		Did the tics only occur because of another medical condition? LIKE HUNTINGTON'S DISEASE OR POSTVIRAL ENCEPHALITIS?	NO	➡ YES

M6 a ARE **M1a** + **M2a** + **M3** CODED **YES**?

AND

ARE **M4** + **M5** CODED **NO**?

SPECIFY IF TOURETTE'S DISORDER IS PRESENT, CURRENT OR LIFETIME, OR BOTH.

CODE LIFETIME IF **M1a** AND **M2a** ARE BOTH CODED YES
CODE CURRENT IF **M1b** AND **M2b** ARE BOTH CODED YES

NO	**YES**
TOURETTE'S DISORDER,	
CURRENT	☐
LIFETIME	☐

M6 b ARE **M1a** + **M3** CODED **YES**?

AND

ARE **M2a** + **M4** + **M5** CODED **NO**?

AND

IS **M6a** CODED **NO** LIFETIME?

SPECIFY IF PERSISTENT MOTOR TIC DISORDER IS PRESENT, CURRENT OR LIFETIME, OR BOTH.

CODE LIFETIME IF **M1a** IS CODED YES
CODE CURRENT IF **M1b** IS CODED YES

NO **YES**

PERSISTENT (CHRONIC)
MOTOR TIC DISORDER,

LIFETIME ☐
CURRENT ☐

M6 c ARE **M2a** + **M3** CODED **YES**?

AND

ARE **M1a** + **M4** + **M5** CODED **NO**?

AND

IS **M6a** CODED **NO** LIFETIME?

SPECIFY IF PERSISTENT VOCAL TIC DISORDER IS PRESENT, CURRENT OR LIFETIME, OR BOTH.

CODE LIFETIME IF **M2a** IS CODED YES
CODE CURRENT IF **M2b** IS CODED YES

NO **YES**

PERSISTENT (CHRONIC)
VOCAL TIC DISORDER,

LIFETIME ☐
CURRENT ☐

M6 d ARE **M1a or M2a** CODED **YES**?

AND

ARE **M3** + **M4** + **M5** CODED **NO**?

AND

ARE **M6a** AND **M6b** AND **M6c** CODED **NO** LIFETIME?

SPECIFY IF PROVISIONAL TIC DISORDER IS PRESENT, CURRENT OR LIFETIME, OR BOTH.

CODE LIFETIME IF **M1a** OR **M2a** OR BOTH ARE CODED YES
CODE CURRENT IF **M1b** OR **M2b** OR BOTH ARE CODED YES

NO **YES**

PROVISIONAL
TIC DISORDER,

LIFETIME ☐
CURRENT ☐

N. ATTENTION - DEFICIT / HYPERACTIVITY DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

		SCREENING QUESTION FOR 3 DISORDERS (ADHD, CD, ODD)		
N1		Has anyone (teacher, baby sitter, friend or parent) ever complained about your behavior or performance in school? **IF NO** TO THIS QUESTION, ALSO CODE **NO** TO **CONDUCT DISORDER** AND **OPPOSITIONAL DEFIANT DISORDER**.	➡ NO	YES
		In the past six months:		
N2	a	Have you often not paid enough attention to details? Made careless mistakes in school?	NO	YES
	b	Have you often had trouble keeping your attention focused when playing or doing schoolwork?	NO	YES
	c	Have you often been told that you do not listen when others talk directly to you?	NO	YES
	d	Have you often had trouble following through with what you were told to do (Like not following through on schoolwork or chores)? Did this happen even though you understood what you were supposed to do? Did this happen even though you weren't trying to be difficult? **IF NO** TO **ANY**, CODE **NO**.	NO	YES
	e	Have you often had a hard time getting organized?	NO	YES
	f	Have you often tried to avoid things that make you concentrate or think hard (like schoolwork)? Do you hate or dislike things that make you concentrate or think hard? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	g	Have you often lost or forgotten things you needed? Like homework assignments, pencils, or toys?	NO	YES
	h	Do you often get distracted easily by little things (Like sounds or things outside the room)?	NO	YES
	i	Do you often forget to do things you need to do every day (like forget to comb your hair or brush your teeth, keeping appointments, doing chores)?	NO	YES
		N2 SUMMARY: ARE **6** OR MORE **N2** ANSWERS CODED **YES?**	NO	YES
		In the past six months:		
N3	a	Did you often fidget with your hands or feet? Or did you squirm in your seat? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	b	Did you often get out of your seat in class when you were not supposed to?	NO	YES
	c	Have you often run around or climbed on things when you weren't supposed to? Did you want to run around or climb on things even though you didn't? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES

	d	Have you often had a hard time playing quietly?	NO	YES
	e	Were you always "on the go"?	NO	YES
	f	Have you often talked too much?	NO	YES
	g	Have you often blurted out answers before the person or teacher has finished the question?	NO	YES
	h	Have you often had trouble waiting your turn?	NO	YES
	i	Have you often interrupted other people? Like butting in when other people are talking or busy or when they are on the phone?	NO	YES
		N3 SUMMARY: ARE **6** OR MORE **N3** ANSWERS CODED **YES**?	NO	YES
N4		Did you have problems paying attention, being hyper, or impulsive before you were 12 years old?	NO	YES
N5		Did these things cause problems at school? At home? With your family? With your friends? CODE **YES** IF **2** OR MORE ARE ENDORSED **YES**.	NO	YES

IS **N2 SUMMARY** AND **N3 SUMMARY** CODED **YES**?

AND

THE ADHD IS NOT RESTRICTED EXCLUSIVELY TO OR BETTER EXPLAINED BY ANOTHER PSYCHIATRIC DISORDER?

NO **YES**

ATTENTION - DEFICIT / HYPERACTIVITY DISORDER
COMBINED PRESENTATION

IS **N2 SUMMARY** CODED **YES** AND **N3 SUMMARY** CODED **NO**?

AND

THE ADHD IS NOT RESTRICTED EXCLUSIVELY TO OR BETTER EXPLAINED BY ANOTHER PSYCHIATRIC DISORDER?

NO **YES**

ATTENTION - DEFICIT / HYPERACTIVITY DISORDER
PREDOMINANTLY INATTENTIVE PRESENTATION

IS **N2 SUMMARY** CODED **NO** AND **N3 SUMMARY** CODED **YES**?

AND

THE ADHD IS NOT RESTRICTED EXCLUSIVELY TO OR BETTER EXPLAINED BY ANOTHER PSYCHIATRIC DISORDER?

NO **YES**

ATTENTION - DEFICIT / HYPERACTIVITY DISORDER
PREDOMINANTLY HYPERACTIVE / IMPULSIVE PRESENTATION

O. CONDUCT DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

		SCREENING QUESTION		
O1		**IF QUESTION N1 IN ADHD** IS ANSWERED **NO**, CODE **NO** TO **CONDUCT DISORDER**. **IF N1** WAS **NOT ASKED** ALREADY, ASK THE QUESTION BELOW. (Has anyone (teacher, baby sitter, friend, parent) ever complained about your behavior or performance in school?)	➡ NO	YES
O2		**In the past year:**		
	a	Have you bullied or threatened other people (excluding siblings)?	NO	YES
	b	Have you started fights with others (excluding siblings)?	NO	YES
	c	Have you used a weapon to hurt someone? Like a knife, gun, bat, or other object?	NO	YES
	d	Have you hurt someone (physically) on purpose (excluding siblings)?	NO	YES
	e	Have you hurt animals on purpose?	NO	YES
	f	Have you stolen things using force? Like robbing someone using a weapon or grabbing something from someone like purse snatching?	NO	YES
	g	Have you forced anyone to have sex with you?	NO	YES
	h	Have you started fires on purpose in order to cause damage?	NO	YES
	i	Have you destroyed things that belonged to other people on purpose?	NO	YES
	j	Have you broken into someone's house or car?	NO	YES
	k	Have you lied many times in order to get things from people or to get out of things? Or tricked other people into doing what you wanted? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES
	l	Have you stolen things that were worth money (like shoplifting or forging a check)?	NO	YES
	m	Have you often stayed out a lot later than your parents let you? Did this start before you were 13 years old? **IF NO** TO **EITHER**, CODE **NO**.	NO	YES
	n	Have you run away from home two times or more?	NO	YES
	o	Have you skipped school often? Did this start before you were 13 years old? **IF NO** TO **EITHER**, CODE **NO**.	NO	YES
		O2 SUMMARY: ARE **3** OR MORE **O2** ANSWERS CODED **YES** WITH AT LEAST **1** PRESENT IN THE PAST 6 MONTHS?	➡ NO	YES

O3 Did these behaviors cause big problems at school? At home? With your family? Or with your friends?

IF YES TO **ANY**, CODE **YES**.

SPECIFY IF THE FIRST SYMPTOM OF CONDUCT DISORDER STARTED:

BEFORE AGE 10 = CHILDHOOD-ONSET TYPE.

AFTER AGE 10 = ADOLESCENT-ONSET TYPE.

UNKNOWN AGE OF ONSET = UNSPECIFIED-ONSET TYPE.

NO	**YES**
CONDUCT DISORDER CURRENT	
CHILDHOOD-ONSET TYPE	☐
ADOLESCENT-ONSET TYPE	☐
UNSPECIFIED-ONSET TYPE	☐

P. OPPOSITIONAL DEFIANT DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

ATTENTION: IF CODED POSITIVE FOR CONDUCT DISORDER, CIRCLE **NO** IN DIAGNOSTIC BOX AND MOVE TO THE NEXT MODULE.

	SCREENING QUESTION			
P1	**IF QUESTION N1 IN ADHD** IS ANSWERED **NO**, CODE **NO** TO **OPPOSITIONAL DEFIANT DISORDER**. **IF N1** WAS **NOT ASKED** ALREADY, ASK THE QUESTION BELOW. (Has anyone (teacher, baby sitter, friend, parent) ever complained about your behavior or performance in school?)	➡ NO	YES	
P2	**At least once a week, over the past six months**:			
	a Have you often lost your temper?	NO	YES	
	b Have you often been "touchy" or easily annoyed by other people?	NO	YES	
	c Have you often been angry and resentful toward others?	NO	YES	
	d Have you often argued with adults?	NO	YES	
	e Have you often refused to do what adults tell you to do? Refused to follow rules? **IF YES** TO **EITHER**, CODE **YES**.	NO	YES	
	f Have you often annoyed people on purpose?	NO	YES	
	g Have you often blamed other people for your mistakes or for your bad behavior?	NO	YES	
	h Have you often been "spiteful" or quick to "pay back" somebody who treats you wrong? Have you done this 2 or more times in the past 6 months? **IF YES** TO **BOTH QUESTIONS**, CODE **YES**.	NO	YES	
	P2 SUMMARY: ARE **4** OR MORE OF **P2** ANSWERS CODED **YES**?	➡ NO	YES	
P3	Did these behaviors last at least 6 months?	➡ NO	YES	
P4	Did these behaviors occur with people outside your brothers or sisters?	➡ NO	YES	
P5	Did these behaviors cause problems at school? At home? With your family? Or with your friends? **IF YES** TO **ANY**, CODE **YES**.	➡ NO	YES	

ARE **P2 SUMMARY** + **P3** + **P4** + **P5** CODED **YES**?

THE OPPOSITIONAL DEFIANT DISORDER IS NOT RESTRICTED EXCLUSIVELY TO OR BETTER EXPLAINED BY ANOTHER PSYCHIATRIC DISORDER, LIKE A MOOD DISORDER, SUBSTANCE USE, PSYCHOTIC DISORDER AND THE PATIENT DOES NOT HAVE A DISRUPTIVE MOOD DYSREGULATION DISORDER.

NO	YES
	OPPOSITIONAL DEFIANT DISORDER **CURRENT**

Q. PSYCHOTIC DISORDERS AND MOOD DISORDERS WITH PSYCHOTIC FEATURES

ASK FOR AN EXAMPLE OF EACH QUESTION ANSWERED POSITIVELY. CODE **YES** ONLY IF THE EXAMPLES CLEARLY SHOW A DISTORTION OF THOUGHT OR OF PERCEPTION OR IF THEY ARE NOT CULTURALLY APPROPRIATE. THE PURPOSE OF THIS MODULE IS TO EXCLUDE PATIENTS WITH PSYCHOTIC DISORDERS. THIS MODULE NEEDS EXPERIENCE.

Now I am going to ask you about unusual experiences that some people have.

Q1	a	Have you ever believed that people were secretly watching you? Have you believed that someone was trying to get you, or hurt you? **IF YES** TO **ANY**, CODE **YES**. **NOTE**: ASK FOR EXAMPLES TO RULE OUT ACTUAL STALKING.	NO	YES
	b	**IF YES**: Do you believe this now?	NO	YES
Q2	a	Have you ever believed that someone was reading your mind or that someone could hear your thoughts? Or that you could actually read someone else's mind or hear what they were thinking? **IF YES** TO **ANY**, CODE **YES**.	NO	YES
	b	**IF YES**: Do you believe this now?	NO	YES
Q3	a	Have you ever believed that someone or something put thoughts in your mind that were not your own? Have you believed that someone or something made you act in a way that was not your usual self? Have you ever felt that you were possessed? CLINICIAN: **IF YES** TO **ANY**, CODE **YES**. **NOTE**: ASK FOR EXAMPLES AND DISCOUNT ANY THAT ARE NOT PSYCHOTIC.	NO	YES
	b	**IF YES**: Do you believe this now?	NO	YES
Q4	a	Have you ever believed that you were being sent special messages through the TV, radio, internet, newspapers, books, magazines, or through your games or toys? Have you ever believed that a person you did not personally know was especially interested in you? **IF YES** TO **ANY**, CODE **YES**.	NO	YES
	b	**IF YES**: Do you believe this now?	NO	YES
Q5	a	Have your family or friends ever thought that any of your beliefs were strange or weird? Please give me an example. CLINICIAN: ASK FOR EXAMPLES. ONLY CODE YES IF THE EXAMPLES ARE CLEARLY DELUSIONAL IDEAS NOT EXPLORED IN QUESTIONS **Q1** TO **Q4**, FOR EXAMPLE, RELIGIOUS, DEATH, DISEASE OR SOMATIC DELUSIONS, DELUSIONS OF GRANDIOSITY, JEALOUSY OR GUILT, OR OF FAILURE, INADEQUACY, RUIN, OR DESTITUTION, OR NIHILISTIC DELUSIONS.	NO	YES
	b	**IF YES**: Do they still think that your beliefs are strange?	NO	YES

Q6	a	Have you ever heard things other people couldn't hear, such as voices?	NO	YES
		IF YES: Did you hear a voice talking about you? Did you hear more than one voice talking back and forth?	NO	YES
	b	**IF YES TO Q6a**: Have you heard these sounds or voices in the past month?	NO	YES
		IF YES: Did you hear a voice talking about you? Did you hear more than one voice talking back and forth?	NO	YES
Q7	a	Have you ever had visions or have you ever seen things other people couldn't see?	NO	YES
		CLINICIAN: CHECK TO SEE IF THESE ARE CULTURALLY INAPPROPRIATE.		
	b	**IF YES**: Have you seen these things in the past month?	NO	YES
		CLINICIAN'S JUDGMENT		
Q8	a	DID THE PATIENT EVER IN THE PAST EXHIBIT DISORGANIZED, INCOHERENT OR DERAILED SPEECH, OR MARKED LOOSENING OF ASSOCIATIONS?	NO	YES
Q8	b	IS THE PATIENT CURRENTLY EXHIBITING INCOHERENCE, DISORGANIZED OR DERAILED SPEECH, OR MARKED LOOSENING OF ASSOCIATIONS?	NO	YES
Q9	a	DID THE PATIENT EVER IN THE PAST EXHIBIT DISORGANIZED OR CATATONIC BEHAVIOR?	NO	YES
Q9	b	IS THE PATIENT CURRENTLY EXHIBITING DISORGANIZED OR CATATONIC BEHAVIOR?	NO	YES
Q10	a	DID THE PATIENT EVER IN THE PAST HAVE NEGATIVE SYMPTOMS OF SCHIZOPHRENIA, E.G. SIGNIFICANT REDUCTION OF EMOTIONAL EXPRESSION OR AFFECTIVE FLATTENING, POVERTY OF SPEECH (ALOGIA) OR AN INABILITY TO INITIATE OR PERSIST IN GOAL-DIRECTED ACTIVITIES (AVOLITION)?	NO	YES
Q10	b	ARE NEGATIVE SYMPTOMS OF SCHIZOPHRENIA, E.G. SIGNIFICANT REDUCTION OF EMOTIONAL EXPRESSION OR AFFECTIVE FLATTENING, POVERTY OF SPEECH (ALOGIA) OR AN INABILITY TO INITIATE OR PERSIST IN GOAL-DIRECTED ACTIVITIES (AVOLITION), PROMINENT DURING THE INTERVIEW?	NO	YES
Q11	a	ARE **1** OR MORE « **a** » QUESTIONS FROM **Q1a** TO **Q7a**, CODED **YES**? **AND IS EITHER:** MAJOR DEPRESSIVE EPISODE, (CURRENT, RECURRENT OR PAST) **OR** MANIC OR HYPOMANIC EPISODE, (CURRENT OR PAST) CODED **YES**? **AND** HOW LONG HAS THE MOOD EPISODE LASTED? _____ HOW LONG HAS THE PSYCHOTIC EPISODE LASTED? _____ IF SUCH A MOOD EPISODE IS PRESENT, CODE **YES** TO **Q11a** ONLY IF THE MOOD DISTURBANCE IS PRESENT FOR THE MAJORITY OF THE TOTAL DURATION OF THE ACTIVE AND RESIDUAL PERIODS OF THE PSYCHOTIC SYMPTOMS. OTHERWISE CODE **NO**.	NO ↳ **Q13**	YES
		IF **NO** TO **Q11a** AND THE TOTAL DURATION OF THE MOOD EPISODE IS **LESS THAN** THE TOTAL DURATION OF THE PSYCHOTIC EPISODE, THEN CIRCLE **NO** IN BOTH 'MOOD DISORDER WITH PSYCHOTIC FEATURES' DIAGNOSTIC BOXES AND MOVE TO **Q13**.		

Q11 b You told me earlier that you had period(s) when you felt (depressed/high/persistently irritable).

Did you have the beliefs and experiences you just described [GIVE EXAMPLES TO PATIENT FROM SYMPTOMS CODED **YES** FROM **Q1a** TO **Q7a**] only when you were feeling depressed? high? very moody? very irritable?

IF THE PATIENT EVER HAD A PERIOD OF AT LEAST **2 WEEKS** OF HAVING THESE BELIEFS OR EXPERIENCES (PSYCHOTIC SYMPTOMS) WHEN THEY WERE NOT DEPRESSED/HIGH/IRRITABLE, CODE **NO** TO THIS DISORDER.

IF THE ANSWER IS **NO** TO THIS DISORDER GROUPING, ALSO CIRCLE **NO** TO **Q12** AND MOVE TO **Q13**.

NO **YES**

MOOD DISORDER WITH PSYCHOTIC FEATURES

LIFETIME

Q12 ARE **1** OR MORE « **b** » QUESTIONS FROM **Q1b** TO **Q7b** CODED **YES**?

AND IS EITHER:

MAJOR DEPRESSIVE EPISODE, (CURRENT)
OR
MANIC OR HYPOMANIC EPISODE, (CURRENT) CODED **YES**?

IF THE ANSWER IS YES TO THIS DISORDER (LIFETIME OR CURRENT), CIRCLE **NO** TO **Q13** AND **Q14** AND MOVE TO THE NEXT MODULE.

NO **YES**

MOOD DISORDER WITH PSYCHOTIC FEATURES

CURRENT

Q13 ARE **1** OR MORE « **b** » QUESTIONS FROM **Q1b** TO **Q8b**, CODED **YES**?

AND

ARE **2** OR MORE « **b** » QUESTIONS FROM **Q1b** TO **Q10b**, CODED **YES**?

AND

DID AT LEAST **2** OF THE PSYCHOTIC SYMPTOMS OCCUR DURING THE SAME **1**-MONTH PERIOD?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

NO **YES**

PSYCHOTIC DISORDER
CURRENT

Q14 IS **Q13** CODED **YES**?

OR

(ARE **1** OR MORE « **a** » QUESTIONS FROM **Q1a** TO **Q8a**, CODED **YES**?

AND

ARE **2** OR MORE « **a** » QUESTIONS FROM **Q1a** TO **Q10a**, CODED **YES**?

AND

DID AT LEAST **2** OF THE PSYCHOTIC SYMPTOMS OCCUR DURING THE SAME **1**-MONTH PERIOD?

AND

IS "RULE OUT ORGANIC CAUSE [**W2 SUMMARY**]" CODED **YES**?)

NO **YES**

PSYCHOTIC DISORDER

LIFETIME

R. ANOREXIA NERVOSA

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

R1	a	How tall are you?	☐☐ ft ☐☐ in ☐☐☐ cm
	B	What was your lowest weight in the past 3 months?	☐☐☐ lb ☐☐☐ kg
	c	IS PATIENT'S WEIGHT EQUAL TO OR BELOW THE THRESHOLD CORRESPONDING TO HIS / HER HEIGHT? (SEE TABLE BELOW) (THIS IS = A BMI OF 17.0 KG/M^2)	NO YES
	d	Have you lost 5 lb or more (2.3 kg or more) in the last 3 months?	NO YES
	e	If you are less than age 14, have you failed to gain any weight in the last 3 months? **IF PATIENT IS 14 OR OLDER**, CODE **NO**.	NO YES
	f	Has anyone thought that you lost too much weight in the last 3 months?	NO YES
		IF YES TO R1c OR R1d OR R1e OR R1f, CODE **YES**. OTHERWISE CODE **NO**.	➡ NO YES

In the past 3 months:

R2		Have you been trying to keep yourself from gaining any weight or to restrict your food intake?	➡ NO YES
R3		Have you been very afraid of gaining weight? Have you been very afraid of getting too fat / big? **IF YES TO EITHER**, CODE **YES**.	➡ NO YES
R4	a	Have you seen yourself as being too big / fat or that part of your body was too big / fat? **IF YES TO EITHER**, CODE **YES**.	NO YES
	b	Has your weight strongly affected how you feel about yourself? Has your body shape strongly affected how you feel about yourself? **IF YES TO EITHER**, CODE **YES**.	NO YES
	c	Did you think that your low weight was normal or overweight?	NO YES
R5		ARE **1** OR MORE **R4** ANSWERS CODED **YES**?	➡ NO YES

IS **R5** CODED **YES**?

NO **YES**

ANOREXIA NERVOSA
CURRENT

HEIGHT / WEIGHT TABLE CORRESPONDING TO A BMI THRESHOLD OF 17.0 KG/M^2

Height/Weight

ft/in	3'0	3'1	3'2	3'3	3'4	3'5	3'6	3'7	3'8	3'9	3'10	3'11	4'0	4'1
lb	32	34	36	38	40	42	44	46	48	50	53	55	57	60
cm	91	94	97	99	102	104	107	109	112	114	117	119	122	125
kg	15	15	16	17	18	19	20	21	22	23	24	25	26	27

ft/in	4'2	4'3	4'4	4'5	4'6	4'7	4'8	4'9	4'10	4'11	5'0	5'1	5'2	5'3
lb	62	65	67	70	72	75	78	79	82	84	87	90	93	96
cm	127	130	132	135	137	140	142	145	147	150	152	155	158	160
kg	28	29	31	32	33	34	35	36	37	38.5	39.5	41	42.5	43.5

ft/in	5'4	5'5	5'6	5'7	5'8	5'9	5'10	5'11	6'0	6'1	6'2	6'3
lb	99	102	106	109	112	115	119	122	125	129	133	136
cm	163	165	168	170	173	175	178	180	183	185	188	191
kg	45.5	46.5	48	49	51	52	54	55	57	58.5	60	62

The weight thresholds above are calculated using a body mass index (BMI) equal to or below 17.0 kg/m^2 for the patient's height using the Center of Disease Control & Prevention BMI Calculator. This is the threshold guideline below which a person is deemed underweight by the DSM-5 for Anorexia Nervosa. For children and adolescents, the above thresholds are only approximate. For a more accurate BMI assessment of each patient, use the date of birth, the date of measurement, sex, height and weight and input this data into the CDC BMI Calculator at www.nccd.cdc.gov

S. BULIMIA NERVOSA

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN THE BULIMIA NERVOSA AND IN THE ANOREXIA NERVOSA BINGE EATING / PURGING TYPE DIAGNOSTIC BOXES. BUT IF ANOREXIA NERVOSA (IN MODULE R) IS CODED YES, CONTINUE WITH THE QUESTIONS TO BE ABLE TO PROPERLY CODE ANOREXIA NERVOSA RESTRICTING TYPE)

	In the past 3 months:		
S1	Did you have eating binges? An "eating binge" is when you eat a very large amount of food within two hours.	➡ NO	YES
S2	During these binges, did you feel that you could not control your eating?	➡ NO	YES
	In the past 3 months:		
S3	Did you have eating binges at least once a week?	➡ NO	YES
S4	Did you do anything to keep from gaining weight? Like making yourself throw up or exercising very hard? Trying not to eat for the next day or more? Taking pills to make you have to go to the bathroom more? Or taking any other kinds of pills to try to keep from gaining weight? **IF YES** TO **ANY**, CODE **YES**.	➡ NO	YES
S4a	Number of Episodes of Inappropriate Compensatory Behaviors per Week? _____		
	Number of Days of Inappropriate Compensatory Behaviors per Week? _____		
S5	Did your weight strongly affect how you felt about yourself? Did your body shape strongly affect how you felt about yourself? **IF YES** TO **EITHER**, CODE **YES**.	➡ NO	YES
S6	DO THE PATIENT'S SYMPTOMS MEET CRITERIA FOR ANOREXIA NERVOSA?	NO ↓ SKIP to S8	YES
S7	Did these binges occur only when you were under (____lb/kg)? INTERVIEWER: WRITE IN THE ABOVE ( ), THE THRESHOLD WEIGHT FOR THIS PATIENT'S HEIGHT FROM THE HEIGHT/WEIGHT TABLE IN THE ANOREXIA NERVOSA MODULE	NO	YES
S8	IS **S5** CODED **YES** AND IS EITHER **S6** OR **S7** CODED **NO**?	**NO**	**YES**

BULIMIA NERVOSA
CURRENT

S9 IS **S7** CODED **YES**?

NO **YES**

ANOREXIA NERVOSA
Binge Eating/Purging Type
CURRENT

DO THE PATIENT'S SYMPTOMS MEET CRITERIA FOR ANOREXIA NERVOSA?

AND

IS **S2** OR **S4** CODED **NO**?

NO **YES**

ANOREXIA NERVOSA
Restricting Type
CURRENT

SPECIFIERS OF EATING DISORDER:

MILD = **1-3** EPISODES OF INAPPROPRIATE COMPENSATORY BEHAVIORS
MODERATE = **4-7** EPISODES OF INAPPROPRIATE COMPENSATORY BEHAVIORS
SEVERE = **8-13** EPISODES OF INAPPROPRIATE COMPENSATORY BEHAVIORS
EXTREME = **14** OR MORE EPISODES OF INAPPROPRIATE COMPENSATORY BEHAVIORS

SPECIFY IF:

MILD ☐
MODERATE ☐
SEVERE ☐
EXTREME ☐

T. BINGE EATING DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOX, CIRCLE **NO** IN THE DIAGNOSTIC BOX, AND MOVE TO THE NEXT MODULE)

T1		DO THE PATIENT'S SYMPTOMS MEET CRITERIA FOR ANOREXIA NERVOSA?	NO	➡ YES
T2		DO THE PATIENT'S SYMPTOMS MEET CRITERIA FOR BULIMIA NERVOSA?	NO	➡ YES
T3		IS **S2** CODED **YES**?	➡ NO	YES
T4		IS **S3** CODED **YES**?	➡ NO	YES
T5		IS **S4** CODED **YES**? IF S4 WAS BYPASSED IN MODULE S (BULIMIA NERVOSA), ASK S4 NOW TO CODE T5	NO	➡ YES
		In the last 3 months during the binging did you:		
T6	a	Eat more rapidly than normal?	NO	YES
	b	Eat until you felt uncomfortably full?	NO	YES
	c	Eat large amounts of food when you were not hungry?	NO	YES
	d	Eat alone because you felt embarrassed about how much you were eating?	NO	YES
	e	Feel guilty, depressed or disgusted with yourself after binging?	NO	YES
		ARE **3** OR MORE **T6** QUESTIONS CODED **YES**?	➡ NO	YES
T7		Does your binging distress you a lot?	➡ NO	YES
T8		Number of Binge Eating Episodes per Week? _____ Number of Binge Eating Days per Week? _____		

IS **T7** CODED **YES**?

NO	YES
BINGE-EATING DISORDER **CURRENT**	

SPECIFIERS OF EATING DISORDER:

MILD = **1-3** EPISODES OF BINGE EATING PER WEEK
MODERATE = **4-7** EPISODES OF BINGE EATING PER WEEK
SEVERE = **8-13** EPISODES OF BINGE EATING PER WEEK
EXTREME = **14** OR MORE EPISODES OF BINGE EATING PER WEEK

SPECIFY IF:

- MILD ☐
- MODERATE ☐
- SEVERE ☐
- EXTREME ☐

U. GENERALIZED ANXIETY DISORDER

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** AND MOVE TO THE NEXT MODULE)

U1	a	**For the past six months**, have you worried a lot or been nervous? Have you been worried or nervous about several things, (like school, your health, or something bad happening)? Have you been more worried than other kids your age? **IF YES TO ANY**, CODE **YES**.	➡ NO	YES
	b	Do you worry most days?	➡ NO	YES
		IS THE PATIENT'S ANXIETY RESTRICTED EXCLUSIVELY TO, OR BETTER EXPLAINED BY, ANY DISORDER PRIOR TO THIS POINT?	NO	➡ YES
U2		Do you find it hard to stop worrying? Do the worries make it hard for you to pay attention to what you are doing? **IF YES TO EITHER**, CODE **YES**.	➡ NO	YES
U3		FOR THE FOLLOWING, CODE **NO** IF THE SYMPTOMS ARE CONFINED TO FEATURES OF ANY DISORDER EXPLORED PRIOR TO THIS POINT.		
		When you are worried, do you, most of the time:		
	a	Feel like you can't sit still?	NO	YES
	b	Feel tense in your muscles?	NO	YES
	c	Feel tired, weak or exhausted easily?	NO	YES
	d	Have a hard time paying attention to what you are doing? Does your mind go blank?	NO	YES
	e	Feel grouchy or annoyed?	NO	YES
	f	Have trouble sleeping ("trouble sleeping" means trouble falling asleep, waking up in the middle of the night, wakening up too early or sleeping too much)?	NO	YES
		ARE **1** OR MORE **U3** ANSWERS CODED **YES**?	➡ NO	YES

U4 Do these worries or anxieties cause a lot of problems at school or with your friends or at home or at work or with other people?

AND

IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

NO	YES
	GENERALIZED ANXIETY DISORDER **CURRENT**

V. ADJUSTMENT DISORDERS

(➡ MEANS: GO TO THE DIAGNOSTIC BOXES, CIRCLE **NO** IN ALL DIAGNOSTIC BOXES, AND MOVE TO THE NEXT MODULE)

ONLY ASK THESE QUESTIONS IF THE PATIENT CODES **NO** TO ALL OTHER DISORDERS.

EVEN IF A LIFE STRESS IS PRESENT OR A STRESS PRECIPITATED THE PATIENT'S DISORDER, **DO NOT** USE AN ADJUSTMENT DISORDER DIAGNOSIS IF **ANY OTHER** PSYCHIATRIC DISORDER IS PRESENT. **CIRCLE N/A** IN DIAGNOSTIC BOX AND **SKIP** THE ADJUSTMENT DISORDER MODULE IF THE PATIENT'S SYMPTOMS **MEET CRITERIA** FOR **ANOTHER SPECIFIC** AXIS I **DISORDER** OR ARE MERELY **AN EXACERBATION** OF A **PREEXISTING** AXIS I OR II **DISORDER**.

V1 Are you stressed out about something? Is this making you upset or making your behavior worse?
IF NO TO **EITHER**, CODE **NO**.

Examples include anxiety/depression/physical complaints; misbehavior such as fighting, driving recklessly, skipping school, vandalism, violating the rights of others, or illegal activity.

IDENTIFIED STRESSOR: _____

DATE OF ONSET OF STRESSOR: _____

➡ NO YES

V2 Did your upset/behavior problems start soon after the stress began? Or was this within 3 months of the onset of the stressor?
IF NO TO **EITHER**, CODE **NO**.

➡ NO YES

V3 a Are you more upset by this stress than other kids your age would be? NO YES

b Do these stresses or upsets cause you problems at home? With your family? At school? With your friends? With other people? Or in some other important way?
IF YES TO **V3a** OR TO ANY PART OF **V3b**, CODE **YES**.

➡ NO YES

V4 BEREAVEMENT IS PRESENT IF THESE EMOTIONAL/BEHAVIORAL SYMPTOMS ARE DUE ENTIRELY TO THE LOSS OF A LOVED ONE AND ARE SIMILAR IN SEVERITY, LEVEL OF IMPAIRMENT AND DURATION TO WHAT MOST OTHERS WOULD SUFFER UNDER SIMILAR CIRCUMSTANCES.

HAS BEREAVEMENT BEEN RULED OUT?

➡ NO YES

V5 Have these problems gone on for 6 months or more after the stress stopped?

➡ NO YES

WHICH OF THESE EMOTIONAL / BEHAVIORAL SUBTYPES ARE PRESENT? **Mark all that apply**

a Depression, tearfulness or hopelessness. ☐

b Anxiety, nervousness, jitteriness, worry. ☐

c Misbehavior (Like fighting, driving recklessly, skipping school, vandalism, violating other's rights, doing illegal things). ☐

d School problems, physical complaints or social withdrawal. ☐

IF MARKED:

- **A only**, then code as Adjustment Disorder, with depressed mood. F43.21
- **B only**, then code as Adjustment Disorder, with anxious mood. F43.22
- **C only**, then code as Adjustment Disorder, of conduct. F43.24
- **A** and **B only**, then code as Adjustment Disorder, with mixed anxiety and depressed mood. F43.23
- **C** and (**A** or **B**), then code as Adjustment Disorder, of emotions and of conduct. F43.25
- **D only**, then code as Adjustment Disorder, unspecified. F43.20
- **C** and **D**, then code as Adjustment Disorder, of conduct. F43.24
- **B** and **D**, then code as Adjustment Disorder, with anxious mood. F43.22
- **B**, **C** and **D**, then code as Adjustment Disorder, with anxious mood and of conduct. F43.22 / F43.24
- **A** and **D**, then code as Adjustment Disorder, with depressed mood. F43.21
- **A**, **C** and **D**, then code as Adjustment Disorder, with depressed mood and of conduct. F43.21 / F43.24
- **A**, **B** and **D**, then code as Adjustment Disorder, with mixed anxiety and depressed mood. F43.23
- **A**, **B** and **C**, then code as Adjustment Disorder, with mixed anxiety and depressed mood, and of conduct. F43.23 / F43.24
- **A**, **B**, **C** and **D**, then code as Adjustment Disorder, with mixed anxiety and depressed mood, and of conduct. F43.23 / F43.24

IF **V1** AND **V2** AND **(V3a or V3b)** ARE CODED **YES**
AND
V5 IS CODED **NO,** THEN CODE THE DISORDER **YES** WITH **SUBTYPES.**

IF **NO,** CODE **NO** TO ADJUSTMENT DISORDER.

NO N / A YES

ADJUSTMENT DISORDER
***with*_____**
(see above for subtypes)

W. RULE OUT MEDICAL, ORGANIC OR DRUG CAUSES FOR ALL DISORDERS

IF THE PATIENT CODES POSITIVE FOR ANY CURRENT DISORDER OR A MAJOR DEPRESSIVE EPISODE OR A MANIC OR A HYPOMANIC EPISODE ASK:

Just before these symptoms began:

W1	a	Were you taking any drugs or medicines or in withdrawal from any of these?	☐ No	☐ Yes	☐ Uncertain
W1	b	Did you have any medical illness?	☐ No	☐ Yes	☐ Uncertain
W2		IF **W1a** OR **W1b** IS CODED **YES,** IN THE CLINICIAN'S JUDGMENT, IS EITHER LIKELY TO BE A DIRECT CAUSE OF THE PATIENT'S DISORDER? IF NECESSARY, ASK ADDITIONAL OPEN-ENDED QUESTIONS.	☐ No	☐ Yes	☐ Uncertain
		W2 SUMMARY: HAS AN "ORGANIC" / MEDICAL / DRUG RELATED CAUSE BEEN RULED OUT?	☐ No	☐ Yes	☐ Uncertain

IF **W2** IS **YES,** THEN **W2** SUMMARY IS **NO.**
IF **W2** IS **NO,** THEN **W2** SUMMARY IS **YES.**
OTHERWISE IT IS **UNCERTAIN.**

X. AUTISM SPECTRUM DISORDER

Patients with Autism Spectrum Disorder (ASD) may not be able to recognize that they exhibit the behaviors described below. Family members may have better insight into the presence or absence of these behaviors. However, where possible the child / adolescent should be involved in this discussion.

X1	Since the age of 4, have you had difficulty making friends? Do you have problems because you keep to yourself? Is it because you are shy or because you don't fit in? **IF YES** TO **ANY**, CODE **YES**.	NO	YES	UNSURE
X2	Has anyone commented that your face lacked expressions or that you appeared to have difficulty communicating non-verbally? Has anyone noticed that it was very difficult to figure out what you were thinking from your facial expression or from your body language? **IF YES** TO **ANY**, CODE **YES**.	NO	YES	UNSURE
X3	Are you fixated on routines and rituals? Do you have interests that are special and interfere with other activities? **IF YES** TO **ANY**, CODE **YES**.	NO	YES	UNSURE
X4	Have you or anyone else noticed that you engage in repetitive movements or repetitive speech that help you calm down or feel better (self-soothing or self-stimulating behaviors)?	NO	YES	UNSURE
X5	Do you react less or do you overreact to touch or sound, or to visual, smell, taste, temperature or pain sensations?	NO	YES	UNSURE
X6	Do other kids think you are weird or strange or awkward?	NO	YES	UNSURE
X7	Do you play mostly alone, rather than with other children?	NO	YES	UNSURE

X8 **IF ALL THE X ANSWERS** ARE CODED **NO**, CODE **NO**.

IF 1 OR MORE OF THE **X ANSWERS** ARE CODED **YES** OR **UNSURE**, CODE **CANNOT BE RULED OUT**.

NO	CANNOT BE RULED OUT *

AUTISM SPECTRUM DISORDER

*Autism Spectrum Disorder is possible, but needs to be more thoroughly investigated by a board-certified child psychiatrist. Based on the above responses, the diagnosis of ASD cannot be ruled out. The above screening is to rule out the diagnosis, rather than to rule it in.

ADDITIONAL OPTIONAL INTERVIEW ASSESSMENTS ON PAGES 56 & 57

MOOD DISORDERS: DIAGNOSTIC ALGORITHM

Consult Modules:
- A Major Depressive Episode
- C (Hypo)manic Episode
- Q Psychotic Disorders

MODULE Q:

1a	IS **Q11b** CODED **YES**?	NO	YES
1b	IS **Q12a** CODED **YES**?	NO	YES

MODULES A and C:		Current	Past
2 a	CIRCLE **YES IF** A DELUSIONAL IDEA IS IDENTIFIED IN **A3e** OR IN **ANY** PSYCHOTIC FEATURE IN **Q1** THROUGH **Q7**.	YES	YES
b	CIRCLE **YES IF** A DELUSIONAL IDEA IS IDENTIFIED IN **C3a** OR IN **ANY** PSYCHOTIC FEATURE IN **Q1** THROUGH **Q7**.	YES	YES

c IS A MAJOR DEPRESSIVE EPISODE CODED **YES** (CURRENT OR PAST)?
AND
IS MANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS HYPOMANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY:

- IF THE DEPRESSIVE EPISODE IS **CURRENT** OR **PAST** OR BOTH.
- WITH PSYCHOTIC FEATURES, CURRENT: IF **1b** OR **2a** (CURRENT) = **YES**
  WITH PSYCHOTIC FEATURES, PAST: IF **1a** OR **2a** (PAST) = **YES**

MAJOR DEPRESSIVE DISORDER

	Current	Past
MDD	☐	☐

With Psychotic Features

Current	☐
Past	☐

d IS MANIC EPISODE CODED **YES** (CURRENT OR PAST)?
AND
IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY:

- IF THE BIPOLAR I DISORDER IS **CURRENT** OR **PAST** OR BOTH.
- WITH SINGLE MANIC EPISODE: IF MANIC EPISODE (CURRENT OR PAST) = **YES**
  AND MAJOR DEPRESSIVE EPISODE (CURRENT AND PAST) = **NO**
- WITH PSYCHOTIC FEATURES, CURRENT: IF **1b** OR **2a** (CURRENT) OR **2b** (CURRENT) = **YES**
  WITH PSYCHOTIC FEATURES, PAST: IF **1a** OR **2a** (PAST) OR **2b** (PAST) = **YES**
- IF THE MOST RECENT EPISODE IS MANIC, DEPRESSED, OR HYPOMANIC (MUTUALLY EXCLUSIVE).
- IF THE MOST RECENT MOOD EPISODE IS WITH MIXED, ANXIOUS OR PSYCHOTIC FEATURES.

  HYPO/MANIC WITH MIXED FEATURES = HYPO/MANIC + AT LEAST **3** SYMPTOMS FROM **A3**

  DEPRESSED WITH MIXED FEATURES = MAJOR DEPRESSIVE EPISODE + AT LEAST **3** SYMPTOMS FROM **C3**

  WITH ANXIOUS DISTRESS = WITH AT LEAST **3** SYMPTOMS FROM **U3**

BIPOLAR I DISORDER

	Current	Past
Bipolar I Disorder	☐	☐
Single Manic Episode	☐	☐

With Psychotic Features
Current ☐
Past ☐

Most Recent Episode
Manic ☐
Depressed ☐
Hypomanic ☐

Most Recent Episode
With mixed features ☐
With anxious distress ☐

Most Recent Episode
Mild ☐
Moderate ☐
Severe ☐

e IS MAJOR DEPRESSIVE EPISODE CODED **YES** (CURRENT OR PAST)?
AND
IS HYPOMANIC EPISODE CODED **YES** (CURRENT OR PAST)?
AND
IS MANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS "RULE OUT ORGANIC CAUSE (**W2 SUMMARY**)" CODED **YES**?

SPECIFY:

- IF THE BIPOLAR DISORDER IS **CURRENT** OR **PAST** OR BOTH.
- IF THE MOST RECENT MOOD EPISODE IS HYPOMANIC OR DEPRESSED (MUTUALLY EXCLUSIVE).
- IF THE MOST RECENT MOOD EPISODE IS WITH MIXED, ANXIOUS OR PSYCHOTIC FEATURES.

  HYPOMANIC WITH MIXED FEATURES = HYPOMANIC + AT LEAST **3** SYMPTOMS FROM **A3**

  DEPRESSED WITH MIXED FEATURES = MAJOR DEPRESSIVE EPISODE + AT LEAST **3** SYMPTOMS FROM **C3**

  WITH ANXIOUS DISTRESS = WITH AT LEAST **3** SYMPTOMS FROM **U3**

BIPOLAR II DISORDER

	Current	Past
Bipolar II Disorder	☐	☐

Most Recent Episode
Hypomanic ☐
Depressed ☐

Most Recent Episode
With mixed features ☐
With anxious distress ☐

Most Recent Episode
Mild ☐
Moderate ☐
Severe ☐

f IS MAJOR DEPRESSIVE EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS MANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS **C4b** CODED **YES** FOR THE APPROPRIATE TIME FRAME?
AND
IS **C8b** CODED **YES**?

OR

IS MANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS HYPOMANIC EPISODE CODED **NO** (CURRENT AND PAST)?
AND
IS **C4a** CODED **YES** FOR THE APPROPRIATE TIME FRAME?
AND
IS **C8c** CODED **YES**?

SPECIFY IF THE OTHER SPECIFIED BIPOLAR AND RELATED DISORDER IS **CURRENT** OR **PAST** OR BOTH.

OTHER SPECIFIED BIPOLAR AND RELATED DISORDER

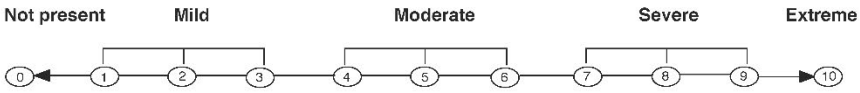
	Current	Past
Other Specified Bipolar and Related Disorder	☐	☐

OPTIONAL ASSESSMENT MEASURES TO TRACK CHANGES OVER TIME

A: CROSS CUTTING MEASURES

SEVERITY OF SYMPTOM

Use this scale to rate the severity of your symptom in the score column in the table below:



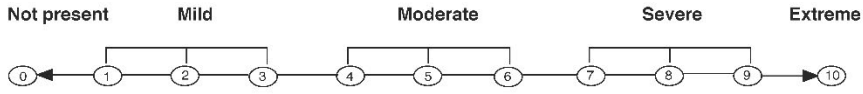
Assessment of Symptoms That Cut Across Disorders

	Symptom Name	Score
1	Depression	
2	Anger	
3	Mania (feeling up or high or hyper or full of energy with racing thoughts)	
4	Anxiety	
5	Physical (somatic) symptoms	
6	Suicidal thoughts, impulses, plans, intent, (ANY thoughts of killing yourself), or any preparations to kill yourself or ANY attempt to kill yourself	
7	Hearing sounds or voices others can't hear or fearing someone can hear or read your thoughts or believing things others don't accept as true e.g. that people are spying on you or plotting against you or talking about you (Psychosis)	
8	Sleep problems	
9	Memory problems	
10	Repetitive or obsessive thoughts or compulsive behaviors	
11	Feeling things around you are strange, unreal, detached or unfamiliar, or feeling outside or detached from part or all of your body (Dissociation)	
12	Ability to function at work, at home, in your life, or in your relationships	
13	Overusing alcohol or drugs	

B: DISABILITY / FUNCTIONAL IMPAIRMENT

SEVERITY OF DISABILITY / IMPAIRMENT

Use this scale to rate in the score column of the table below, how much your symptoms have disrupted your ability to function in the following areas of your life:



Assessment of Impairment of Functioning /Disability

	Domain Name	Score
1	Work or school work	
2	Social life or leisure activities (like hobbies or things you do for enjoyment)	
3	Family life and / or home responsibilities	
4	Ability to get along with people	
5	Personal and social relationships	
6	Ability to understand and to communicate with others	
7	Ability to take care of yourself (washing, showering, bathing, dressing properly, brushing teeth, laundry, combing / brushing hair, eating regularly)	
8	Made you disruptive or aggressive towards others	
9	Financially (ability to manage your money)	
10	Ability to get around physically	
11	Spiritual or religious life	
12	How much did your condition have an impact on other people in your family?	

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KEY REFERENCES on MINI Kid or MINI

1. Sheehan DV, Sheehan KH, Shytle RD, Janavs J, Bannon Y, Rogers JE, Milo KM, Stock SL, Wilkinson B. Reliability and Validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI–KID). J Clin Psychiatry; 2010;71(3):313-326.

2. Sheehan DV, Lecrubier Y, Harnett-Sheehan K, Janavs J, Weiller E, Bonara I, Keskiner A, Schinka J, Knapp E, Sheehan MF, Dunbar GC. Reliability and Validity of the MINI International Neuropsychiatric Interview (M.I.N.I.): According to the SCID-P. European Psychiatry. 1997;12:232-241.

3. Lecrubier Y, Sheehan DV, Weiller E, Amorim P, Bonora I, Sheehan K, Janavs J, Dunbar G. The MINI International Neuropsychiatric Interview (M.I.N.I.) A Short Diagnostic Structured Interview: Reliability and Validity According to the CIDI. European Psychiatry. 1997;12: 224-231.

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International Advisory Committee for MINI Kid version 2.0

Manuel Bouvard	Phillipe Mazet
Lars von Knorring	Marie Christine Mouren-Simeoni
Naomi Breslau	Stephan Renou
Martine Flament	Frank Verhulst
Donald Klein	Lars von Knorring
Rachel Gittelman Klein	Anne-Liis von Knorring

Translations	**M.I.N.I. KID 5**
English	DV. Sheehan, D. Shytle, K.Milo, J Janavs.
Spanish	M. Soto, R Hidalgo
French	Y. Lecrubier, T. Hergueta
Hungarian	J. Balazs
Turkish	A. Engeler
German	B. Plattner
Hebrew	D. Gothelf, A. Pardo

Translations	**M.I.N.I. KID 6 and 7**
All	Mapi in France in collaboration with many international consultants (http://www.mapigroup.com)

12.8 Vitiello Aggression Scale

Predatory-Affective Aggression Scale

Patient_____

Rater_____ Date_____

Check if any these behaviors is usual for this patient (i.e., it has occurred at least 3 times during the last month):

		YES	NO
1.	Non profitable damaging of own property	1	0
2.	Hides aggressive acts	1	0
3.	Exposes self to physical harm when aggressive	1	0
4.	Is aggressive without a purpose	1	0
5.	Can control own behavior when aggressive	1	0
6.	Aggression is unplanned, out of the blue	1	0
7.	Very careful to protect self when aggressive	1	0
8.	Completely out of control when aggressive	1	0
9.	Plans aggressive acts	1	0
10.	Steals	1	0

Scoring:

Predatory score: sum of items 2, 5, 7, 9, and 10
Affective score: sum of items 1, 3, 4, 6, and 8
Total score: difference of Predatory score minus Affective score/
Possible range of total score: from 5 (completely predatory) to –5 (completely affective)

Reference:

B. Vitiello et al. (1990), J. Neuropsychiatry Clin. Neurosciences 2:189-192.

12.9 Edinburgh Handedness Inventory

Subject Number: _____ Date: _____

EDINBURGH HANDEDNESS INVENTORY

Please indicate your preferences in the use of hands in the following activities *by putting + in the appropriate column.* Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, *put* + +. If in any case you are really indifferent, *put + in both columns.*
Some of the activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in brackets.
Please try to answer all the questions, and only leave a blank if you have no experience at all of the object or task.

		LEFT	RIGHT
1	Writing		
2	Drawing		
3	Throwing		
4	Scissors		
5	Toothbrush		
6	Knife (without fork)		
7	Spoon		
8	Broom (upper hand)		
9	Striking Match (match)		
10	Opening box (lid)		
i	Which foot do you prefer to kick with?		
ii	Which eye do you use when using only one?		

# of LEFT	# of RIGHT	# RIGHT- #LEFT	# RIGHT + #LEFT
Final Score: (# RIGHT- #LEFT) * 100 (# RIGHT+ #LEFT)			

Oldfield, R.C. "*The Assessment and Analysis of Handedness: The Edinburgh Inventory.*" Neuropsychologia, 9(1):97-113. 1971

12.10 PSAP Questionnaire

Subject ID: _____ Date Imaging Procedures Performed: _____

810P204 Imaging Center Visit

Section I:

1.) Were all imaging procedures completed for the subject? Y N
2.) Were the two PSAP fMRI sessions completed? Y N
3.) How many game points were earned by the subject? _____
4.) For the fMRI visit on treatment only:
   a. What time did the subject report taking their study medication dose? _____
   b. What time did the fMRI session start? _____

Section II:

Administer below questionnaire to the subject at the end of the visit

"Thank you for participating in this study and playing the game, we hope that you have enjoyed it. We would like to hear from you to understand if there is something that we can do to improve the game. We are asking if you could please answer a few questions."

1. How easy was the game? On a scale from 1 to 5, where 1 is very difficult and 5 is very easy, how would you rate the game?

◯	◯	◯	◯	◯
1	2	3	4	5

2. What was the most difficult part of the game?

_____

_____

3. What don't you like about the game? Choose up to 3.

◯ It takes up too much time
◯ I didn't earn too much
◯ It's pointless
◯ It's frustrating
◯ It's boring

4. Choose one to describe the other player:

◯ Unbeatable player
◯ Good player
◯ Bad player
◯ Other _____

Administered By (Initials/Date): _____

Version 1.0

12.11 MR Safety Questionnaire

Name: Acct#: Date:

SAND LAKE IMAGING

MAGNETIC RESONANCE (MR) PROCEDURE SCREENING FORM

Please read and **CIRCLE YES OR NO** if you have any of the following:

ABSOLUTE CONTRAINDICATIONS		
YES	NO	Aneurysm clip (s)
YES	NO	Pacemaker
YES	NO	Implanted cardioverter defibrillator (ICD)
YES	NO	Electronic implant or device
YES	NO	Magnetically – activated implant or device
YES	NO	Neuro-stimulation System
YES	NO	Spinal Cord Stimulator
YES	NO	Internal electrodes or wires
YES	NO	Bone growth/ Bone fusion stimulator
YES	NO	Cochlear, otologic, or other ear implant
YES	NO	Tissue expander (ex: breast)
Other		

POSSIBLE CONTRAINDICATIONS		
YES	NO	Any type of prosthesis (eye, penile, etc.)
YES	NO	Heart valve prosthesis
YES	NO	Eyelid spring or wire
YES	NO	Any metallic fragment or foreign body
YES	NO	Metallic Stent, filter, or coil
YES	NO	Insulin or other infusion pump
YES	NO	Shunt (spinal or intraventricular)
YES	NO	Medication patch (nicotine, nitroglycerine)
YES	NO	Implanted drug infusion device
Other		

NEED TO KNOW FOR POSSIBLE ARTIFACT		
YES	NO	Wire Mesh Implant
YES	NO	Dentures
YES	NO	Surgical staples, clips, metallic sutures
YES	NO	Joint Replacement (hip, knee, etc)
YES	NO	Bone/joint pin, screw, nail, wire, plate, etc
YES	NO	IUD, diaphragm, or pessary
YES	NO	Tattoo or permanent makeup
YES	NO	Body Piercing
YES	NO	Hearing Aid (removed before entering MR room)
Other		

Surgical Hx:
Pregnancy Status:
LMP:

CAUTION:

Before entering the MR environment or MR system room, you must remove all metallic objects including: weapons including pistols, hearing aids, dentures, partial plates, keys, beeper, cell phone, eyeglasses, hair pins, barrettes, jewelry, body piercing jewelry, watch, safety pins, paperclips, money clips, credit cards, bank cards, magnetic strip cards, coins, pens, pocket knife, nail clipper, tools, clothing with metal fasteners, clothing with metallic threads.

Please consult the MRI Technologist or Radiologist if you have any question or concerns BEFORE entering the MRI system room.

NOTE: You may be advised or required to wear ear plugs or other hearing protection during the MR system room.

I have read the above statement and acknowledge it is my responsibility to remove the listed items before entering the MRI room in order to prevent damage to Sand Lake Imaging equipment and my personal items. Sand Lake Imaging is no responsible for damage to personal items not removed before entering MRI room

Patient or Guardian Signature:

_____

Date: _____

HEIGHT: _____

WEIGHT: _____