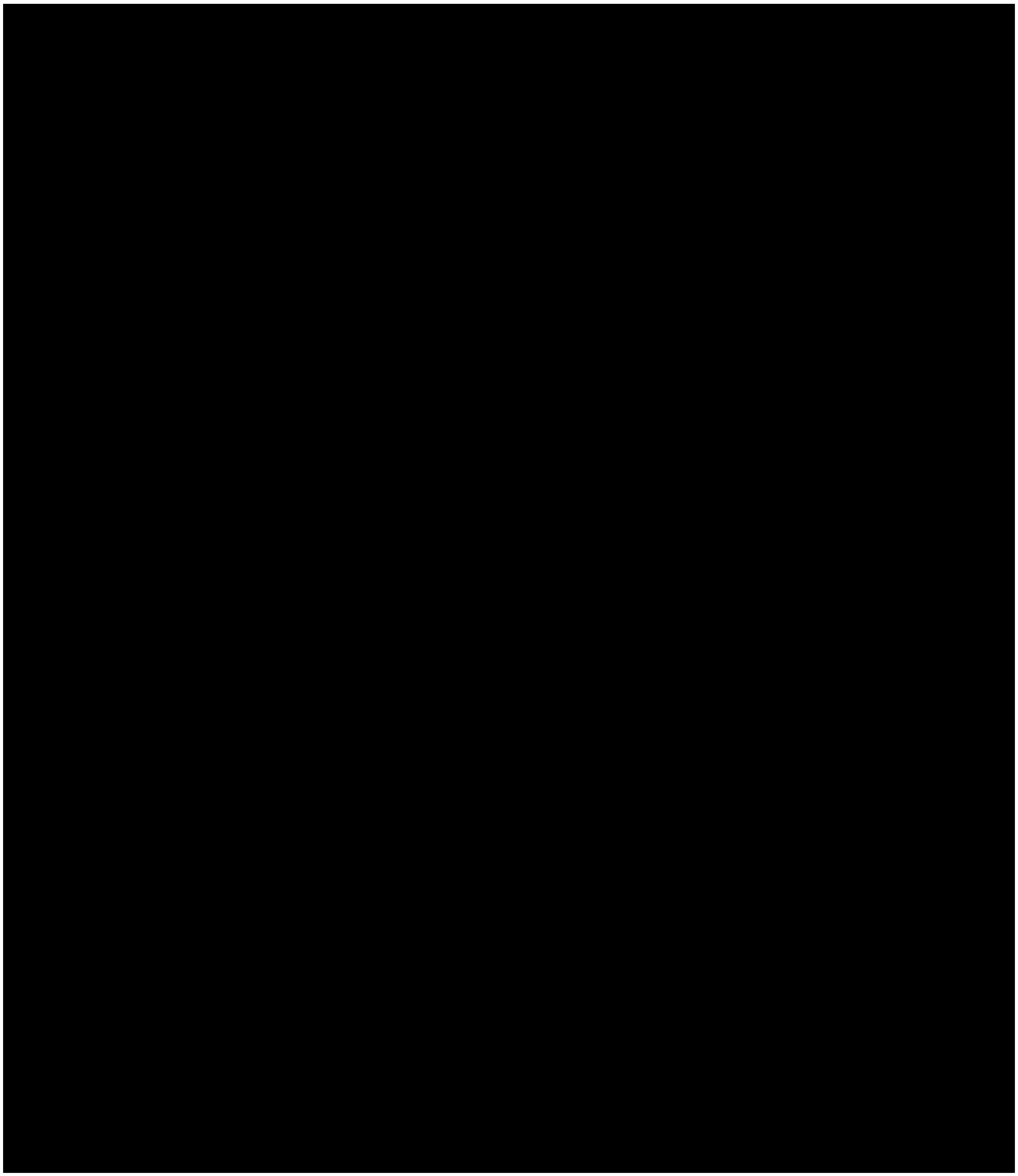
TITLE PAGE

Protocol Number:	810P503
Title:	Assessment of Efficacy and Safety of SPN-810 for the Treatment of Impulsive Aggression (IA) in Adolescent Subjects 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 in subjects with Attention Deficit/Hyperactivity Disorder (ADHD) in conjunction with standard ADHD treatment
Medical Monitor	[redacted]
Phase:	3
Protocol Version:	3.0
Release Date:	01 Nov 2018
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.

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 International Conference on Harmonization (ICH) and all applicable local Good Clinical Practice (GCP) guidelines, including the Declaration of Helsinki and all its accepted amendments to date.

Principal Investigator	Signature	Date

SUPERNUS PHARMACEUTICALS, INC. PROTOCOL APPROVAL PAGE



SUMMARY OF CHANGES

This summary table lists all clarifications, administrative changes or amendments to Supernus protocol 810P503. Additions are denoted by bold letters and deletions by strikethrough.

Section	Page	Description of Change	Rationale
Changes to 810P503 V1.0 Dated 31 May 2018			
Title Page	1	The following was changed: ~~A Phase III Trial to~~ Assess**ment** ~~the~~**of** Efficacy and Safety of **SPN810** for the Treatment of Impulsive Aggression (IA) in Adolescent ~~**Patient**~~**Subjects** with Attention Deficit/Hyperactivity Disorder (ADHD) in Conjunction with Standard ADHD Treatment.	Administrative
Title Page	1	Protocol version and date was updated	Administrative
Synopsis	6	The following was changed: ~~A Phase III Trial to~~ Assess**ment** ~~the~~**of** Efficacy and Safety of **SPN810** for the Treatment of Impulsive Aggression (IA) in Adolescent ~~**Patient**~~**Subjects** with Attention Deficit/Hyperactivity Disorder (ADHD) in Conjunction with Standard ADHD Treatment.	Administrative
Sec. 4.1	30	The following was changed: The incidence of these infrequent IA behaviors will be assessed **on paper at Visit 2 and** using the checklist in the same IA diary **from Visit 3 to Visit 7.**	Clarification
Sec. 4.3.1.2	34	The following was added: **At Visit 2 infrequent behaviors will also be recorded.**	Clarification
Table 1	39,40	Infrequent Behavior Checklist was added at Visit 2 The footnote was added: **k. The checklist will be recorded on a paper source and entered on EDC only at Visit 2.**	Clarification
Sec. 5.3.2	41	The following was added: **5. Record Infrequent IA Behaviors**	Clarification
Sec. 6.4.10	63	The following was changed:	Clarification

Section	Page	Description of Change	Rationale
		At Visit 2 the c~~C~~aregivers will be asked which, if any, of these behaviors have been observed since screening. At the following visits (Visit 3-7) any of these behaviors will be recorded if they were observed since the patient's last visit. ~~**This assessment will be administered at Visit 3-7**~~	
Sec. 7.1	63	The following was added: **All the modules will be administered except for modules R, S, T, U, V and W.**	Clarification
Changes to 810P503 V2.0 Dated 08 Jun 2018 **Version 2.0 (dated 08 June, 2018) of the protocol was amended to include a clarification of the R-MOAS score as well as a definition of the R-MOAS remission, an update to schedule of assessments for blood collection for PK analysis to facilitate enrollment, inclusion of urine drug screen at each visit and vital signs at Visit 3 for safety. A complete list of all changes is summarized below.**			
Synopsis	18	<u>Additional secondary objectives</u> **These additional secondary objectives are to assess the effect of treating adolescents with SPN-810 on the following**: 4. Inattention, Hyperactivity-Impulsivity **and ODD** measured by the SNAP-IV; 5. Child's overall health as measured by the Child Health Questionnaire Parent Form 28-item (CHQ-PF28); 6. **Parental stress measured by the** Stress Index for Parents of Adolescents (SIPA); 7. Safety of SPN-810 in adolescent subjects.	To clarify
Synopsis	19	The following text was changed: • Treatment Phase: ~~45~~**36** days Titration period: 2 weeks	To clarify
Synopsis	20	The following text was added: **Dose reduction will be allowed during maintenance in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.**	To clarify
Synopsis	21	The following were added: 3. R-MOAS remission rate **defined as a score ≤10** <u>Additional **Secondary** Endpoints:</u>	To clarify

Section	Page	Description of Change	Rationale
		Additional Secondary Safety and Tolerability Endpoints: **Exploratory Endpoints:**	
Synopsis	22	The following text was added: **Pharmacogenomic testing is optional.**	Administrative
Synopsis	22	The following was changed: Assuming a mean **difference** ~~deviation~~ of 15 between SPN-810 dose group and placebo with a common standard deviation of 35, a sample of 93 subjects per arm will yield 80 % power to detect a non-zero difference between the median of SPN-810 treatment group and the placebo group using the Wilcoxon rank-sum test with a 2-sided significance level α=0.05.	Administrative
Synopsis	22	The following text was added: **It is assumed that approximately 20% subjects will dropout before the completion of the study and hence, an adjusted total of 186 subjects will be randomized in a 1:1 ratio to obtain approximately 150 subjects at the completion of the study.**	Improve study design
Synopsis	22	The following text was changed: Per-Protocol (PP) Population: will include all of the subjects ~~in the FAS~~ who completed the Treatment Phase ~~with 70% diary completion compliance~~ and ~~who~~ did not have major protocol deviations **(as defined in the SAP).**	Improve study design
Synopsis	23	The following was added: For the efficacy endpoint, the frequency of IA behaviors during the Treatment Phase will be calculated over the number of days with non-missing IA diary data in the Treatment Phase **(titration + maintenance).**	To clarify
Synopsis	23	The following text was added:	Improve study design

Section	Page	Description of Change	Rationale
		Each of the secondary endpoints will be analyzed using a Mixed-Effect Model for Repeated Measure (MMRM). MMRM assumes missing data as Missing at Random. The model includes treatment, visit, and interaction between treatment and visit as fixed factors, baseline as covariate. The model parameters will be estimated using restricted maximum likelihood method with unstructured variance-covariance matrix and Kenward-Roger approximation to estimate denominator degrees of freedom. The between-group comparison will be performed using the simple contrast at the respective visits. The following text was removed: ~~As a key secondary analysis, the above analysis will be repeated for percent change (PCHM) in the frequency of IA behaviors per 7 days in the Maintenance period relative to the Baseline period calculated over the number of days with non-missing IA diary data.~~ ~~Key and additional secondary endpoints (Investigator and Caregiver-completed-CGI-S, R-MOAS, Investigator and Caregiver-completed-CGI-I, SNAP-IV, CHQ-PF28 and SIPA) will be analyzed using the analysis of covariance method based on the FAS population with missing data imputed using the Last Observation Carried Forward (LOCF) method. The model includes treatment and baseline as fixed independent covariates and change from baseline to final maintenance visit as a response variable.~~	
Sec 2.5	38	The following was changed: The primary objective of 810P301 and 810P302 is to assess the efficacy and safety of SPN-810 in reducing the frequency of IA behaviors in children 6 to 12 years of age with ADHD and ~~comorbid~~**associated features** of IA when taken in conjunction with standard ADHD treatment.	To clarify
Sec 3.2	39 and 40	The following text were changed:	To clarify

Section	Page	Description of Change	Rationale
		3. ~~R-MOAS remission rate~~ **Percent of children whose IA behaviors were remitted at the end of the study measured by R-MOAS score ≤ 10.** Additional secondary objectives are to assess the effect of **treating adolescents with** SPN-810 on the following: 1. Caregiver-rated CGI-I **Scale**; 2. Caregiver-rated **Clinical Global Impression – Severity Scale (**CGI-S**)**; 3. Inattention and Hyperactivity-Impulsivity **and ODD** measured by the SNAP-IV rating scale; 7. Safety Monitoring **a. Incidence of Adverse Events** **b. Incidence of Extrapyramidal Symptoms (EPS) as assessed by Simpson-Angus Scale Barnes Akathisia Scale, Abnormal Involuntary Movement Scale** **c. Columbia Suicide Severity Rating Scale (C-SSRS)** **d. Laboratory Parameters (Hematology, Chemistry, Urinalysis, Insulin and Prolactin)** **e. Vital signs, Standardized BMI, Physical Examination and ECG (12-lead)** **f. Infrequent Behaviors Checklist**	
Sec. 4.1	41	The following text was changed. "**Key** secondary measures of efficacy of SPN-810 will include the Clinical Global Impression - Severity Scale (CGI-S) scores completed by the Investigator, R-MOAS score and the percent of adolescents whose IA behaviors were remitted at the end of study (R-MOAS score ≤ 10). Additional secondary measures include the Investigator and Caregiver-rated Clinical Global Impression- Improvement Scale (CGI-I) scores, the Caregiver-rated Clinical Global Impression - Severity Scale (CGI-S) score, the inattention, hyperactivity-impulsivity **and ODD** measured by the SNAP-IV…"	To clarify
Sec 4.1	41	The following text was changed:	To clarify

Section	Page	Description of Change	Rationale
		The incidence of these infrequent IA behaviors will be assessed on paper at Visit 2 and using the checklist in the **electronic** IA diary from Visit 3 to Visit 7.	
Sec. 4.2	42	The following text was added: **Dose reduction will be allowed during maintenance in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.**	To clarify
Sec. 4.2	42	The following text was changed: 	Improve study design
Sec 4.3	42	The following was changed; Treatment Phase: **36**~~46~~ days	Administrative
Figures 1 and 2	44 and 45	Figures 1 and 2 were updated to clarify the increase of dosage at Visit 5 and to specify option for dose reduction from 45mg to 36mg/day during the third week of titration.	To clarify
Sec. 4.3.1.1	46	The following were changed: Both these scales measure severity of aggressive behaviors; only those subjects with an R-MOAS score of **≥ 20** ~~≥ 24~~ and scoring of at least "moderately ill" (score of ≥ 4) on CGI-S will be eligible for the study The following was added:	To increase study enrollment

Section	Page	Description of Change	Rationale
		Serum pregnancy test will be performed at Screening for all female subjects.	
Sec 4.3.1.2	46	The following text was added: At Visit 2 infrequent behaviors will also be recorded **on paper source.**	To clarify
Sec 4.3.1.2	47	The following text was changed: Although there are up to 30 days available for each of the Screening ~~and~~**or** the Baseline period, the total duration of Screening and Baseline periods may not exceed 45 days.	To clarify
Sec 4.3.2	47	The following text was changed: Treatment Phase: (2-~~8~~ **5** weeks)	Administrative
Sec 4.3.2.2	47	Flexible Maintenance period (3 weeks), Day 15 to Day ~~36~~**35** The following text was added: **Dose reduction will also be allowed during the second week of the Maintenance period in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.**	Administrative
Sec 4.3.3	47	Conversion Phase (10 days), Day 36 to day ~~46~~**45**	Administrative
Sec 4.3.4	48	Taper Phase (10 days), Day 36 to day ~~46~~**45**	Administrative
Sec 5.1	48	The following was changed: The population will be male and female subjects diagnosed with ADHD, ~~comorbid~~**with associated features of IA** and currently being treated with an FDA-approved standard ADHD treatment (psychostimulants and non-stimulants).	To clarify
Sec. 5.1.1	49	The following were changed: 4. Retrospective Modified Overt Aggression Scale (R-MOAS) score of **≥ 20** ~~≥ 24~~ at Screening **and Visit 3**	To increase study enrollment

Section	Page	Description of Change	Rationale
		5. CGI-S score at least moderately ill (≥4) at Screening **and Visit 3.**	
Sec. 5.1.2	49 and 50	The following was changed: 2. **History or ~~C~~c**urrent ~~or lifetime~~ diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia and other psychotic disorders, personality disorder, Tourette's disorder, dissociative disorder, ~~substance abuse disorder~~ or autism spectrum disorder. **14. Use of an investigational drug or participation in an investigational study within 30 days prior Visit 2.**	Administrative
Table 1	51 and 52	The following were changed: • Recording of vital signs was added at each visit. • Urine drug screen was added at each visit. • PK sampling at Visits 4 and 7 were removed. • PK sampling at Visits 5 and 6 were added. • Footnote 'e" was changed: Urine pregnancy test will be performed for **al**l female subjects**. ~~p~~P**rior to the administration of the first dose of SM **subjects** will have to be tested as negative to continue in the study. **If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed.** • Serum pregnancy test was added at Screening for all female subjects and pregnancy test was added at Visit 2. • Footnote "f" was changed: Serum pregnancy test will be performed at ~~Visit 2~~ **Screening for all female subjects.** • Footnote "i" was changed: **PK blood samples will be obtained over two visits.** ~~Visit 4, 6 and 7 the study medication will be taken at the clinic prior the first blood drawn.~~ • Footnote "**l: Optional"** was added • Footnote **"j" was changed: Only the Investigator-rated CGI-S will be completed at**	Procedural

Section	Page	Description of Change	Rationale
		Screening; Caregiver and Investigator-rated CGI-S will be collected at ~~every visit after~~ randomization and every visit thereafter.	
Sec. 5.3.1	53	The following were changed: 11. Collect ~~U~~**u**rine **sample for** drug screen~~,~~ **and** urinalysis ~~and pregnancy test~~. 12. **Collect blood for serum pregnancy test (If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed)** 13. Record vital signs (HR, BP, temperature, and RR) 15. Collect blood samples for **optional** PGx **testing**	Administrative
Sec. 5.3.2	53	The following was changed: ~~Collect blood for serum pregnancy~~ **Collect urine for drug screen and pregnancy test (If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed)**	Procedural
Sec. 5.3.3	54	The following was added: **8. Record vital signs (HR, BP, temperature, and RR)**	Procedural
Sec. 5.3.4	54	The following were added: 3. Collect urine sample for pregnancy test **and drug screen.** ~~4. Collect blood for PK analysis~~ 5. **Record vital signs (HR, BP, temperature, and RR)** The following text was removed. ~~Subject will arrive at the clinic in the morning and will take the first dose of SM at the clinic~~	Procedural
Sec. 5.3.5	55	The following were added: **(Refer to Section 5.3.9 for details regarding timing of the dose of SM prior PK sampling.)** 4. Collect urine sample for pregnancy test **and drug screen.** 6. **Record vital signs (HR, BP, temperature, and RR)**	Procedural

Section	Page	Description of Change	Rationale
		7. **Collect blood for PK analysis**	
Sec. 5.3.6	55	The following text was added: **(Refer to Section 5.3.9 for details regarding timing of the dose of SM prior to PK sampling.)** The following were added: 4. Record vital signs **(HR, BP, temperature, and RR)** 5. Collect urine sample for pregnancy test **and drug screen** The following text was removed. ~~Subject will arrive at the clinic in the morning and will take the first dose of SM at the clinic~~	Procedural
Sec. 5.3.7	56	The following were added: 6. Collect urine sample for urinalysis, ~~and~~ pregnancy test **and drug screen.** 7. **Record vital signs (HR, BP, temperature, and RR)** The following were removed. ~~Subject will arrive at the clinic in the morning and will take the first dose of SM at the clinic~~ ~~Collect blood for PK analysis~~	Procedural
Sec. 5.3.8	56	The following was changed: ~~2. Collect urine for pregnancy test~~ Collect urine for urinalysis**, drug screen and pregnancy test**	Procedural
Sec 5.3.9	57	The following text was changed: [redacted]	Procedural

Section	Page	Description of Change	Rationale
		[redacted]	
Sec. 5.4.1	57	Subjects will take up to (6) six 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 the stable dose of the optimized ADHD medication. **During the conversion phase, subjects will take up to (8) eight molindone hydrochloride extended release tablet (SPN-810) or placebo twice each day (BID).**	To clarify

Section	Page	Description of Change	Rationale
Sec. 5.4.1	57 and 58	The following text was changed. Subjects will remain at the target dose of 36 mg/day or placebo for one week during maintenance. In the second week of maintenance (Visit ~~6~~**5**), the treatment dose could be increased in a blinded fashion to 45 mg (TTD) based on Investigator discretion or maintained at 36mg (TDD) or placebo. In the following week **(Visit 6)**, the Investigator will re-assess the dosage: the subject may remain at 36 mg (TDD) or 45 mg (TDD) or matching placebo (depending on the dosage from the previous week) or titrate up to the higher dose of 45 mg or 54 mg (TDD) or placebo. **At the same Visit, dose reduction will be allowed in consultation with the Medical Monitor and the Sponsor: the Investigator may adjust the dose based upon tolerability.**	To clarify
Sec. 5.4.2	58	The following text was changed The Investigator is not allowed to adjust the FDA-approved ADHD monotherapy **(either IR or ER not both)** medication and/or its dose at any time during the course of this study.	To clarify
Sec. 5.5	61	The following was added: 5. **For the treatment of Akathisia, propranolol is recommended up to 90 mg /day in divided doses, three times per day, starting at 10 mg BID and up to 30 mg TID, as needed.**	To clarify
Sec 6.2	63	The following text was changed Secondary Efficacy ~~Variables~~Endpoints **The secondary efficacy endpoint is the** ~~The effect of SPN-810 on the following scales will be measured as a~~ change from Baseline to the end of the study **where the Baseline is defined as the last observation prior to the first dose, Visit 3. The effect of SPN-810 will be measured on** the following efficacy scales ~~will be~~ administered at visits designated in the Schedule of Visits and Procedures (Table 1).	Administrative

Section	Page	Description of Change	Rationale
Sec. 6.2.3	64	The following was changed: **6.2.3~~2~~ Additional Secondary ~~Variables~~ Efficacy Endpoints**	Administrative
Sec 6.2.3.3	64	The following was changed • ADHD-Combined subscales **(items #1-18)** • **ODD (items #19-26)** ~~the first two subscales are combined~~	Administrative
Sec. 6.3.3.3	66	The following was added: **Pharmacogenomic testing is optional.**	Administrative
Sec 6.4.2.2	68	"…occurrence of AEs will be assessed starting at Visit ~~7~~ **8** of this study (810P503) or Visit 1 in the OLE."	Administrative
Sec. 6.4.3.1	70	The following was changed: All SAEs must be reported to the Drug Safety Contact ~~and DSC~~ within 24 hours of first becoming aware of the SAE.	Administrative
Sec. 6.4.4.4	72	The following was added: **For the treatment of Akathisia, propranolol is recommended up to 90 mg /day in divided doses, three times per day, starting at 10 mg BID and up to 30 mg TID, as needed.**	To clarify
Sec. 6.4.6	73	The following was changed: 	To adjust for PK sampling change
Table 3	74	Table 3 was updated to specify Urine tests Urinalysis: Glucose, protein (total), ketones, bilirubin, urobilinogen, hemoglobin, leucocyte esterase, nitrite Urine: Cocaine, amphetamines, barbiturates, benzodiazepines, cannabinoids, opioids, phencyclidine, propoxyphene, methadone and alcohol Urine Pregnancy tests: hCG	To clarify

Section	Page	Description of Change	Rationale
Sec 6.4.10	75	The following was added: At the following visits (Visit 3-7) any of these behaviors will be recorded on the **electronic IA** diary if they were observed since the patient's last visit.	Administrative
Sec. 8.2	76	The following was added: For the primary efficacy end point, the frequency of IA behaviors during the Treatment Phase will be calculated over the number of days with non-missing IA diary data in the Treatment Phase **(titration + maintenance).**	To clarify
Sec. 8.3	77	The following was changed: Safety Population: will include all subjects ~~screened~~ who received at least 1 dose of study drug **and had at least one post-baseline safety assessment**. Per-Protocol (PP) Population: will include all ~~of the~~ subjects ~~in the FAS~~ who completed the Treatment Phase ~~with 70% diary completion compliance~~ and who did not have major protocol deviations **as defined in the SAP)**.	To clarify
Sec. 8.7	78	The following was added: $\{(D-R)/T*(D_L- D_F)\}*100$ changed to $\{(D-R)/T*(D_L- D_F$**+1**$)\}*100$	To clarify
Sec. 12.10	180	SIPA scale was added	Administrative

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: 810P503	**Phase of Development:** 3
Full Title of Study: Assessment of Efficacy and Safety of SPN-810 for the Treatment of Impulsive Aggression (IA) in Adolescent Subjects with Attention Deficit/Hyperactivity Disorder (ADHD) in Conjunction with Standard ADHD Treatment.	
Investigator(s) / Center(s): Approximately 35-40 US centers	

Objectives:

Primary

Efficacy and safety of SPN-810 treatment in reducing the frequency of impulsive aggression (IA) behaviors in adolescents with ADHD when taken in conjunction with standard ADHD treatment.

Secondary

Key secondary objectives of the study are to assess the effect of SPN-810 on the following:

1. Investigator-rated Clinical Global Impression – Severity Scale (CGI-S)
2. Retrospective Overt Modified Aggression Scale (R-MOAS)
3. Percent of children whose IA behaviors were remitted at the end of the study measured by R-MOAS score ≤ 10.

Additional secondary objectives

These additional secondary objectives are to assess the effect of treating adolescents with SPN-810 on the following:

1. Investigator-rated Clinical Global Impression – Improvement Scale (CGI-I);
2. Caregiver-rated Clinical Global Impression – Improvement Scale (CGI-I);
3. Caregiver-rated Clinical Global Impression – Severity Scale (CGI-S);
4. Inattention, Hyperactivity-Impulsivity and ODD measured by the SNAP-IV;
5. Child's overall health as measured by the Child Health Questionnaire Parent Form 28-item (CHQ-PF28);
6. Parental stress measured by the Stress Index for Parents of Adolescents (SIPA);
7. Safety of SPN-810 in adolescent subjects.

Exploratory

1. Cross-validation of the electronic impulsive aggression (IA) Diary in adolescents;
2. [redacted]
3. Pharmacogenomics (PGx).

Study Design: This is a double-blind, randomized, parallel group, two-arm, placebo-controlled study with flexible dosing (36, 45 or 54 mg/day) of SPN-810. Subjects will be randomized to the two arms in 1:1 ratio of SPN-810 or placebo.

Number of Subjects: Approximately 372 subjects aged 12-17 years (inclusive) will be screened to randomize approximately 186 subjects; 93 in the SPN-810 arm, 93 in the placebo arm.

The sample size for the trial may be revised after the results of the ongoing 810P301 and 810P302 studies become available.

Key Criteria for Inclusion:
Otherwise, healthy non-smoking, male and females adolescents (12-17 years of age at the time of screening) with a primary diagnosis of ADHD and currently taking an optimized FDA-approved ADHD medication. IA will be confirmed at screening using R-MOAS scale and Vitiello Aggression Questionnaire.

Key Criteria for Exclusion:
History or current diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia and other psychotic disorders, personality disorder, Tourette's syndrome or dissociative disorder, autism spectrum disorder, pervasive developmental disorder, obsessive compulsive disorder, post-traumatic stress disorder, or intermittent explosive disorder. Known or suspected intelligence quotient (IQ) <70, active suicidal plan/intent or active suicidal thought, criminal arrest, alcohol or drug use or pregnancy.

Treatment, Dose, and Mode of Administration:
Molindone hydrochloride extended-release tablet dosage forms of 3 mg and 9 mg with matching placebo tablets. Treatment to be administered orally twice daily with or without food. Subjects will be force-titrated over a period of 2 weeks to 36 mg/day.

- Treatment 1: Placebo
- Treatment 2: Flexible dose of SPN-810 titrated to 36 mg, 45 mg, or 54 mg

Duration of Treatment and Study Duration:
Total duration of study: Approximately 13 weeks

- Pre-treatment Phase: Up to 45 days
  - Screening period: Up to 30 days
  - Baseline period: At least 15 days
- Treatment Phase: 36 days
  - Titration period: 2 weeks
  - Maintenance period: 3 weeks

Conversion/taper Phase: 10 days

Pre-Treatment Phase:

Screening and Baseline

Subjects will be screened approximately 45 days before the Treatment Phase. 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 scale and the Vitiello Aggression Questionnaire will be administered to determine the subject's IA eligibility for the study by evaluating the severity and the subtype of aggression, respectively.

Following screening eligible subjects will enter a two-week flexible baseline period, at which time the caregivers will receive the IA diary and will receive training on how to use the diary to identify IA behaviors.

Treatment Phase:

After completing the Baseline period, eligibility criteria will be confirmed: only those subjects who achieve ≥70% compliance in completing the IA diary during Baseline period and have a baseline score of IA behaviors per 7 days ≥ 6 will be randomized. A dose titration schedule will be followed, where dosing will be initiated at [redacted] for all subjects in the active treatment group and will increase approximately every three days in the first two weeks of drug administration until 36 mg/day dose is reached.

All subjects will remain at 36 mg/day during the first week of the Maintenance period. At the following week during maintenance, the Investigator will assess whether to increase the dose to 45 mg/day SPN-810 or placebo, or remain on 36 mg/day of SPN-810 or placebo. A week later, the Investigator will re-assess whether the subject will remain at 36 mg or 45 mg/day or titrate up to the higher dose of 45 mg or 54 mg/day of SPN-810 or placebo. Dose reduction will be allowed during maintenance in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.

After completing the three-week Maintenance period, subjects will enter a taper down period if they decide to discontinue from the study, or will be given the option to convert to an open label extension (OLE) study (810P304). Subjects who choose to participate in the OLE will receive a blinded double-dummy conversion card to down or up-titrate the study medication and matching placebo to enter the study at a dose of 36 mg/day SPN-810.

Endpoints:

Primary Efficacy Endpoint:

The primary efficacy variable will be based on a checklist of 15 IA behaviors collected in an electronic IA diary.

The primary efficacy endpoint is the percent change (PCH_T) in the frequency (unweighted score) of IA behaviors per 7 days in the Treatment Phase (titration + maintenance) relative to the Baseline period calculated over the number of days with non-missing IA diary data.

The primary efficacy endpoint PCH_T will be calculated by $PCH_T = 100*(T – B)/B$, where T and B are IA behavior frequencies per 7 days during the Treatment Phase and Baseline period, respectively. The IA behavior frequency per 7 days is defined as (SUM/DAY) x 7, where SUM is the total of the 15 IA behaviors reported in IA diary, and DAY is the number of days with non-missing IA score in the IA diary during the specified study period.

Key Secondary Efficacy Endpoints:

1. Investigator-rated CGI-S scale
2. R-MOAS rating scale
3. R-MOAS remission rate defined by a score ≤ 10

Additional Secondary Endpoints:

1. Investigator-rated CGI-I scale
2. Caregiver-rated CGI-I scale
3. Caregiver-rated CGI-S scale
4. SNAP-IV rating scale
5. CHQ-PF28 rating scale
6. SIPA rating scale

Additional Secondary Safety and Tolerability Endpoints:

1. Incidence of Adverse Events
2. Incidence of Extrapyramidal Symptoms (EPS) as assessed by Simpson-Angus Scale Barnes Akathisia Scale, Abnormal Involuntary Movement Scale
3. Columbia Suicide Severity Rating Scale (C-SSRS)
4. Laboratory Parameters (Hematology, Chemistry, Urinalysis, Insulin and Prolactin)
5. Vital signs, Standardized BMI, Physical Examination and ECG (12-lead)
6. Infrequent Behaviors Checklist

Exploratory Endpoints:

1. IA Diary Cross-Validation

   The data generated from 810P301 and 810P302 pediatric studies during the diary validation process may be used for cross-validation of the IA Diary in adolescents. If the decision is made to proceed with the analysis, the cross-validation plan and results will be provided in a separate stand-alone report.

2. Population Pharmacokinetics/Pharmacodynamics:

[redacted]

3. Pharmacogenomics (PGx) Testing:

Pharmacogenomic testing is optional. The DNA will be extracted and tested for any genetic variations associated with CYP2D6 enzyme. This enzyme is involved in the metabolism of molindone and genetic variations of the CYP2D6 gene may affect the pharmacokinetics of the drug. Test results in this study will identify the subject's metabolizer phenotype.

Sample size:

Assuming a mean difference of 15 between SPN-810 dose group and placebo with a common standard deviation of 35, a sample of 93 subjects per arm will yield 80 % power to detect a non-zero difference between the median of SPN-810 treatment group and the placebo group using the Wilcoxon rank-sum test with a 2-sided significance level α=0.05.

It is assumed that approximately 20% subjects will dropout before the completion of the study and hence, an adjusted total of 186 subjects will be randomized in a 1:1 ratio to obtain approximately 150 subjects at the completion of the study.

Sample size may be recalculated based on the effect size of the ongoing 810P301 and 810P302 studies.

Analysis Populations:

Safety Population: will include all subjects who received at least 1 dose of study drug and had at least one post-baseline safety assessment.

FAS (Full Analysis Set): include all subjects who received at least 1 dose of study drug and have completed baseline and at least 1 valid post-randomization assessment of frequency of IA behaviors based on IA diary entry.

Per-Protocol (PP) Population: will include all of the subjects who completed the Treatment Phase and did not have major protocol deviations (as defined in the SAP).

PK population: will include all subjects in the safety population who have received at least 1 dose of active study medication and had one PK sample drawn which had quantifiable concentration for molindone.

Efficacy Hypothesis:

Let μ_1, and μ_2 represent the median percent change in the frequency of IA behaviors per 7 days in the Treatment Phase relative to the Baseline period in the FAS population for subjects treated with placebo and SPN-810 treatment, respectively. The null (H_0) and the alternative (H_a) hypotheses are as in the following:

> H_0: $\mu_2 = \mu_1$, [there is no difference between the median of the SPN-810 treatment group and the median of placebo group] vs. H_a: $\mu_2 \neq \mu_1$, [there is a difference between the median of the SPN-810 treatment group and the median of placebo].

Handling Missing Data:

For the efficacy endpoint, the frequency of IA behaviors during the Treatment Phase will be calculated over the number of days with non-missing IA diary data in the Treatment Phase (titration + maintenance).

For subjects who have partial IA diary data during Maintenance period (<7 days with non-missing IA diary data), the IA behaviors from both Titration and partial Maintenance period will be counted together and used for the Maintenance period. For subjects with IA diary data only available during Titration period, the IA behaviors from the Titration period will be used for the Maintenance period.

Statistical Methods:

Summaries for continuous variables will include the sample size, mean, and standard deviation, median, minimum, and maximum. Summaries for discrete variables will include the tabulation of frequencies and percentages.

Analysis of PCH_T will be performed using the Wilcoxon rank-sum test to test the hypothesis of equality of the median of SPN-810 treatment group with the median of the placebo group. The Hodges-Lehmann estimate and the associated 95% confidence interval (CI) will be calculated.

Each of the secondary endpoints will be analyzed using a Mixed-Effect Model for Repeated Measure (MMRM). MMRM assumes missing data as Missing at Random. The model includes treatment, visit, and interaction between treatment and visit as fixed factors, baseline as covariate. The model parameters will be estimated using restricted maximum likelihood method with unstructured variance-covariance matrix and Kenward-Roger approximation to estimate denominator degrees of freedom. The between-group comparison will be performed using the simple contrast at the respective visits.

The least squares mean of the treatment groups, the difference in the least squares mean (SPN-810 minus placebo), and the 2-sided 95% CI for the difference will be obtained.

Safety Monitoring:
An independent and unblinded Data and Safety Committee (DSC) will be established to assess the safety of the subjects participating in the study. An interim safety data analysis will be performed if required to support a registration filing. The DSC will consist of 3 individuals.

Safety Analysis:

Safety analyses will be based on the safety population. All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and preferred term. All AEs with onset date on or after the first dose of double-blind study medication and prior to 7 days after the permanent discontinuation of study medication (onset date – last date of dose <=7) will be summarized using discrete summaries at the subject and event level by system organ class and preferred term for each treatment group. AEs with onset date after Visit 7, will be summarized in the OLE study (810P304) for subjects who decide to enroll in the OLE. Similarly, treatment-emergent AEs will be summarized by severity and relationship separately. Vital signs and all other safety endpoints will be summarized using descriptive statistics by treatment groups. If applicable, categorical laboratory tests will be summarized using number and percent of subjects by treatment groups. Data on infrequent behaviors will be listed.

IA Diary Cross-Validation:

Cross-validation model generated based on the results from the validation of the IA diary in the 810P301 and 810P302 studies may be used to predict and estimate the accuracy of electronic IA diary to measure aggressive behaviors in adolescents.

Pharmacokinetic Analysis:

Bioanalytical Analysis:

[redacted]

Pharmacogenomics (PGx) Analysis:

The DNA will be extracted and tested for any genetic variations associated with CYP2D6 enzyme. The residual DNA will be stored for possible testing of genes involved in the efficacy and possible association with particular adverse events of the drug (e.g., understand the non-responders to treatment and/or individuals who show unusual safety profile). The DNA analysis will not be used for individual genetic characterization and the subject identity will be kept confidential. The PGx report will be a stand-alone document.

TITLE PAGE 1

SUPERNUS PHARMACEUTICALS, INC. PROTOCOL APPROVAL PAGE 3

SUMMARY OF CHANGES 4

CLINICAL PROTOCOL SYNOPSIS 18

LIST OF TABLES AND FIGURES 29

LIST OF ABBREVIATIONS 30

1. ETHICS 32
- **1.1 Institutional Review Boards / Independent Ethics Committees** 32
- **1.2 Ethical Conduct of the Study** 32
- **1.3 Investigators and Study Personnel** 32
- **1.4 Subject Information and Consent/Assent** 33

2. INTRODUCTION 33
- **2.1 Background** 33
- **2.2 Impulsive Aggression Comorbid with ADHD** 34
- **2.3 Current Treatment Options** 35
- **2.4 Sponsor's Phase 2 Studies** 36
- **2.5 Sponsor's Phase 3 Studies** 38
- **2.6 IA Diary** 38
- **2.7 Study Rationale** 38

3. STUDY OBJECTIVES 39
- **3.1 Primary Objective** 39
- **3.2 Secondary Objectives** 39
- **3.3 Exploratory Objectives** 40

4. INVESTIGATIONAL PLAN 40
- **4.1 Rationale for Study Design and Appropriateness of Measurements** 40
- **4.2 Overall Study Design and Plan** 41

4.3 Duration of Study Treatment 42
4.3.1 Pre-Treatment Phase 46
4.3.2 Treatment Phase: (2-5 weeks) 47
4.3.3 Conversion Phase (10 days), Day 36 to day 45 47
4.3.4 Taper Phase (10 days), Day 36 to day 45 48
4.3.5 End of the Study (EOS)/Early Termination, Day 46 48
4.3.6 Early Termination 48

5. STUDY METHODS 48
5.1 Selection of Study Population 48
5.1.1 Inclusion Criteria 48
5.1.2 Exclusion Criteria 49
5.2 Schedule of Visits and Procedures 50
5.3 Study Procedures 53
5.3.1 Screening/ Visit 1 (Day -45) 53
5.3.2 Baseline/ Visit 2, Day -15 53
5.3.3 Visit 3, Day 1 54
5.3.4 Visit 4, Day 15 54
5.3.5 Visit 5, Day 22 55
5.3.6 Visit 6, Day 29 55
5.3.7 Visit 7, Day 36 56
5.3.8 Visit 8/ End of the Study, Day 46 56
5.3.9 Pharmacokinetic Blood Sampling 57
5.4 Treatments 57
5.4.1 Treatment Administered 57
5.4.2 ADHD medication 58
5.4.3 Identity of Investigational Product(s) 58
5.4.4 Study Medication Handling and Accountability 58
5.4.5 Methods of Assigning Subjects to Treatment Group 59
5.4.6 Treatment Replacement 59
5.4.7 Dosing Schedule 59
5.4.8 Method of Administration 60
5.4.9 Blinding 60
5.5 Allowed Concomitant Medications 61
5.6 Prohibited Medications 61
5.7 Completion of Study and Discontinuation of Subjects 61

6. STUDY ENDPOINTS 62
6.1 Primary Efficacy Endpoint 62
6.1.1 Primary Efficacy Variable 62
6.2 Secondary Efficacy Endpoints 63

6.2.1 Investigator-Rated Clinical Global Severity of Illness Scale (CGI-S) 63
6.2.2 Retrospective-Modified Overt Aggression Scale (R-MOAS) 63
6.2.3 Additional Secondary Efficacy Endpoints 64
6.3 Exploratory Endpoints 65
6.3.1 IA Diary Cross-Validation 65
6.3.2 Pharmacokinetic Measurements 65
6.3.3 Pharmacogenomics (PGx Testing) 66
6.4 Safety and Tolerability Endpoints 66
6.4.1 Data Safety Committee (DSC) 67
6.4.2 Adverse Events 67
6.4.3 Serious Adverse Events (SAE) 69
6.4.4 Assessment of Neurological Side Effects and EPS 72
6.4.5 Columbia Suicide Severity Rating Scale (C-SSRS) 72
6.4.6 Laboratory Measurements 73
6.4.7 Vital Signs and Weight Measurements 74
6.4.8 Medical History and Physical Examinations 74
6.4.9 Electrocardiograms (ECGs) 74
6.4.10 Infrequent Behaviors Checklist 75

7. OTHER SPECIAL TESTS 75
7.1 MINI-KID 75
7.2 Vitiello Aggression Questionnaire 75

8. STATISTICAL METHODS 76
8.1 Statistical and Analytical Plans 76
8.2 Handling Missing Data 76
8.3 Analysis Populations 77
8.4 Demographics 77
8.5 Subject Disposition 77
8.6 Protocol Deviations 78
8.7 Study Medication Exposure and Compliance 78

9. EFFICACY ANALYSES 79
9.1 Primary Efficacy Analysis 79
9.2 Secondary Efficacy Analyses 79
9.2.1 Key secondary endpoints are: 79
9.2.2 Additional secondary endpoints: 80
9.2.3 Sensitivity Analysis 81
9.3 Sample Size and Power Consideration 82
9.4 Exploratory Analyses 82

9.4.1 IA Diary Cross Validation 82
9.4.2 Pharmacokinetic 82
9.4.3 Pharmacogenomic (PGx) 83
9.5 Safety Analysis 83
9.5.1 Adverse Events 83
9.5.2 C-SSRS 84
9.5.3 Extrapyramidal Signs 84
9.5.4 Laboratory Values 84
9.5.5 Vital Signs, Height, Weight and BMI 84
9.5.6 ECG Results 84
9.5.7 Physical Examinations 85
9.5.8 Infrequent Behaviors Checklist 85

10. PROCEDURES AND INSTRUCTIONS 85
10.1 Adherence to the Protocol 85
10.2 Changes to the Protocol 85
10.3 Protocol Deviations 86
10.4 Data Quality Assurance 86
10.4.1 Data Collection 86
10.4.2 Clinical Data Management 87
10.4.3 Database Quality Assurance 87
10.5 Retention of Records 87
10.6 Auditing Procedures 88
10.7 Publication of Results 88
10.8 Financing and Insurance 89
10.9 Disclosure and Confidentiality 89
10.10 Discontinuation of Study 89

11. REFERENCE LIST 89

12. APPENDICES 94
12.1 Retrospective-Modified Overt Aggression Scale (R-MOAS) 94
12.2 Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) 96
12.3 Clinical Global Impression (CGI) Scale 154

12.4 Columbia-Suicide Severity Rating Scales (C-SSRS) 155
12.4.1 C-SSRS, Lifetime/Recent 155
12.4.2 C-SSRS, Since Last Visit 158
12.5 Simpson-Angus Scale 161
12.6 Barnes Akathisia Rating Scale (BARS) 165

12.7 Abnormal Involuntary Movement Scale (AIMS) 167
12.8 Swanson, Nolan, Pelham Rating Scale-Revised (SNAP-IV)..... 171
12.9 Child Health Questionnaire Parent Form 28-item (CHQ-PF28) 172
12.10 Stress Index for Parents of Adolescents (SIPA) 180

LIST OF TABLES AND FIGURES

Table 1 Schedule of Visits and Procedures..... 51
Table 2 Titration Dosing Schedule..... 60
Table 3 Clinical Laboratory Tests..... 74

Figure 1 Schematic of Conversion to Open Label Study 44
Figure 2 Schematic of Tapering for Subjects who Discontinue 45

LIST OF ABBREVIATIONS

ADHD	Attention-Deficit Hyperactivity Disorder
ADR	Adverse Drug Reaction
AE	Adverse Event
AIMS	Abnormal Involuntary Movement Scale
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BARS	Barnes Akathisia Rating Scale
BID	Twice a Day
BMI	Body Mass Index
BP	Blood Pressure
CFR	Code of Federal Regulations
CGI-S	Clinical Global Impression – Severity of Illness
CGI-I	Clinical Global Impression – Global Improvement
CHQ-PF28	Child Health Questionnaire Parent Form 28 item
CK	Creatine Kinase
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
C-SSRS	Columbia Suicide Severity Rating Scale
DSC	Data Safety Committee
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eOBsRO	Electronic Observer-Reported Outcome
EOS	End of Study
EPS	Extrapyramidal Symptoms
ER	Extended Release
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transpeptidase
HCT	Hematocrit
HDL	High Density Lipoprotein
Hgb	Hemoglobin
HR	Heart Rate
IA	Impulsive Aggression
IAF	Informed Assent Form
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee

IR	Immediate Release
IRB	Institutional Review Board
[redacted]	[redacted]
LAR	Legal Authorized Representative
LDL	Low Density Lipoprotein
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MedDRA	Medical Dictionary for Regulatory Activities
MINI-KID	Mini International Neuropsychiatric Interview for Children and Adolescents
MTA	Multimodal Treatment of Children with ADHD
ODD	Oppositional Defiant Disorder
OLE	Open Label Extension
RBC	Red Blood Cells
R-MOAS	Retrospective Modified Overt Aggression Scale
RR	Respiratory Rate
SADR	Suspected Adverse Drug Reaction
SAE	Serious Adverse Event
SIPA	Stress Index for Parents of Adolescents
SM	Study Medication
SNAP-IV	Swanson, Nolan and Pelham-IV
SOP	Standard Operating Protocol
TEAE	Treatment Emergent Adverse Event
TEOSS	Treatment of Early-Onset Schizophrenia Spectrum Disorders Study
TID	Three Times a Day
TOSCA	Treatment of Severe Childhood Aggression
WBC	White Blood Cells

1. ETHICS

1.1 Institutional Review Boards / Independent Ethics Committees

A list of the Institutional Review Board(s) (IRB) and/or Independent Ethics Committee(s) (IEC) that approved this study 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 before subjects are enrolled. IRB Approval is required and will be acquired prior to the distributing SM to investigational sites. The Investigators or Sponsor will submit, depending on local regulations, periodic reports and inform the IRB of any reportable adverse events (AEs) per International Conference on Harmonization (ICH) guidelines and local IRB standards of practice.

1.2 Ethical Conduct of the Study

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

- 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.

1.3 Investigators and Study Personnel

This study will be conducted by qualified Investigators under the sponsorship of Supernus Pharmaceuticals, Inc. (Sponsor) at US 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 Sponsor. The Sponsor will oversee and review the monitoring activities for the study. 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.

1.4 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 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 consent/assent form and the original will be retained in the investigational site study records.

All 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 consent form. All ongoing subjects must be reconsented per the IRB guidelines. All versions of the signed consent forms (including reconsents) must be retained by the sites.

2. INTRODUCTION

2.1 Background

Aggression refers to a behavior that can result in both physical and psychological harm to oneself, others or objects in the environment. Aggression is manifested verbally, mentally, and physically. Such behavior becomes maladaptive when it persists, occurs outside an acceptable social context, and is of an intensity, frequency, severity and/or duration detrimental to the child's interests (Jensen, et al., 2007; Connor & McLauglin, 2006).

Aggression can be categorized into two broad subtypes based on the aggressor's motivation – 1) reactive or impulsive and 2) proactive or instrumental (Vitiello & Stoff, 1997). Impulsive aggression (IA) is angry, retaliatory aggression arising out of frustration, annoyance, or hostility

triggered by real or perceived provocations – stressors that non-affected youth of the same age can typically control in a more socially acceptable manner. IA is an unplanned, immediate response and an out-of-control emotional state, reflecting the inability to contain rage in response to apparent threat that usually does not lead to a secondary benefit. In contrast, instrumental aggression is consciously planned, goal-oriented behavior with the specific intent of benefiting the aggressor, a planned act, used for personal gain (Jensen, et al., 2007). IA is then a behavior that implies an immediate action without thinking: this type of impulsivity seems to nurture internalizing behaviors leading to depression and anxiety due to poor parent-child interaction, peer rejection or sensitivity to stress.

2.2 Impulsive Aggression Comorbid with ADHD

ADHD is the most prevalent neurological disorder in youth with a parent-reported prevalence of 6.8-10.2% in children and adolescents (Visser, et al., 2010; Visser, et al., 2014). IA is a common feature in the clinical presentation of ADHD patients and has a much greater impact on parents' overall impairment ratings than the core ADHD symptoms themselves. Among participants of the Multimodal Treatment of Children with ADHD (MTA) study, 54% of subjects with ADHD exhibited clinically significant aggression at baseline (Jensen, et al., 2007). IA amplifies the psychological, academic, emotional, and social problems associated with ADHD (Shelton, et al., 1998), markedly increasing the risk of persistent behavioral problems, conduct disorder, encounters with the justice system, deficits in academic achievement, behavioral and disciplinary problems at school, and substance experimentation/abuse. In adolescents, reactive aggression is strongly correlated with anxiety and ADHD problems. (Smeets, et al., 2017).

Prospective longitudinal studies have established that consequences of childhood ADHD persist through adolescence. In younger adolescents, low or moderate levels of IA are considered normal as coping skills are not fully developed yet at younger age. However, in pediatric ADHD patients, IA may become more persistent and severe at older age (Smeets, et al., 2017). Pervasive IA in children, which is characterized by impulsive thoughts, emotional lability, and impulsive behavior is thought to represent a high-risk profile for progression from childhood ADHD to adult antisocial disorders (McKay & Halperin, 2001). Physical and emotional changes occur while transitioning from childhood to adolescence. A lack of self-regulation during this period adversely affects these changes and results in low self-esteem and sociability in adolescents with ADHD. While inattention and impaired executive functions mostly impact academic achievement, impulsivity affects the non-academic aspects of functionality that may lead to development of oppositional defiant disorder (ODD), drug experimentation, speeding while driving, risky sexual behavior, impulsive verbal behaviors and reactive aggression (Wehmeier, et al., 2010). Adolescents are at higher risks for more severe reactive aggression at older age hence, treatment is needed to prevent the progression of unwanted behaviors.

Children and adolescents are an especially vulnerable population that bear the brunt of ADHD-related morbidity, and may therefore benefit from the addition of a drug specifically targeting residual aggressive behaviors refractory to primary ADHD therapy. A stepped-care approach with aggression-targeted therapy, such as an antipsychotic added to ADHD therapy has been recommended to treat residual aggressive behaviors (Scotto-Rosato, et al., 2012). IA represents a serious clinical and public health concern and requires effective and timely intervention (Saylor & Amann, 2016). For these reasons, it is important to understand and characterize IA behaviors and to assess the response to medication in adolescents with ADHD for an effective treatment.

2.3 Current Treatment Options

Based largely on the beneficial effects of risperidone on disruptive behavior disorders in children of sub-average intelligence, antipsychotics are used as adjunctive therapy for treating aggression in children with ADHD (Pappadopulos, et al., 2003; Pliszka, 2007; Pliszka, et al., 2006). The TOSCA (Treatment of Severe Childhood Aggression) study has provided empirical evidence to support a stepped-care approach in which children with ADHD and severe aggression are initially treated with primary ADHD therapy followed by adjunctive antipsychotic therapy targeting residual aggressive behaviors (Farmer, et al., 2011; Aman, et al., 2014; Gadow, et al., 2014). However, risperidone had only a limited impact on aggression in the TOSCA study even though the dosage was flexible for optimal effect. Moreover, the TOSCA study confirmed that stimulant co-therapy does not attenuate the long-term effects of risperidone or similar agents on body composition, metabolic parameters, prolactin, or sedation (Penzner, et al., 2009; Calarge, et al., 2009). Use of the antipsychotics olanzapine, quetiapine, risperidone, and aripiprazole in children were all associated with significant increase in weight and BMI (8.5 kg/3.01 kg/m^2, 6.1 kg/2.12 kg/m^2, 5.3 kg/1.92 kg/m^2, and 4.4 kg/1.67 kg/m^2, respectively) (Correll, et al., 2009). Olanzapine and quetiapine also produced significant increases in multiple metabolic parameters and risperidone significantly increased triglyceride levels.

Molindone hydrochloride is a first-generation mid-potency compound for which the Sponsor has developed an extended release (ER) formulation (SPN-810), administered orally for the treatment of IA in children with ADHD. The immediate-release molindone (Moban®) was approved in 1974 for the management of schizophrenia in adults and adolescents but was discontinued due to commercial reasons by the original manufacturer. Its effects relative to the second-generation antipsychotics (olanzapine and risperidone) were evaluated in a pediatric population with early-onset schizophrenia and schizoaffective disorder in the Treatment of Early-Onset Schizophrenia Spectrum Disorders Study (TEOSS) (McClellan, et al., 2007). Molindone was selected as the first generation antipsychotic based on its favorable safety profile in comparison with the second generation agents. At the average dose of 60 mg/day molindone was shown to be safe and well tolerated (Sikich, et al., 2008). Molindone was not associated with significant increases in weight/BMI in contrast to olanzapine.

Molindone has been shown to be effective in treating aggressive behavior in children with undersocialized conduct disorder, aggressive type, in an open label and a double-blind study (Greenhill, et al., 1981; Greenhill, et al., 1985).

Results of randomized controlled trials such as TEOSS and other studies has stimulated interest in the potential usefulness of molindone as a weight- and metabolically-neutral D2-receptor antagonist in children with ADHD and comorbid IA. The overall clinical profile of molindone in children makes it an attractive candidate for the treatment of IA in children and adolescents with ADHD, especially with the anticipated benefits of an ER formulation.

2.4 Sponsor's Phase 2 Studies

Study 810P201 was a proof-of-concept, open label, parallel-group, randomized, dose-ranging, safety and tolerability study using the investigational immediate-release (IR) formulation of molindone (Molindone IR) dosed three times a day (TID) in children with ADHD and persistent serious conduct problems (Stocks, et al., 2012). Target subjects were healthy male or female children aged 6 to 12 years, with a diagnosis of ADHD accompanied by persistent serious conduct problems. A total of 78 subjects (19-20 per treatment group) in ten U.S sites were randomized. The primary objective was to evaluate the safety and tolerability of four weight-based dosages of Molindone IR dosed three times daily in children with ADHD and persistent serious conduct problems [redacted]). The secondary objectives were to 1) explore the relationship between molindone plasma concentration exposure and safety/tolerability endpoints and 2) assess the effect of Molindone IR after 6 weeks of maintenance treatment in reducing persistent serious conduct problems as measured by the Conduct Problem Subscale of the Nisonger Child Behavior Rating Form-Typical Intelligence Quotient (NCBRF-TIQ).

[redacted]

Study 810P202 was a Phase 2b multicenter, randomized, double-blind, placebo-controlled trial in a pediatric population of subjects 6-12 years of age diagnosed with ADHD and IA that was not controlled by optimal stimulant and behavioral therapy (Study 810P202, 2013). The primary objective of the study was to assess the effect of an extended-release (ER) tablet formulation of molindone hydrochloride (SPN-810) (12 to 54 mg/day) in reducing IA as measured by the Retrospective-Modified Overt Aggression Scale (R-MOAS) after at least three weeks of assigned treatment. Secondary endpoints included the rate of remission of IA and measurement of the effectiveness of SPN-810 on Clinical Global Impression (CGI) and ADHD scales as well as evaluation of the safety and tolerability of the drug. Patients who completed the study could continue into an open-label phase of six months duration.

SPN-810 dose within treatment groups was stratified by weight (below/above 30 kg). Both the Medium (24/36 mg) and Low (12/18 mg) dose groups showed a statistically significant difference from the Placebo group in the change from baseline to final visit (Visit 10) in R-MOAS but the High (36/54 mg) dose group was not significantly different from the Placebo group.

SPN-810 ER formulation exhibited a satisfactory safety and tolerability profile, with low incidence of AEs and no unexpected, life threatening or dose-limiting safety issues. The adverse events (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 events was relatively low, as were discontinuations due to AEs. The frequency of AEs associated with extrapyramidal symptoms (EPS) was also low and the two serious adverse events that occurred were not drug-related.

Other study results further supported a beneficial treatment effect on IA behaviors. The CGI results (Severity and Improvement) were consistent with the findings for the R-MOAS; notable improvement occurred primarily in the Low dose and Medium dose groups. Scores for Swanson, Nolan and Pelham Questionnaire (SNAP-IV) Hyperactivity and Impulsivity did not exhibit statistically significant differences across groups. Numeral trends in SNAP-IV Oppositional Defiant Disorder (ODD) scores, while not always significant, consistently favored the Low dose and Medium dose groups over Placebo.

Study 810P203 was a multicenter open label extension (OLE) to the Phase 2b trial in a pediatric population of subjects 6-12 years of age diagnosed with ADHD and IA (Study 810P203, 2013). The starting dose for this open-label extension study was based on subjects' weight at the end of 810P202. Subjects were initiated at doses of 18 and 36 mg/day, in children weighing less than 30 kg, and more than 30 kg, respectively. The dose was gradually adjusted based on tolerability or effectiveness, regardless of weight group to 9 mg/day, 18 mg/day, 27 mg/day or 36 mg/day. Of the 121 subjects randomized into the double blind Study 810P202, 78 subjects continued on to the OLE study and received SPN-810 for up to 6 months.

[redacted]

2.5 Sponsor's Phase 3 Studies

The Sponsor is conducting three Phase 3 multicenter studies, of which two are randomized, double-blind, placebo-controlled trials in pediatric population (810P301 and 810P302) and one is an open-label extension (OLE) study, 810P304. After completing the 810P301 or 810P302 studies, subjects will have the option to enroll in the 810P304 study that is designed to assess long-term safety and tolerability of SPN-810.

The primary objective of 810P301 and 810P302 is to assess the efficacy and safety of SPN-810 in reducing the frequency of IA behaviors in children 6 to 12 years of age with ADHD and associated features of IA when taken in conjunction with standard ADHD treatment. In these two studies, the percent change in the frequency of 15 identified IA behaviors per 7 days during the treatment, is measured using and electronic diary that was developed by the Sponsor to characterize the nature of impulsive aggressive behaviors in children (6-12 years old) with a confirmed diagnosis of ADHD.

2.6 IA Diary

From 2013 to 2015, Endpoint Outcomes (EO) in partnership with [redacted] developed a new impulsive aggression diary (IA diary). The IA diary is an electronic observer-reported outcome (eObsRO) instrument that is comprised of an episodic diary (to be reported as soon as possible after the parent or other guardian or observer witnesses the child's IA behavior) and an evening diary (to enable at a minimum, completion of the diary once each day). The development of this diary was as per FDA's "Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims" (US FDA, 2009).

Psychometric testing of the electronic diary was conducted in parents of children aged 6 to 12 years with a primary diagnosis of ADHD (Sponsor Study 810P501, 2015) to establish the validity and reliability of the IA diary. The results indicate that 15 items of the original diary (30 items) best describe IA and demonstrate sufficient reporting prevalence at baseline and across all diaries exhibiting acceptable psychometric properties. The following 15 items are: Yelling, Screaming, Threatening, Scratching, Throwing, Slamming, Hitting Self, Arguing, Cursing, Name Calling, Shoving, Hair Pulling, Fighting, Hitting Others, and Kicking Others. Hence, the IA diary is currently used for the first time in the pediatric studies (810P301 and 810P302) to monitor the frequency of these 15-items in children 6-12 years old with a primary diagnosis of ADHD.

2.7 Study Rationale

Supernus was interested in expanding the potential age range of the subjects in future trials of SPN-810 and has conducted a preliminary concept elicitation and cognitive interviews, using

the original IA diary (15 items) in an adolescent (13-17 years old) population (Sponsor Study 810P502, 2016). The results from the study found the concepts that are present in the 15-item IA diary developed for children as relevant in the older population (i.e., Yelling, Arguing, Cursing, Name Calling, Threatening, Shoving/Pushing, Fighting, Throwing, Slamming, and Hitting were each reported by >60% of the subjects). Two items in the IA diary were not endorsed as frequently (Scratching and Pulling Hair) and were each reported by <25% of the population. The low reporting of these two behaviors may suggest them as outlier concepts in a sample of mostly boys who tend to have shorter hair and/or nails than girls, and therefore less likely to pull hair or scratch in the context of fighting. Even though these concepts were reported less frequently than other concepts, keeping these items in the current 15-item IA diary may help to comprehensively cover and adequately characterize the IA experience in girls.

This research finding supports the content validity of the 15-item IA diary developed for children 6-12 years old as an adequate measure IA behaviors that can be applied to an older population (13-17 years old). Furthermore, the results suggested the appropriateness of a common parent/caregiver reported eObsRO diary for children and adolescents diagnosed with ADHD and exhibiting significant IA behaviors.

3. STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of this study is to assess the efficacy and safety of flexible doses of SPN-810 (36 to 54 mg/day) in the improvement of IA behaviors in adolescents diagnosed with ADHD when taken in conjunction with standard ADHD treatment.

3.2 Secondary Objectives

The key secondary objectives of this study are to assess the effect of SPN-810 on the following scales:

1. Investigator-rated Clinical Global Impression – Severity Scale (CGI-S);
2. Retrospective Overt Modified Aggression Scale (R-MOAS);
3. Percent of children whose IA behaviors were remitted at the end of the study measured by R-MOAS score ≤ 10.

Additional secondary objectives are to assess the effect of treating adolescents with SPN-810 on the following:

1. Investigator- rated Clinical Global Impression – Improvement Scale (CGI-I);
2. Caregiver-rated CGI-I Scale;
3. Caregiver-rated Clinical Global Impression – Severity Scale (CGI-S);
4. Inattention, Hyperactivity-Impulsivity and ODD measured by the SNAP-IV rating scale;
5. Child Health Questionnaire Parent Form 28-item (CHQ-PF28);

6. Stress Index for Parents of Adolescents (SIPA);
7. Safety monitoring.
    a. Incidence of Adverse Events
    b. Incidence of Extrapyramidal Symptoms (EPS) as assessed by Simpson-Angus Scale Barnes Akathisia Scale, Abnormal Involuntary Movement Scale
    c. Columbia Suicide Severity Rating Scale (C-SSRS)
    d. Laboratory Parameters (Hematology, Chemistry, Urinalysis, Insulin and Prolactin)
    e. Vital signs, Standardized BMI, Physical Examination and ECG (12-lead)
    f. Infrequent Behaviors Checklist

3.3 Exploratory Objectives

The following objectives will also be evaluated; the report from each results analysis will be a stand-alone document:

1. A cross-validation of the electronic IA diary will be conducted using the parameters obtained from the psychometric validation in the two pediatric Phase 3 studies (810P301 and 810P302) to assess the minimal clinically important changes (MCIC) in this population;
2. [redacted]
3. Pharmacogenomics (PGx) of molindone.

4. INVESTIGATIONAL PLAN

4.1 Rationale for Study Design and Appropriateness of Measurements

The study is designed to assess the efficacy and safety of an extended release oral formulation of molindone as a treatment for reducing impulsive aggression in adolescents with ADHD when given in conjunction with each subject standard prescribed ADHD medication.

The IA diary will serve as the primary assessment tool to measure the improvement in the frequency of the IA behaviors as it is used in the Phase 3 studies (810P301 and 810P302) in pediatric population. The content validity of the 15-item IA diary as an adequate measure of IA behaviors for older children (13-17 years old) was confirmed by the concept elicitation interviews study (Sponsor Study 810P502, 2016) conducted in adolescents (13-17 years of age) suggesting that the 15-item IA diary developed for children (i.e., Yelling, Screaming, Threatening, Scratching, Throwing, Slamming, Hitting Self, Arguing, Cursing, Name Calling, Shoving, Hair Pulling, Fighting, Hitting Others and Kicking Others) may also be used as an appropriate instrument to assess the frequency of the IA behaviors in adolescents with ADHD.

Key secondary measures of efficacy of SPN-810 will include the Clinical Global Impression - Severity Scale (CGI-S) scores completed by the Investigator, R-MOAS score and the percent of adolescents whose IA behaviors were remitted at the end of study (R-MOAS score ≤ 10). Additional secondary measures include the Investigator and Caregiver-rated Clinical Global Impression- Improvement Scale (CGI-I) scores, the Caregiver-rated Clinical Global Impression - Severity Scale (CGI-S) score, the inattention, hyperactivity-impulsivity and ODD measured by the SNAP-IV, the treatment effect of the child's overall heath as measured by the Child Heath Questionnaire Parent Form 28-item (CHQ-PF28), and parental and child stress measured by the Stress Index for Parents of Adolescents (SIPA).

Besides routine safety monitoring, incidence of extrapyramidal symptoms will be assessed by special scales, i.e., Simpson-Angus Scale, the Barnes Akathisia Scale, and the Abnormal Involuntary Movement Scale (AIMS). Suicidal thoughts and ideation will be assessed by the Columbia Suicide Severity Rating Scale (C-SSRS).

A list of 15 behaviors such as Teasing, Spitting, Biting, Weapons, Ripping, Breaking, Vandalizing, Destroying, Fire Setting, Hitting Animal, Kicking self, Kicking Animal, Severe Injury Self, Severe Injury Others and Severe Injury Animal, were considered infrequent in the qualitative study conducted during the IA diary development (Sponsor Study 810501, 2015). The incidence of these infrequent IA behaviors will be assessed on paper at Visit 2 and using the checklist in the electronic IA diary from Visit 3 to Visit 7.

As an exploratory measure, this study will also permit us to psychometrically cross-validate, if needed, the IA diary as a tool to measure IA behaviors in subjects aged 12 to 17 years with ADHD and comorbid IA.

Additional exploratory analyses include the pharmacokinetic/pharmacodynamics and pharmacogenomics of molindone.

4.2 Overall Study Design and Plan

The study is a randomized, double-blind, multicenter, placebo-controlled, flexible-dose (36, 45 or 54 mg/day), 2-arm, (1:1) parallel group study to evaluate the safety and efficacy of SPN-810 (molindone extended release tablets) for reducing impulsive aggression in adolescents (12-17 years of age) with ADHD as an adjunctive treatment to an approved ADHD medication.

The study will consist of 3 phases: (1) Pre-Treatment Phase, (2) Treatment Phase and (3) Conversion/Taper Phase (Figure 1).

Following Screening, eligible subjects will enter a flexible Baseline period, during which the subject's primary caregiver (or secondary if assigned) will use the IA diary to record daily the occurrence of IA behaviors.

After the completion of the Baseline period, at Visit 3 eligibility criteria will be re-confirmed: only subjects who achieve ≥ 70% in the completion of the IA diary during baseline, with a threshold of ≥ 6 IA behaviors per 7 days observed during the flexible Baseline period, will be randomized in a 1:1 ratio to the SPN-810 group (n=93) or placebo group (n=93).

Subsequently, the randomized subjects will follow a dose titration schedule as shown in (Figure 1). The titration will consist of dosing starting at [redacted] and increasing approximately every 3 days until the target dose of 36 mg/day is reached within 2 weeks. This will be followed by a flexible three-week Maintenance period during which the Investigator will have the option to gradually increase the total daily dose (TDD) of SPN-810.

During the first week of the Maintenance period, all subjects will remain at 36 mg/day. After the first week of maintenance, the Investigator will assess whether to increase the dose to 45 mg/day SPN-810 or placebo, or remain on 36 mg/day of SPN-810 or placebo. In the following week, the Investigator will re-assess the dosage: the subject may remain at 36 mg/day or 45 mg/day or matching placebo (depending on the dosage from the previous week) or titrate up to the higher dose of 45 mg/day or 54 mg/day of SPN-810 or placebo, respectively. Dose reduction will be allowed during maintenance in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.

At the end of the Maintenance period, all subjects who complete the study will have the option to participate in an OLE study (Study Protocol 810P304) in which all subjects will receive active SM treatment. Subjects choosing to participate will receive a blinded double-dummy conversion medication card which will adjust the subject's TDD to 36 mg for initiation into the open label extension study (Figure 1). Those subjects who do not elect to participate in this extension will be tapered down prior to discontinuation of SM (Figure 2).

A subject who discontinues early in the Maintenance period, i.e., prior to Visit 7 may be allowed to participate in the OLE on a case-by-case basis after consultation between the Investigator, Medical Monitor, and the Sponsor.

[redacted]

4.3 Duration of Study Treatment

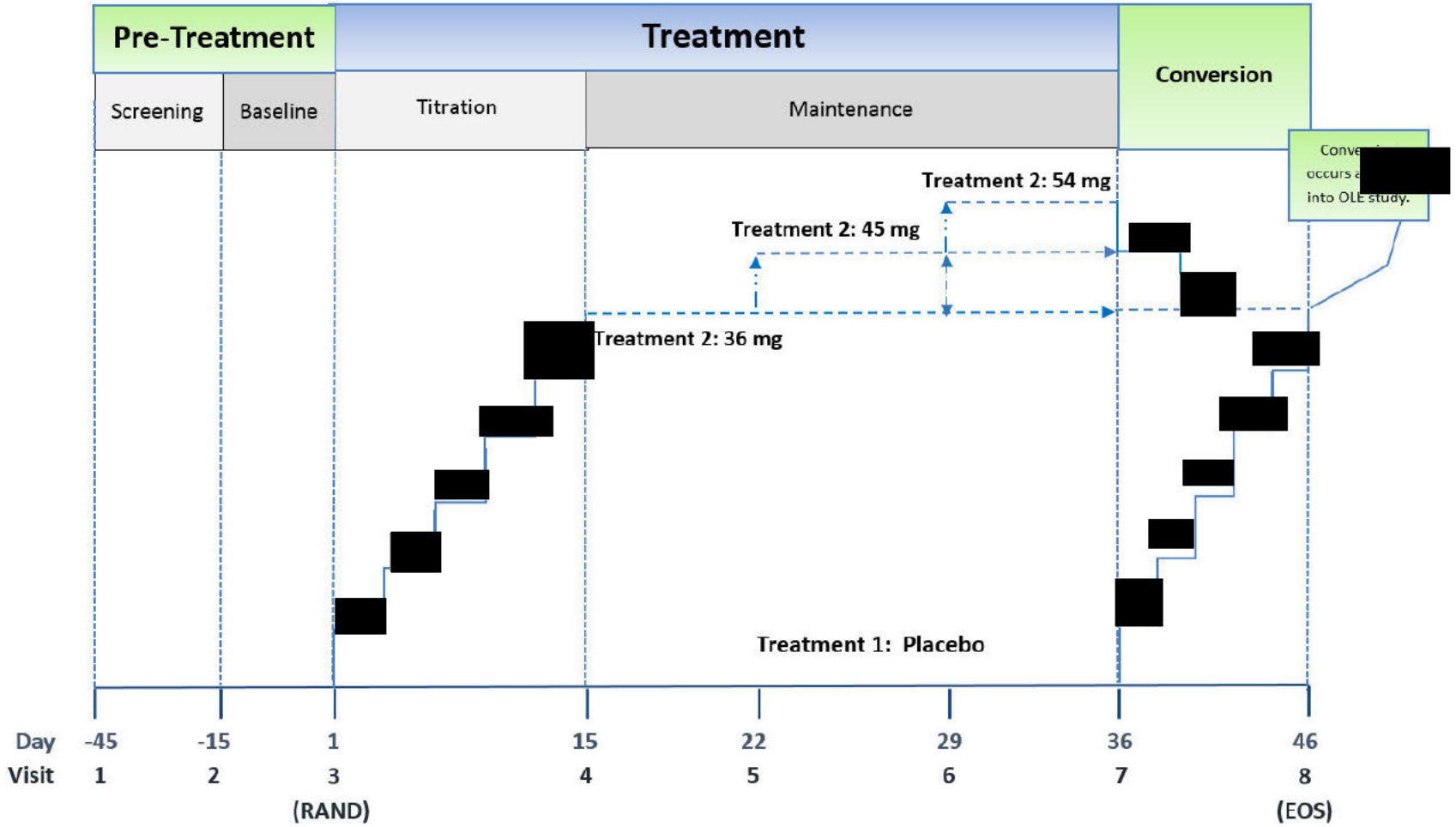
Total duration of study: Approximately 13 weeks

- Pre-treatment Phase: Up to 45 days
  - Screening period: Up to 30 days
  - Baseline period: At least 15 days
- Treatment Phase: 36 days

- Titration period: 2 weeks
- Maintenance period: 3 weeks

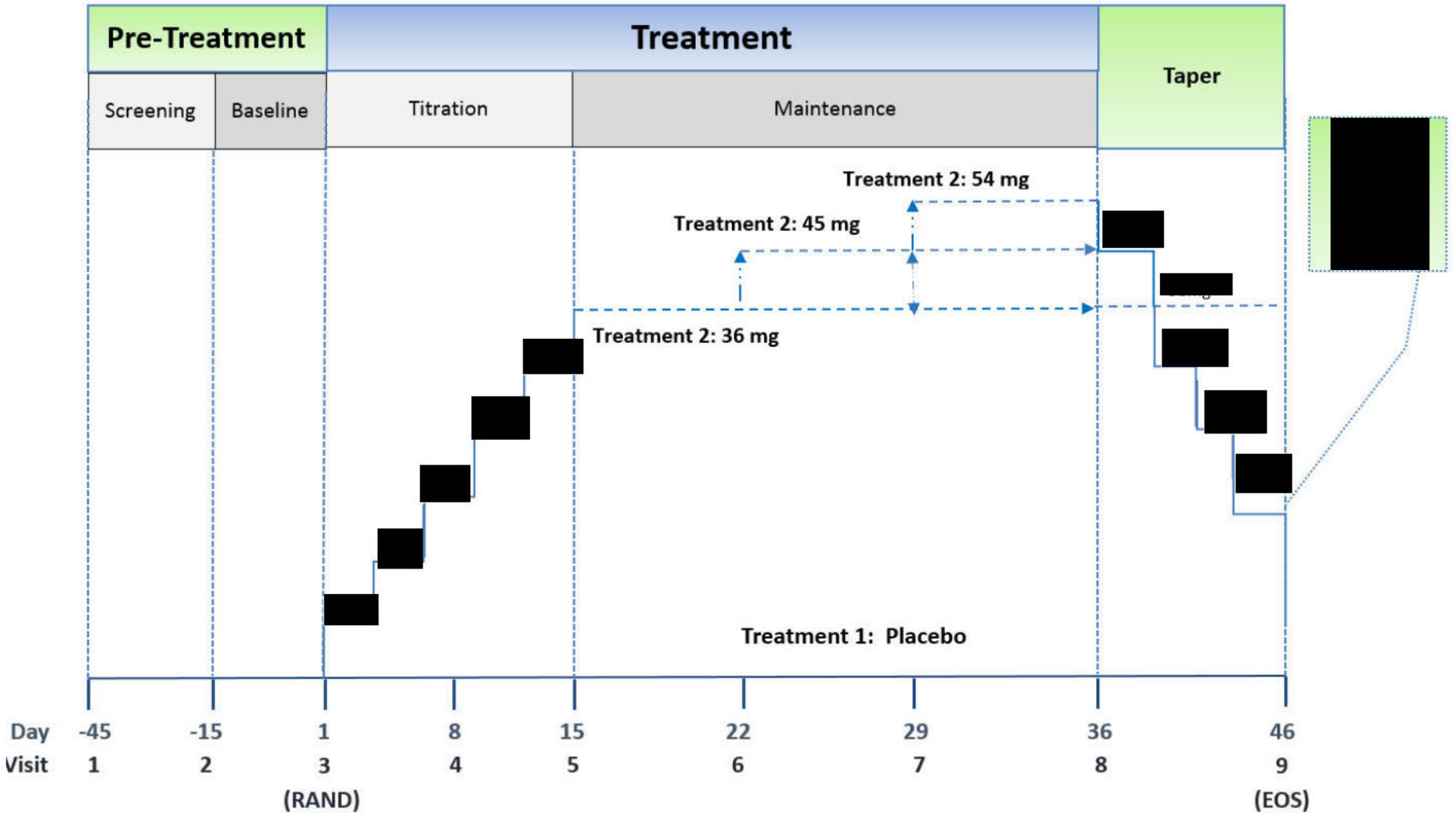
- Conversion/Taper Phase: 10 days

Figure 1 Schematic of Conversion to Open Label Study



1. A blinded double-dummy conversion card will be distributed to down or up-titrate the study medication and matching placebo.

Figure 2 Schematic of Tapering for Subjects who Discontinue



4.3.1 Pre-Treatment Phase

4.3.1.1 Screening Period

Screening procedures will be conducted within 45 days prior to subject randomization (Visit 3) and may be carried out over more than one visit if needed. Prior to conducting any study related procedures, a written informed consent/assent must be obtained from the parent or legal representative, and subject (when required). Abnormal results on screening laboratory tests may be repeated only at the discretion of the Investigator, in consultation with the Medical Monitor and the Sponsor on a case by case basis. Re-screening of subjects is not allowed. Each screened subject will be assigned a subject number starting from 5001 to 5999 in a sequential order. **Staff and study sites are encouraged to complete screening procedures as early as possible to allow more flexibility on the Baseline period for the caregiver to achieve the IA diary compliance.**

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 R-MOAS and CGI-S completed by the Investigator will be administered to determine if the subject is eligible to participate in the study. Both these scales measure severity of aggressive behaviors; only those subjects with an R-MOAS score of ≥ 20 and scoring of at least "moderately ill" (score of ≥ 4) on CGI-S will be eligible for the study.

The Vitiello Aggression Questionnaire 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.

Serum pregnancy test will be performed at Screening for all female subjects.

4.3.1.2 Baseline Period

Subjects who meet all study criteria will proceed to the flexible 15-day Baseline period. At Visit 2 an IA diary electronic device will be issued: the subject's primary caregiver and a secondary caregiver (if assigned) will be trained on how to use the device. Every effort will be made to provide adequate caregiver training on the use of the diary and acknowledgment of training will be captured on the device. At Visit 2 infrequent behaviors will also be recorded on paper source.

Following at least 15 days of using the diary, caregiver's compliance with the IA diary will be assessed. Compliance will be calculated as percentage of days over the past 15 days during the Baseline period for which an evening diary was completed. A diary compliance ≥70 % in the completion of the diary is for eligibility.

Subjects whose caregivers do not reach 70% compliance (at least 11 out 15 days) during the first 15 days of the Baseline period may be allowed to continue to use the diary for up to 15 additional days to improve caregivers' performance with the IA diary and demonstrate ≥ 70% compliance over the past 15-day rolling window. For these subjects, caregivers will receive remedial training on the use of the IA diary. During this time, caregiver compliance with the IA diary will be monitored daily by study site personnel over the past 15-days as a "rolling window".

Although there are up to 30 days available for each of the Screening or the Baseline period, the total duration of Screening and Baseline periods may not exceed 45 days.

A baseline score of ≥6 of IA behaviors per 7 days is required for randomization. The score represents the frequency of IA behaviors per 7 days and, will be calculated as the sum of the scores of the IA behaviors collected during the entire Baseline period, divided by the number of days with non-missing IA behaviors, then multiplied by 7 days.

Subjects whose caregivers demonstrate ≥ 70% diary compliance and an IA baseline score ≥6 will be eligible for randomization and continue into the Titration period.

4.3.2 Treatment Phase: (2-5 weeks)

4.3.2.1 Titration period (2 weeks), Day 1 to Day 14

Inclusion/exclusion criteria will be re-assessed to verify eligibility prior to study randomization at the end of Visit 3. Eligible subjects will be randomized at Visit 3 (Day 1) in a 1: 1 ratio to receive 36 mg/day SPN-810 or placebo and proceed to the two-week Titration period in order to reach the maintenance dose of 36 mg/day over a period of 2 weeks.

4.3.2.2 Flexible Maintenance period (3 weeks), Day 15 to Day 35

Following dose titration, all subjects will remain at the reached dose of SPN-810 (36 mg/day) or placebo on the first week of the Maintenance period. After the first week, the Investigator will clinically assess whether to increase the dose to 45 mg/day SPN-810 or placebo, or remain at 36 mg/day of SPN-810 or placebo. On the following week, the Investigator will re-assess the dosage: the subject may remain at 36 mg/day or 45 mg/day or matching placebo (depending on the dosage from the previous week) or titrate up to the higher dose of 45 mg/day or 54 mg/day of SPN-810 or placebo, respectively. Dose reduction will also be allowed during the second week of the Maintenance period in consultation with the Medical Monitor and the Sponsor; at Visit 6 the Investigator may adjust the dose based upon tolerability.

4.3.3 Conversion Phase (10 days), Day 36 to day 45

At the end of the 3-week Maintenance period (Visit 7), subjects will enter a 10 day Conversion Phase if the subject chooses to enroll into an ongoing open-label extension (OLE) study (i.e., 810P304). A blinded double-dummy conversion card will be distributed to down or up-titrate

the study medication and matching placebo. Subjects will return to the study site for a final end-of-study (EOS) visit, (Visit 8), after completing the Conversion Phase (Figure 1).

4.3.4 Taper Phase (10 days), Day 36 to day 45

At Visit 7, subjects who opt to discontinue from the study will receive a blinded taper card to titrate down the study medication. At the completion of the Taper Phase, subjects will return to the study site to complete the EOS procedures (Figure 2).

Subjects who choose to continue into the OLE, will enter the study at a dose of 36 mg/day SPN-810. A subject who discontinues early in the Maintenance period, i.e., prior to Visit 7 may be allowed to participate in the OLE on a case-by-case basis after consultation between the Investigator, Medical Monitor, and the Sponsor.

4.3.5 End of the Study (EOS)/Early Termination, Day 46

Subjects will return to the study site for a final visit, after completing the 10 day period of Taper or Conversion Phase. Those subjects who choose to continue in the OLE study (810P304) will have baseline procedures performed for that study; eligibility criteria will be confirmed (at Visit 1 of study protocol 810P304) or EOS (Visit 8) in this study (810P503).

4.3.6 Early Termination

All subjects who discontinue early (i.e. during Titration period, Day 1 to Day 14) will be instructed to return to the study site for a final visit (EOS), one week after discontinuation. Subjects who discontinue from the study following Day 15 in the Titration period or during the Maintenance period will be offered a taper card and will return to the study site for a final visit (EOS).

5. STUDY METHODS

5.1 Selection of Study Population

Approximately 372 subjects aged 12-17 years (inclusive) will be screened to enroll and randomize 186 subjects; 93 in the SPN-810 arm and 93 in the placebo arm. The population will be male and female subjects diagnosed with ADHD, with associated features of IA and currently being treated with an FDA-approved standard ADHD treatment (psychostimulants and non-stimulants).

5.1.1 Inclusion Criteria

The following inclusion criteria must be met in order for a subject to be enrolled and randomized to treatment:

1. Healthy male or female subjects, age 12-17 years at the time of screening, including outpatients in foster care living at home.

2. Diagnosis of ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders-5* (DSM-5) confirmed by MINI-KID.
3. Monotherapy treatment with an FDA-approved optimized ADHD medication (psychostimulants and non-stimulants for at least one month prior to Screening and willing to maintain the dose throughout the duration of the study.
4. Retrospective Modified Overt Aggression Scale (R-MOAS) score of ≥ 20 at Screening and Visit 3.
5. CGI-S score at least moderately ill (≥4) at Screening and Visit 3.
6. Vitiello Aggression Questionnaire score from -2 to -5 at Screening.
7. Free of antipsychotic medication for at least 2 weeks or 5x drug's half-life or whatever is longer prior to Visit 2.
8. Discontinuation of α2-adrenergic agonists (e.g. clonidine and guanfacine) used for any other reason except for monotherapy treatment of ADHD (e.g. aggression or insomnia) at least two-weeks prior to Visit 2.
9. Medically healthy with clinically normal laboratory profiles, vital signs and electrocardiograms (ECGs).
10. Able and willing to swallow tablets whole and not chewed, cut or crushed.
11. Written informed consent/assent obtained from the subject's parent or legal authorized representative (LAR), and written informed assent from the subject if required.
12. Compliance ≥ 70% for completion of the IA Diary during the Baseline period.
13. IA score ≥ 6 during the Baseline period.

5.1.2 Exclusion Criteria

Any of the following will disqualify a subject from being enrolled and randomized:

1. Body Mass Index (BMI) less than 25th and above 99th percentile.
2. History or current diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia and other psychotic disorders, personality disorder, Tourette's disorder, dissociative disorder, or autism spectrum disorder.
3. Currently meeting DSM-5 criteria for 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 strongly inhibit and induce CYP2D6 activity within (2) two weeks or 5x drug's half-life or whatever is longer, before Screening.
5. Use of herbal supplements one week prior Screening.
6. Known or suspected intelligence quotient (IQ) < 70, including speech/language problems, non-verbal learning disabilities, lead intoxication and traumatic brain injury.
7. Suicidality, defined as either active suicidal plan/intent or active suicidal thought in the six months before the Screening Visit or more than one lifetime suicide attempt confirmed by the Columbia-Suicide Severity Rating Scale (C-SSRS).
8. Historical and current evidence of violence abuse or neglect.

9. Pregnancy, breastfeeding or refusal to use birth control during the study (for female subjects of childbearing potential and sexually active males).
10. Substance or alcohol/abuse use during the last three months prior to Screening.
11. Criminal arrest reports at least six months prior to Screening.
12. Known allergy or sensitivity to molindone hydrochloride or inactive ingredients.
13. Any reasons which, in the opinion of the Investigator or the Sponsor, would prevent the subject and the subjects' caregiver from participating in the study or complying with the study procedures.
14. Use of an investigational drug or participation in an investigational study within 30 days prior Visit 2.

5.2 Schedule of Visits and Procedures

All subjects who are consented are required to follow the protocol procedures regardless of the number of doses of SM taken. The Sponsor, or the Sponsor's designee, must be notified of all deviations from the Schedule of Visits 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 site personnel to report any issues or abnormal reactions during the intervals in 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 Visits and Procedures

Phase	Pre-Treatment		Treatment					Conversion/Taper
Period	Screening	Baseline	Titration		Maintenance			
VISIT NUMBER	1	2	3	4	5	6	7	8 (EOS)
DAY	-45	-15	1	15	22	29	36	46
WINDOW (DAYS)	≤45d prior to Visit 3	≥15d prior to Visit 3	14d±2d from Visit 2	14d±2d from Visit 3	21d±2d from Visit 3	28d±2d from Visit 3	7d±2d from Visit 6	10d±1d from Visit 7
Informed Consent/Assent[a]	X[b]							
R-MOAS Scale	X	X	X	X	X	X	X	X
MINI-KID & Vitiello Aggression Scales	X							
Medical History	X		X[c]					
Demographics	X							
Physical Examination & ECG (12-lead)	X						X	
Inclusion/Exclusion Criteria	X		X[d]					
Randomization			X[b]					
Urine Drug Screen	X	X	X	X	X	X	X	X
Pregnancy Test[e]	X[f]	X	X	X	X	X	X	X
Diary Training & Distribution or Evaluation		X	X[g]	X	X	X	X	
Vital Signs[h]	X		X	X	X	X	X	X
Weight, Height, BMI	X		X			X		X
Hematology/Chemistry/Urinalysis	X		X				X	X
PK Blood Sampling[i]					X	X		
PGx sampling[l]	X							

Columbia Suicide Severity Rating Scale (CSSRS)	X		X	X	X	X	X	X
Caregiver and Investigator CGI-S	X[j]		X	X	X	X	X	
Caregiver and Investigator CGI-I				X	X	X	X	
SNAP-IV, CHQ-PF28, SIPA			X				X	
Infrequent Behaviors Checklist		X[k]	X	X	X	X	X	
Simpson-Angus, Barnes & AIMS			X	X	X	X	X	X
Adverse Events			X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X
Drug Dispensation			X[b]	X	X	X	X	
Drug Return and Compliance				X	X	X	X	X
Diary Return								X

a. Written consent must be obtained prior to performing any study-related procedure.
b. Subject number will be assigned via [redacted]
c. Assess for any clinically significant change in Medical History since screening.
d. Confirm inclusion/exclusion criteria.
e. Urine pregnancy test will be performed for all female subjects. Prior to the administration of the first dose of SM subjects will have to be tested as negative to continue in the study. If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed.
f. Serum pregnancy test will be performed at Screening for all female subjects.
g. Diary compliance must be at least 70% (minimum of 11 days out of 15) to qualify for randomization.
h. Heart Rate (HR), blood pressure (BP), temperature, and respiratory rate will be measured.
i. PK blood samples will be obtained over two visits
j. Only the Investigator-rated CGI-S will be completed at Screening; Caregiver and Investigator-rated CGI-S will be collected at randomization and every visit thereafter.
k. The checklist will be recorded on a paper source and entered on EDC only at Visit 2.
l. Optional

5.3 Study Procedures

5.3.1 Screening/ Visit 1 (Day -45)

Prior to conducting any procedures, written Informed Consent will be obtained from the parent or LAR, and, if appropriate, Informed Assent from the subject. Subjects screening procedures will be performed within 45 days prior Visit 3 and may be done on more than one day. Abnormal results on screening laboratory tests may be repeated at the discretion of the Investigator.

The following procedures will be performed at screening (Visit 1):

1. Obtain written informed consent and assent
2. Administer R-MOAS scale
3. Administer MINI-KID for ADHD diagnosis
4. Administer Vitiello Aggression Questionnaire
5. Record medical history
6. Record demographic information
7. Perform physical examination
8. Perform 12-lead ECG
9. Confirm Inclusion/Exclusion criteria
10. Access [redacted] for subject number
11. Collect urine sample for drug screen and urinalysis
12. Collect blood for serum pregnancy test (If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed)
13. Record vital signs (HR, BP, temperature, and RR)
14. Record weight, height, BMI
15. Collect blood samples for hematology and chemistry
16. Collect blood samples for optional PGx testing
17. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
18. Administer Investigator CGI-S scale
19. Record concomitant medications

5.3.2 Baseline/ Visit 2, Day -15

Visit 2 will occur at least 15 days prior to Visit 3 as per the Schedule of Events and Procedures.

1. Administer R-MOAS scale
2. Collect urine for drug screen and pregnancy test (If Visit 1 and Visit 2 occur on the same day then both urine and serum pregnancy tests must be performed)
3. Conduct training for the electronic IA diary
4. Distribution of IA diary

5. Record Infrequent IA Behaviors
6. Record and assess concomitant medications

5.3.3 Visit 3, Day 1

Visit 3 will occur at least 14 days (±2 days) following Visit 2 as per the Schedule of Events and Procedures.

1. Administer R-MOAS scale
2. Assessment for any clinically significant changes in medical history
3. Confirm eligibility to randomize subject
4. Assess IA diary compliance/review training as necessary
5. Randomize subject
6. Collect urine sample for drug screen, urinalysis and pregnancy test
7. Record weight, height and BMI
8. Record vital signs (HR, BP, temperature, and RR)
9. Collect blood samples for hematology and chemistry
10. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
11. Administer Caregiver and Investigator-completed CGI-S scale
12. Administer SNAP-IV, CHQ-PF 28 and SIPA scales
13. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)
14. Record adverse events
15. Record Infrequent IA Behaviors
16. Record concomitant medications
17. Dispense SM via [redacted]

5.3.4 Visit 4, Day 15

Visit 4 will occur 14 days (±2 days) following Visit 3 according to the Schedule of Visits and Procedures.

1. Administer R-MOAS scale
2. Review IA diary compliance and provide training as needed
3. Record dosing diary compliance and provide training as needed
4. Collect urine sample for pregnancy test and drug screen
5. Record vital signs (HR, BP, temperature, and RR)
6. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
7. Administer Caregiver and Investigator-completed CGI-S scale
8. Administer Caregiver and Investigator- completed CGI-I scale
9. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)
10. Record adverse events
11. Record Infrequent IA Behaviors
12. Record concomitant medications
13. Collect returned SM assess treatment compliance

14. Dispense SM

5.3.5 Visit 5, Day 22

Visit 5 will occur 21 days (±2 days) following Visit 3 according to the Schedule of Visits and Procedures. Refer to Section 5.3.9 for details regarding timing of the dose of SM prior PK sampling.

1. Administer R-MOAS scale
2. Review IA diary compliance and provide training as needed
3. Record dosing diary compliance and provide training as needed
4. Collect urine sample for pregnancy test and drug screen
5. Record vital signs (HR, BP, temperature, and RR)
6. Collect blood for PK analysis
7. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
8. Administer Caregiver and Investigator-completed CGI-S scale
9. Administer Caregiver and Investigator- completed CGI-I scale
10. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)
11. Record adverse events
12. Record Infrequent IA Behaviors
13. Record concomitant medications
14. Collect returned SM; assess treatment compliance
15. Dispense SM

5.3.6 Visit 6, Day 29

Visit 6 will occur 28 days (±2 days) following Visit 3 according to the Schedule of Visits and Procedures. Refer to Section 5.3.9 for details regarding timing of the dose of SM prior to PK sampling.

1. Administer R-MOAS scale
2. Review IA diary compliance and provide training as needed
3. Record dosing diary compliance and provide training as needed
4. Record vital signs (HR, BP, temperature, and RR)
5. Record weight, height and BMI
6. Collect blood for PK analysis
7. Collect urine sample for pregnancy test and drug screen
8. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
9. Administer Caregiver and Investigator-completed CGI-S scale
10. Administer Caregiver and Investigator- completed CGI-I scale
11. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)
12. Record adverse events
13. Record Infrequent IA Behaviors
14. Record concomitant medications

15. Collect returned SM; assess treatment compliance
16. Dispense SM

5.3.7 Visit 7, Day 36

Visit 7 will occur 7 days (±2 days) following Visit 6 according to the Schedule of Visits and Procedures.

1. Administer R-MOAS scale
2. Perform physical examination
3. Perform 12-lead ECG
4. Review IA diary compliance and provide training as needed
5. Record dosing diary compliance and provide training as needed
6. Collect urine sample for urinalysis, pregnancy test and drug screen
7. Record vital signs (HR, BP, temperature, and RR)
8. Collect blood samples for hematology and chemistry
9. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
10. Administer Caregiver and Investigator-completed CGI-S scale
11. Administer Caregiver and Investigator-completed CGI-I scale
12. Administer SNAP-IV, CHQ-PF 28 and SIPA scales
13. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)
14. Record adverse events
15. Record Infrequent IA Behaviors
16. Record concomitant medications
17. Collect returned SM; assess treatment compliance
18. Dispense SM (either taper or conversion card based upon the subject's decision about participation in the open-label extension)

5.3.8 Visit 8/ End of the Study, Day 46

Visit 8 will occur 10 days (±1 day) following Visit 7 according to the Schedule of Visits and Procedures. These procedures will be performed for all subjects who complete the Maintenance period and for those who discontinue early. Subjects who discontinue after Visit 4 will be offered a taper kit and return to the study site to complete Visit 8. Any subject, who discontinues between Visit 3 and Visit 4, will be instructed to return to the study site for the final visit, within one week after discontinuation.

1. Administer R-MOAS scale
2. Record vital signs (HR, BP, temperature, and RR)
3. Record height, weight and BMI
4. Collect blood for hematology and chemistry
5. Collect urine for urinalysis, drug screen and pregnancy test
6. Administer Columbia Suicide Severity Rating Scale (C-SSRS)
7. Administer safety scales (Simpson-Angus, Barnes-Akathisia, AIMS)

8. Record adverse events
9. Record concomitant medications
10. Collect SM and assess treatment compliance
11. Collect Diary
12. Complete/Discontinue subject

5.3.9 Pharmacokinetic Blood Sampling

[redacted]

5.4 Treatments

5.4.1 Treatment Administered

Subjects will take up to (6) six 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 the stable dose of the optimized ADHD medication. During the conversion phase, subjects will take up to (8) eight molindone hydrochloride extended release tablet (SPN-810) or placebo twice each day (BID).

If dosing starts before noon, the subject should start with the morning dose; if dosing starts after noon, the subject should start with the evening dose. Subjects will be randomized to one of the two treatments at Visit 3 and will be titrated to the final randomized total daily dose (TDD) of 36 mg/day.

- Treatment 1: Placebo, PO, BID
- Treatment 2: Flexible dose titrated to one of SPN-810 45 mg, or 54 mg, PO, BID

Subjects will remain at the target dose of 36 mg/day or placebo for one week during maintenance. In the second week of maintenance (Visit 5), the treatment dose could be increased in a blinded fashion to 45 mg (TTD) based on Investigator discretion or maintained at

36mg (TDD) or placebo. In the following week (Visit 6), the Investigator will re-assess the dosage: the subject may remain at 36 mg (TDD) or 45 mg (TDD) or matching placebo (depending on the dosage from the previous week) or titrate up to the higher dose of 45 mg or 54 mg (TDD) or placebo. At the same Visit, dose reduction will be allowed in consultation with the Medical Monitor and the Sponsor: the Investigator may adjust the dose based upon tolerability.

5.4.2 ADHD medication

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

5.4.3 Identity of Investigational Product(s)

SM and reference (matching placebo) products are either purple (3mg) or yellow (9mg) round tablets printed on one side with the tablet dose strength ("3" or "9") that will be supplied in labeled blister cards by the Sponsor. The Sponsor will package the SM in a double-blind configuration.

Each SM blister card will contain combinations of molindone extended-release and/or placebo tablets, which will supply a subject with 7 (seven) days of dosing as well as some extras to account for visit delays associated with patient/site schedules. A single SM kit contains a total of 7 pre-packaged blister cards (two Titration blister cards, three maintenance blister cards, one tapering blister card and one conversion blister card) and is marked with a unique 4-digit SM kit number.

Instructions will be provided to site staff and caregiver(s) on how to move between the different dose-levels during the Maintenance period (36mg, 45mg and 54mg TDD).

5.4.4 Study Medication Handling and Accountability

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

Following Sponsor instructions and in compliance with 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, shipment, dispensing, inventory, and record keeping) in a SM 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 SM 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; dispensing of SM to the subject; collection of unused supplies returned by the subject; and subsequent return of

unused SM to the Sponsor must be maintained with dates. This SM accountability log includes, but may not be limited to: (a) documentation of receipt of clinical supplies, (b) SM inventory log, (c) SM 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 CRA will review these documents along with all other study conduct documents at each and every visit to the study site once SM 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 subject 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 SM accountability and reconciliation procedures by study site personnel and documentation procedures by Sponsor personnel, SM is to be returned to the Sponsor with a copy of the completed SM disposition form as outlined in the Study Medication Manual.

5.4.5 Methods of Assigning Subjects to Treatment Group

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. Dispending of the SM will be completed centrally through the use of an [redacted] that will determine which kit to assign to the subject.

Upon enrollment to the study, subjects will be assigned site (01-99) and subject numbers (5001-5999), in the sequence that they are entered. On Visit 3, subjects who complete the IA Diary Baseline period and met all eligibility criteria will be assigned kit numbers, according to the randomization schedule, by using the [redacted]

5.4.6 Treatment Replacement

In the event that a subjects' original kit is lost, damaged or consumed prior to the end of treatment, the Investigator will use the [redacted] which will specify a new kit number to be dispensed to that subject from the supplies already at that site. Separate reserve will not be provided to the Investigators.

5.4.7 Dosing Schedule

At Visit 3, subject will be randomized to Placebo or SPN-810 in a 1:1 ratio and the dosing will begin. Table 2 below presents the details of the dosing for each treatment group throughout the 2-week titration phase for this study. During Maintenance period, the Investigator will assess the dosage at his discretion. Dose reduction will be discussed with the Medical Monitor.

Table 2 Titration Dosing Schedule

Treatment Arm	Final Dose	Study Days					
		1-2	3-5	6-8	9-11	12-14	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
[1]36 mg (TDD) will be maintained for the first week into Maintenance period, in the following two weeks the dose could be adjusted to 45 mg or 54 mg (TDD) or placebo.

5.4.8 Method of Administration

The SM must be swallowed whole. SM must not be crushed, chewed or cut. The SM may be taken with or without food in the morning and in the evening, no more than 12 hours between doses (i.e., if the morning dose is taken at 8:00 am, the evening dose should be taken at 8:00 pm).

5.4.9 Blinding

The subject and all study personnel involved with the conduct and interpretation of the study, including the Investigators, site personnel, the Sponsor, DSC and clinical staff 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 are not associated with the clinical conduct of the study and will not have access to the randomization schedule, nor will 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 [redacted] vendor, and accessible only to authorized persons until the time of unblinding.

The SM tablets have matching placebo tablets. The blind is maintained through the [redacted] The blind will be maintained through the end of the Conversion/Taper period.

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 [redacted] 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.

5.5 Allowed Concomitant Medications

The dose of the ongoing ADHD therapy will not be adjusted during the study, starting at Visit 1. No additional concomitant medications are allowed, with the following exceptions:

1. Emla or other numbing cream for PK venipuncture
2. Standard childhood vaccinations and prophylactic flu shots
3. Nutritional supplements (e.g. multivitamins, fish oil)
4. 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 three times daily) and clonazepam (0.25 to 1 mg per dose not to exceed twice daily) is also permitted to treat extrapyramidal symptoms.
5. For the treatment of Akathisia, propranolol is recommended up to 90 mg /day in divided doses, three times per day, starting at 10 mg BID and up to 30 mg TID, as needed.
6. Common over-the-counter (OTC) therapies for minor transient ailments (e.g. acetaminophen for headache, ibuprofen for fever) will be allowed without exception.
7. Treatment for AEs other than EPS or minor transient ailments is permitted in consultation with the Medical Monitor and Sponsor.

All concomitant medications will be recorded in the eCRF.

5.6 Prohibited Medications

1. 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.
2. Use of herbal supplements.
3. α2-adrenergic agonists (e.g. clonidine and guanfacine) used for other reasons except for monotherapy treatment of ADHD.

5.7 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 8. Any subject, who discontinues from the study during the Maintenance period or following day 15 in the Titration period, will be offered a taper kit, whereas subjects who

discontinue prior Visit 4 (i.e. during Titration period, Day 1 to Day 14) will be instructed to return to the study site for a final visit, one week after discontinuation. All subjects who discontinue early will complete Visit 8, EOS procedures.

The Investigator(s) or subjects themselves may stop SM 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 should be discussed where possible and as applicable with the Medical Monitor, the Investigator and the Sponsor before the subject stops SM. 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. STUDY ENDPOINTS

6.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the percent change (PCH_T) in the frequency (unweighted score) of IA behaviors per 7 days in the Treatment Phase (titration + maintenance) relative to the Baseline period calculated over the number of days with non-missing IA diary data.

The primary efficacy endpoint PCH_T will be calculated by $PCH_T = 100*(T - B)/B$, where T and B are IA behavior frequencies per 7 days during the Treatment Phase and Baseline period, respectively. The IA behavior frequency per 7 days is defined as (SUM/DAY) x 7, where SUM is the total of the 15 IA behaviors reported in the subject IA diary, and DAY is the number of days with non-missing IA score in the subject IA diary during the specified study period.

6.1.1 Primary Efficacy Variable

The primary efficacy outcome variable will be based on a checklist of 15 IA behaviors collected in the electronic IA diary. These behaviors were described in the non-interventional study (Sponsor Study 810P502, 2016); they include Yelling, Screaming, Threatening, Scratching, Throwing, Slamming, Hitting Self, Arguing, Cursing, Name Calling, Shoving, Hair Pulling, Fighting, Hitting Others and Kicking Others. The IA diary consists of two parts: 1) an episodic diary that will be used by the primary or alternate caregiver to enter events as soon as possible after they are observed; and 2) an evening diary that will prompt the caregiver to review events for the

day and to enter any events that were not previously captured. Events can be directly observed by the caregiver or could be reported to the caregiver by another observer such as a teacher, a friend of the subject or the parent of a friend.

Each event will be characterized by a checklist of one or more behaviors observed during the day. The checklist will indicate whether each behavior was observed (coded 1) or was not observed (coded 0) during the incidence of an event. Each day can have multiple events. A day can have no event, as can be attested in the evening diary. In this case, if no event is reported during a day, and the evening diary confirms this, the daily event score for that subject will be 0. Behaviors not on this list will not be captured.

6.2 Secondary Efficacy Endpoints

The secondary efficacy endpoint is the change from Baseline to the end of the study where the Baseline is defined as the last observation prior to the first dose, Visit 3. The effect of SPN-810 will be measured on the following efficacy scales administered at visits designated in the Schedule of Visits and Procedures (Table 1).

6.2.1 Investigator-Rated Clinical Global Severity of Illness Scale (CGI-S)

Effect of SPN-810 on the Clinical Global Impression – Severity of Illness Scale (CGI-S) completed by the Investigator will be assessed as a key secondary efficacy measure. The CGI scale was developed to provide a brief, stand-alone assessment of the clinician's view of a subject's global functioning (Guy, 1976). Successful therapy is indicated by a lower overall score in subsequent testing. Investigators should consider their total clinical experience with children who have IA comorbid with ADHD and rate how severe the subject's condition is at the time.

CGI-S will be evaluated on a 7-point scale:

- 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 assessed at Screening and at each visit after randomization (Visit 3).

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

The treatment effect on the Retrospective-Modified Overt Aggression Scale (R-MOAS) will be assessed to capture the severity of the aggressive behaviors and to correlate with the IA behaviors in the diary.

This scale was developed to gauge the severity of aggressive behavior (Blader, et al., 2010). Parents rate the frequency over the past week of 16 aggressive behaviors in four areas: verbal aggression; physical aggression toward others; aggression toward oneself; and destruction or hostile misuse of property.

The remission rate will be defined as a score ≤ 10.

The scale will be administered at each visit.

6.2.3 Additional Secondary Efficacy Endpoints

6.2.3.1 Clinical Global Impression – Improvement Scale (CGI-I)

Effect of SPN-810 on the Clinical Global Impression – Improvement Scale (CGI-I) completed by the Investigator and the Caregiver will be assessed as an additional secondary efficacy measure.

CGI-I, relative to the condition at baseline, will be evaluated by the Investigator and the Caregiver on a 7-point scale:

- 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 assessed at Visit 4-7.

6.2.3.2 Caregiver-Rated Clinical Global Severity of Illness Scale (CGI-S)

The Clinical Global Impression – Severity of Illness Scale (CGI-S) completed by the Caregiver will be assessed as an additional secondary efficacy measure.

CGI-S will be evaluated on a 7-point scale:

- 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 assessed at each visit after randomization (Visit 3).

6.2.3.3 Swanson, Nolan, Pelham Rating Scale-Revised (SNAP-IV)

The SNAP-IV rating scale includes 18 ADHD and 8 oppositional defiant disorder (ODD) symptoms as specified in the DSM-IV-TR and International Statistical Classification of Diseases and Health Related Problems 10th Revision (ICD-10) Classification of Mental and Behavioral Disorders. The symptoms are scored by assigning a severity estimate for each symptom on a 4-point scale (Swanson 2001). The SNAP-IV rating should be performed by the same parent or legal representative.

The ratings from the SNAP-IV scale are grouped into the following 4 subscales:

- ADHD-Inattention (items #1-9),
- ADHD-Hyperactivity/Impulsivity (items #10-18)
- ADHD-Combined subscales (items #1-18)
- ODD (items #19-26)

Each subscale score is calculated by averaging the items scores within each subscale.

The SNAP-IV rating scale will be administered at Visit 3 and Visit 7.

6.2.3.4 Child Health Questionnaire Parent Form 28-Item (CHQ-PF28)

The Child Health Questionnaire Parent Form 28-item (CHQ-PF28) is a short generic measure of health status and health related quality of life (Landgraf 1996). CHQ-PF28 items have four, five, or six response options, divided over eight multi-item scales (physical functioning, general behavior, mental health, self-esteem, general health perceptions, parental impact: emotional, parental impact: time, and family activities) and five single item concepts (role functioning: emotional/behavior, role functioning: physical, bodily pain, family cohesion, and change in health). The CHQ-PF28 should be performed by the primary caregiver.

The CHQ-PF28 will be administered at Visit 3 and Visit 7.

6.2.3.5 Stress Index for Parents of Adolescents (SIPA)

The Stress Index for Parents of Adolescents (SIPA) is a screening and diagnostic instrument that identifies areas of stress in parent–adolescent interactions, allowing examination of the relationship of parenting stress to adolescent characteristics, parent characteristics, the quality of the adolescent–parent interactions, and stressful life circumstances in parents of adolescents (11-19 years old). The SIPA consists of 90 items divided in three major domains, the Adolescents Domain (AD), the Parent Domain (PD) and the Adolescent-Parent Relationship Domain (APRD), which include the following subscales: moodiness/emotional lability, social isolation/withdrawal, delinquency/antisocial, failure to achieve and persevere, relationship with spouse/partner, social alienation and incompetence/guilt. The SIPA includes 22 item Life Stressors (LS) Scale and the Index of Total Parenting Stress (TS).

Parents respond to the first 90 items using a 5-point rating scale ranging from *Strongly Disagree* (5) to *Strongly Agree* (1) and the final 22 items by indicating *Yes* (Y) or *No* (N).

The SIPA will be administered at Visit 3 and Visit 7.

6.3 Exploratory Endpoints

6.3.1 IA Diary Cross-Validation

The data generated from 810P301 and 810P302 pediatric studies during the diary validation process will be used for cross-validation of the IA Diary in adolescents. The parameters used will be specified in the statistical analysis plan (SAP).

6.3.2 Pharmacokinetic Measurements

[redacted]

6.3.2.1 Pharmacokinetic Variables

The pharmacokinetic variables are:

- Apparent clearance (CL/F) of molindone
- Apparent volume of distribution (V/F) of molindone

6.3.2.2 Additional Pharmacokinetic Variables

[redacted]

6.3.3 Pharmacogenomics (PGx Testing)

Blood samples will be collected at Visit 1 after confirmation of subject's eligibility. Pharmacogenomic testing is optional. The DNA will be extracted and tested for any genetic variations associated with CYP2D6 enzyme. This enzyme is involved in the metabolism of molindone and genetic variations of the CYP2D6 gene may affect the pharmacokinetics of the drug. Test results in this study will identify the subject's metabolizer phenotype.

The residual DNA will be stored for possible testing of genes involved in the efficacy and possible association with particular adverse events of the drug (e.g., to understand the non-responders to treatment and/or individuals who show unusual safety profile). The DNA analysis will not be used for individual genetic characterization and the subject identity will be kept confidential.

6.4 Safety and Tolerability Endpoints

The secondary outcome measures include the safety and tolerability of the SM. Safety assessment will consist of monitoring and recording of all AEs, concomitant medications and assessment of suicidality ideation and behaviors at every visit. Clinical laboratory tests, including prolactin and insulin plasma levels, vital signs, physical examinations, 12-lead ECG are performed at visits specified in the Schedule of Events and Procedures and can be repeated as necessary as per the judgment of the Investigator and the Medical Monitor.

Assessment of possible neurological side effects and EPS will be performed using the Simpson-Angus scale, the Barnes Akathisia scale and the Abnormal Involuntary Movement scale. A positive rating or finding on any safety scale will be captured as an Adverse Event at the discretion of the Investigator if it satisfied the criteria for Adverse Event.

6.4.1 Data Safety Committee (DSC)

An independent and unblinded Data and Safety Committee (DSC) will be established to assess the safety of the subjects participating in the study. An interim safety data analysis will be performed if required to support a registrational filing. The DSC will not evaluate the efficacy data. The duties and responsibilities of the DSC will be described in a separate DSC charter.

6.4.2 Adverse Events

As defined by the ICH Guideline for 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:

- 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.
- Any new disease, intercurrent injuries, or exacerbation of an existing disease.
- Any deterioration in a laboratory value or other clinical test (e.g., ECG) that results in symptoms, a change in treatment, or discontinuation from SM.
- Recurrence of an intermittent medical condition (e.g., headache) not present at baseline.

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.

6.4.2.1 Causality

AEs may be categorized as either Adverse Drug Reactions or Suspected Adverse Drug Reactions based on their relationship to SM and the degree of certainty about causality.

- **Suspected adverse drug reactions** (SADRs) are a subset of adverse events 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 adverse event.

- **Adverse drug reactions** (ADRs) are a subset of all SADRs for which there is reason to conclude that the drug caused the event.

6.4.2.2 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/procedure, 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/procedure has started. TEAEs occurring prior to the administration of the study medication (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.

All AEs occurring after enrollment and throughout the study period must be recorded. A treatment-emergent adverse event (TEAE) is defined as an AE with a start date on or after the first dose of study drug, or that worsened following first administration of study drug. For subjects who receive SM, TEAEs will be collected starting from the first dose of SM. The clinical course of each AE should be followed until resolution or until, in the medical judgment of the Investigator, the event has stabilized or is assessed as chronic.

For subjects who opt to enroll in the OLE (810P304) study, occurrence of AEs will be assessed starting at Visit 8 of this study (810P503) or Visit 1 in the OLE. AEs occurred in this double-blind study or ongoing after Visit 7, will be part of the medical history in the OLE study.

An increase in the CSSRS, Simpson Angus Scale, Barnes Akathisia Scale, or the AIMS will not necessarily be rated as an AE unless the event meets AE criteria.

The Investigator is responsible for evaluating AEs and determining the following:

- **Serious vs. Non-serious:** Is the event a Serious Adverse Event (SAE)?
- **Causality:** Was AE related or possibly related to the SM?
- **Severity:** How pronounced is the incapacity/discomfort caused by an AE?

6.4.2.3 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.

6.4.2.4 Criteria for Assessing Causality

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

Not suspected: The temporal relationship of the AE to SM 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 SM administration is missing or implausible, or there is an evident other cause.
- **Unlikely related**: Temporal relationship to SM administration makes a causal relationship improbable; and other drugs, chemicals, or underlying disease provide plausible explanations.

Suspected: The temporal relationship of the AE to SM 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 SM administration is plausible, but concurrent disease or other drugs or chemicals could also explain event. Information on drug withdrawal may be lacking or unclear. This will be reported as a **Suspected Adverse Drug Reaction (SADR)**.
- **Definitely related:** Temporal relationship to SM administration is plausible, and concurrent disease or other drugs or chemicals cannot explain event. The response to withdrawal of the medication (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary. This will be reported as an **Adverse Drug Reaction (ADR)**.

6.4.3 Serious Adverse Events (SAE)

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.)
- in-patient 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 in-patient hospitalization, or intensive treatment for allergic bronchospasm in an emergency department would typically be considered serious.

6.4.3.1 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.

All SAEs must be reported to the Drug Safety Contact within 24 hours of first becoming aware of the SAE. The Investigator must complete an SAE eCRF in EDC 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). Should the site be unable to access EDC, a paper SAE form must be completed and sent to [redacted] Drug Safety by email or fax. The Investigator will keep a copy of this SAE Report form on file at the study site. Once EDC becomes available, the site must complete the SAE eCRF in EDC.

The Investigator or study physician, after thorough consideration of all facts that are available, must include an assessment of causality of an AE to SM 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]

6.4.3.2 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 Medical Monitor; the Investigator must follow any pregnant subject for 3 months after the child is born. The Investigator must complete a Pregnancy Outcome Form as a follow up. Any AEs concerning the pregnancy of the subject during pregnancy or the child after birth must be documented and reported to the Sponsor.

Treatment-emerging **EPS** (e.g. akathisia, dystonia, Parkinsonism, tardive dyskinesia) and neuroleptic malignant syndrome should be reported to the Drug Safety Contact person(s) by completing the Adverse Event of Special Interest (AESI) eCRF in EDC. Should the site be unable to access EDC, a paper AESI form must be completed and sent to [redacted] Drug Safety by email or fax within 24 hours of first becoming aware of the event. Once EDC becomes available the site must complete AESI eCRF in EDC. EPS incidence will be summarized and shared with study Investigators throughout the 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 molindone which is freely soluble in water. Since the adsorption of molindone 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 molindone in animals, this blocking effect has not been determined in humans.

6.4.3.3 Sponsor Responsibilities for Expedited Reporting of SAEs

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

Investigators must comply with the applicable regulatory requirements related to the reporting of SAEs to the IRB/IEC. Investigators must also submit the safety information provided by the Sponsor to the IRB/IEC unless the country legal regulation requires that the Sponsor should be responsible for the safety reporting to the IRB/IEC.

It is the responsibility of the Sponsor to notify all participating Investigators, in a written IND safety report, of any SADR that is both serious and unexpected. The Sponsor will also notify participating Investigators of any findings from other sources (other studies, animal and in vitro testing, etc.) that suggest a significant risk for human subjects. Such findings will typically lead to safety-related changes in the study protocol, Informed Consent, and/or Investigator's Brochure.

6.4.4 Assessment of Neurological Side Effects and EPS

6.4.4.1 Simpson-Angus Scale

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

6.4.4.2 Barnes Akathisia Scale

The Barnes Akathisia scale 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 3 and all subsequent visits.

6.4.4.3 Abnormal Involuntary Movement Scale (AIMS)

The AIMS test is a rating scale used to measure tardive dyskinesia (Munetz 1988). There are 12 items that rate involuntary movements of various areas of the subject's body. This assessment will be administered at Visit 3 and all subsequent visits.

6.4.4.4 Management of Treatment-Emerging EPS

If a subject experiences treatment-emerging 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 three times daily) and clonazepam (0.25 to 1 mg per dose not to exceed twice daily) will also be permitted to treat emerging EPS.

For the treatment of Akathisia, propranolol is recommended up to 90 mg /day in divided doses, three times per day, starting at 10 mg BID and up to 30 mg TID, as needed.

A positive finding on an EPS safety assessment scale (Barnes Akathisia, Simpson-Angus, 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.

6.4.5 Columbia Suicide Severity Rating Scale (C-SSRS)

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

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 all the other study visits.

6.4.6 Laboratory Measurements

With the exception of urine pregnancy test, 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 detailed 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. A subject will be excluded if the Screening blood test results indicates > 2 times the upper limit of normal (ULN) of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transpeptidase (GGT), and/or serum creatinine. Laboratory tests will not be repeated for these subjects.

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 testing at the discretion of the Investigator. Any repeat laboratory testing will be conducted under **fasting condition**. Any laboratory abnormality may qualify as an AE in the Investigator's judgment.

[redacted]

Table 3 Clinical Laboratory Tests

Category	Parameters
Hematology	RBC, WBC, Hgb, HCT, MCH, MCHC, MCV, platelet count, and WBC with differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils, large unstained cells)
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, gammaGT (GGT), Iron, Lipase, Magnesium
Urinalysis	Glucose, protein (total), ketones, bilirubin, urobilinogen, hemoglobin, leucocyte esterase, nitrite
Urine	Cocaine, amphetamines, barbiturates, benzodiazepines, cannabinoids, opioids, phencyclidine, propoxyphene, methadone and alcohol
Urine Pregnancy Test	hCG

6.4.7 Vital Signs and 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.

6.4.8 Medical History and Physical Examinations

Medical history will be taken at screening. Physical examinations will be performed at screening and at the end of the study as designated on the Schedule of Visits and Procedures (Table 1).

6.4.9 Electrocardiograms (ECGs)

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 measure the PR, QRS, QT, and QTc intervals, and heart rate.

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).

6.4.10 Infrequent Behaviors Checklist

The infrequent behaviors checklist is a list of 15 behaviors that (along with the 15 IA Diary behaviors) were qualitatively linked to IA during the development of the IA diary (Sponsor Study 810P501, 2015). These behaviors include *Teasing, Spitting, Biting, Weapons, Ripping, Breaking, Vandalizing, Destroying, Fire Setting, Hitting Animal, Kicking Self, Kicking Animal, Severe Injury Self, Severe Injury Others and Severe Injury Animal*. At Visit 2 the caregivers will be asked which, if any, of these behaviors have been observed since Screening. At the following visits (Visit 3-7) any of these behaviors will be recorded on the electronic IA diary if they were observed since the patient's last visit.

7. OTHER SPECIAL TESTS

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

7.1 MINI-KID

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.

7.2 Vitiello Aggression Questionnaire

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

8. STATISTICAL METHODS

8.1 Statistical and Analytical Plans

Tabular summaries of the data collected during the study will be presented to provide a general description of the subjects studied and an overview of the efficacy, PK and safety results. Data from all sites will be combined in the computation of these summaries and summaries will be presented by treatment group. Continuous variables will be summarized using descriptive statistics (number of subjects, mean, standard deviation [SD], median, and minimum and maximum values). Categorical (nominal) variables will be summarized using frequency tables (number 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. Additional subject data listings to be provided for this study are listed under the relevant subsections below. All data analyses will be performed by [redacted] which is designated CRO, after the study is completed and the database is released. Statistical programming and analyses will be performed using SAS® and/or other validated statistical software as required.

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 database lock and will be included in the Clinical Study Report (CSR) as an appendix. The SAP will supersede the statistical analysis methods described in this clinical protocol. Any deviation from the statistical plan will be documented and described in the CSR. 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.

In general, the baseline value for a variable is defined as the last observation prior to the first dose of double-blind study medication, ideally Visit 3, but including the screening value, if necessary.

8.2 Handling Missing Data

For the primary efficacy end point, the frequency of IA behaviors during the Treatment Phase will be calculated over the number of days with non-missing IA diary data in the Treatment Phase (titration + maintenance). For subjects who have partial IA diary data during Maintenance period (<7 days with non-missing IA diary data), the IA behaviors from both titration and partial maintenance period will be counted together and used for the maintenance period. For subjects with IA diary data only available during titration period, the IA behaviors from the titration period will be used for the maintenance period.

8.3 Analysis Populations

The population of "all enrolled subjects" consists of all those screened subjects who meet the requirements for study participation and are entered in the Baseline period of the study. The population of "all randomized subjects" consists of all those enrolled subjects who complete the Baseline Period, meet the inclusion/exclusion criteria and are randomized.

Safety Population: will include all subjects who received at least 1 dose of study drug and had at least one post-baseline safety assessment.

Full Analysis Set (FAS): will include all screened subjects who received at least 1 dose of study drug and have completed baseline and at least 1 valid post-randomization assessment of frequency of IA behaviors based on IA diary entry.

Per-Protocol (PP) Population: will include all subjects who completed Treatment Phase and did not have major protocol deviations (as defined in the SAP).

PK population: will include all subjects in the safety population who have received at least 1 dose of study drug and had one PK sample drawn which had quantifiable concentration for molindone.

The safety, psychometric, FAS, PP, and PK populations are based on randomized treatment received.

8.4 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 safety, psychometric, FAS, and PP populations, except for medical history, which will be summarized for the safety population.

8.5 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 in the FAS population
- Subjects treated (safety population)
- Subjects in the PP study population

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

- Subject withdrew consent

- Lost to follow-up
- 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.

8.6 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
- Non-compliance with study treatment
- Disallowed concomitant medications
- Non-compliance with study inclusion or exclusion criteria
- Non-compliance with study assessment procedures

8.7 Study Medication Exposure and Compliance

Duration of 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:

> $\{(D-R)/T*(D_L- D_F + 1)\}*100$, where D=number of tablets dispensed, R= number of tablets returned, T= number of tablets administered, D_L = date of last visit (dose) and D_F= date of first visit (dose)

The number of tablets (T) taken each day may vary during the flexible Maintenance period: during the first week of maintenance a total of 6 tablets per day will be taken, whereas during week 2 and 3 of maintenance, the number of tablets taken will be between 4 and 6 depending upon the 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.

9. EFFICACY ANALYSES

9.1 Primary Efficacy Analysis

The primary efficacy analysis is the percent change (PCH_T) in the frequency (unweighted score) of IA behaviors per 7 days in the Treatment Phase (titration + maintenance) relative to the Baseline period calculated over the number of days with non-missing IA diary data. The frequency of the IA behaviors per 7 days is the sum of the scores for all the events collected in a given period of sequential days, adjusted per 7 days.

The primary efficacy endpoint PCH_T will be calculated by $PCH_T = 100*(T - B)/B$, where T and B are IA behavior frequencies per 7 days during the Treatment Phase and Baseline period, respectively. The IA behavior frequency per 7 days is defined as (SUM/DAY) x 7, where SUM is the sum of the IA behaviors reported in the subject IA diary, and DAY is the number of days with non-missing IA frequency data in the subject IA diary during the specified study period.

Let μ_1, and μ_2 represent the median percent change in the frequency of IA behaviors per 7 days in the Treatment Phase, relative to the Baseline period in the FAS population for subjects treated with placebo and SPN-810 treatment, respectively. The null (H_0) and the alternative (H_a) hypotheses are as in the following:

> H_0: $\mu_2 = \mu_1$, [there is no difference between the median of the SPN-810 treatment group and the median of placebo group] vs. H_a: $\mu_2 \neq \mu_1$, [there is a difference between the median of the SPN-810 treatment group and the median of placebo].

To test the above hypothesis, the primary efficacy analysis will be performed using the Wilcoxon rank-sum test to compare the median of SPN-810 with the median of the Placebo. The Hodges-Lehmann estimate of the difference (SPN-810 minus placebo) and the associated 95% confidence interval (CI) around the difference will be calculated.

When the median PCH_T from subjects in SPN-810 treatment group is significantly different from the placebo, further exploratory testing may be performed between other doses (45mg and 54mg) and placebo depending on the available sample size at each dose level.

9.2 Secondary Efficacy Analyses

9.2.1 Key secondary endpoints are:

1. Change from Visit 3 to Visit 7 in the Investigator-rated CGI-S score

2. Change from Visit 3 to Visit 7 in R-MOAS score
3. R-MOAS remission rate at Visit 7

9.2.2 Additional secondary endpoints:

1. Actual Investigator CGI-I score at Visit 7 and change from Visit 4
2. Actual Caregiver CGI-I score at Visit 7 and change from Visit 4
3. Change from Visit 3 to Visit 7 in the Caregiver-rated CGI-S score
4. Change from Visit 3 to Visit 7 in the SNAP-IV ADHD scores in:
    a. Inattention ratings
    b. Hyperactivity/Impulsivity ratings
    c. ODD ratings
    d. Combined scale ratings
5. Change from Visit 3 to Visit 7 in the CHQ-PF28 score
6. Change from Visit 3 to Visit 7 in the SIPA scores in:
    a. Adolescents domain
    b. Parent domain
    c. Adolescents-Parents Relationship domain
    d. Life Stressor domain

Each of the secondary endpoints will be analyzed using a Mixed-Effect Model for Repeated Measure (MMRM). MMRM assumes missing data as Missing at Random. The model includes treatment, visit, and interaction between treatment and visit as fixed factors, baseline as covariate. The model parameters will be estimated using restricted maximum likelihood method with unstructured variance-covariance matrix and Kenward-Roger approximation to estimate denominator degrees of freedom. The between-group comparison will be performed using the simple contrast at the respective visits. The least squares mean of the treatment group, the difference in the least squares mean (SPN-810 minus placebo), and the 2-sided 95% CI for the difference will be obtained.

To preserve the overall type I error rate at 0.05 for the secondary endpoints, only SPN-810 treatment group is significantly different from placebo for the primary endpoint will be tested for secondary endpoints.
The ordering of the three (3) key secondary endpoints from first to be tested to third is: Investigator-completed Clinical Global Impression – Severity Scale (CGI-S) (Endpoint 1); Retrospective Modified Aggression Scale (R-MOAS)(Endpoint 2); Retrospective Modified Aggression (R-MOAS) remission (Endpoint 3).

The ordering for the additional six (6) secondary endpoints from the first to the sixth is: Investigator-completed Clinical Global Impression – Improvement Scale (CGI-I)(Endpoint 1); Caregiver-completed Clinical Global Impression – Improvement Scale (CGI-I)(Endpoint 2); Caregiver-completed Clinical Global Impression – Severity Scale (CGI-S)(Endpoint 3);SNAP-IV

Rating Scale (Endpoint 4); Child Health Questionnaire (CHQ-PF28) (Endpoint 5) and SIPA Rating scale (Endpoint 6).

9.2.3 Sensitivity Analysis

The purpose of the sensitivity analysis is to see whether different methods of handling missing data provide consistent and similar results for the primary efficacy analysis. To this end, the following sensitivity analysis will be considered:

1. Multiple imputation under MAR
2. Placebo-based imputation under MNAR
3. Percent change (PCH_M) in the frequency of IA behaviors per 7 days in the Maintenance period relative to the Baseline period calculated over the number of days with non-missing IA diary data.

9.2.3.1 Multiple imputation under Missing at Random (MAR)

The multiple imputation (MI) method assumes that the missing data are missing at random (MAR), that is, the probability that an observation is missing may depend on the observed values but not the missing values. For example, if a subject's Diary values are available on Day 1 and Day 2 but missing on Day 3, then the missing value on Day 3 is related to the non-missing value on Day 1 and Day 2.

MI is implemented using the following three steps.

1. SAS PROC MI is applied with input dataset containing some missing values for all days during the titration and maintenance period to create 100 datasets. The data sets will include separate columns for the frequency of incidences during each day starting from baseline. The Markov Chain Monte Carlo (MCMC) method will be used to complete the missingness pattern to a monotone pattern separately by treatment arm. The monotone patterns will be achieved by applying sequential imputation based on Bayesian regression with the treatment arm included as a covariate. All copies contain identical values of the non-missing data items, but different values imputed for missing values.

2. For each of these MI data sets, the percent change will be computed as in the observed data set and the primary analysis based on the Wilcoxon rank-sum test will be conducted and asymptotic 95% confidence intervals will be constructed.

3. To produce a single confidence interval for each dose placebo comparison (e.g., Dose 1 versus placebo), PROC MIANALYZE will be used and Rubin's combination rules will be applied to the treatment effect estimates and associated asymptotic standard errors from the MI data sets. The treatment effect estimates will be defined as the midpoints

of the asymptotic confidence intervals and the standard errors will be defined as the asymptotic standard errors (based on the width of the associated 95% confidence intervals) from the Hodges-Lehmann estimate of the individual datasets (Rubin 1987).

9.2.3.2 Multiple imputation under Missing Not at Random (MNAR)

This approach can be labeled "worst-case" sensitivity analyses as it assumes that after discontinuation subjects from the dosing arms would adopt the outcome model estimated from the placebo arm. To generate missing values from this "placebo-based" imputation model, PROC MI with the MNAR statement (available in SAS 9.3 and later versions) will be used or, alternatively, SAS macros available at the DIA Missing Data Working Group site (Ratitch et al., 2013; Ayele et al., 2014) can be used.

9.2.3.3 Per Protocol Analysis

This analysis will be conducted by repeating the primary analysis on the per protocol population.

9.3 Sample Size and Power Consideration

Assuming a mean difference of 15 between SPN-810 dose group and placebo with a common standard deviation of 35, a sample of 93 subjects per arm will yield 80 % power to detect a non-zero difference between the median of SPN-810 treatment group and the placebo group using the Wilcoxon rank-sum test with a 2-sided significance level α=0.05.

It is assumed that approximately 20% subjects will dropout before the completion of the study and hence, an adjusted total of 186 subjects will be randomized in a 1:1 ratio to obtain approximately 150 subjects at the completion of the study.

Sample size may be recalculated based on the effect size of the ongoing 810P301 and 810P302 studies.

9.4 Exploratory Analyses

9.4.1 IA Diary Cross Validation

Cross-validation model will be generated based on the results from the IA diary validation in the 810P301 and 810P302 studies. The model will estimate the minimal clinical important change (MCIC) for improvement of IA behaviors in adolescents. The cross-validation plan and results will be provided in a separate report.

9.4.2 Pharmacokinetic

A population PK model will be developed for molindone using the nonlinear mixed-effects modeling program NONMEM. The structural model for molindone will incorporate data from

studies in which sampling was more intensive than in the present study. Results from the data analysis will be provided in a separate and stand-alone report.

9.4.3 Pharmacogenomic (PGx)

Genetic variations associated with CYP2D6 enzyme will be analyzed using the FAS population. Paired t-test will be used to compare the treatment groups, results will be summarized by treatment group using descriptive statistics. A stand-alone analysis and report will be generated.

9.5 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 3 to each subsequent visit for each of the Simpson-Angus scale, Barnes Akathisia scale, and AIMS. Suicidal ideation and suicidal behavior will be measured by C-SSRS.

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

9.5.1 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 first dose of study medication (after Visit 3) to the end of the study. These AEs include those that emerge 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 two 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). For the combined Titration and Maintenance Periods, the incidence of TEAEs will also be presented by highest severity reported and the dose of SM 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.

9.5.2 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 applicable if appropriate.

9.5.3 Extrapyramidal Signs

The occurrence of neurological side effects will be assessed by looking at the changes in scores from Baseline to each of the post-Baseline visit for each of the Simpson-Angus scale, Barnes Akathisia 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.

9.5.4 Laboratory Values

Clinical laboratory values will be summarized by visit and by treatment group using descriptive statistics for hematology and chemistry. 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 three by three tables (shift tables) that, for a particular laboratory test, compare the LNH classification at baseline to the LNH classification at visit. By subject-listings of all abnormal laboratory values, i.e., those with L or H classification will be provided.

9.5.5 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 by treatment group.

9.5.6 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.

9.5.7 Physical Examinations

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

9.5.8 Infrequent Behaviors Checklist

Infrequent behaviors will be listed for each subject by treatment group.

10. PROCEDURES AND INSTRUCTIONS

10.1 Adherence to the Protocol

The Investigator agrees, when signing the 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 IRB constituted and functioning in accordance with ICH E6 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 with a copy to the Sponsor prior to study start and the release of SM to the site by the Sponsor or its designee. If the IRB decides to suspend or terminate the study, the Investigator will immediately send the notice of study suspension or termination by the IRB to the Sponsor.

Study progress is to be reported to 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.

10.2 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 IRB [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 the IRB for the site must be informed promptly.

Changes affecting only administrative aspects of the study 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.

10.3 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.

10.4 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.

10.4.1 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 Good Clinical Practice (GCP).

The Investigator will permit representatives of the Sponsor to inspect all CRFs and corresponding study subject original medical records (source documents) at regular intervals throughout the study. Subject original medical records and other relevant data must be available to support all data recorded in the eCRF. 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 is being entered on the case report forms. A Monitoring Log will be maintained at each study site. The Monitoring Log will be signed by the monitor, dated and stated the type of visit. The Investigator should be aware that the study site and subject records may be inspected by the Sponsor and/or their designees, 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.

10.4.2 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.

10.4.3 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.

10.5 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, SM inventory records, Investigator's Brochure, and regulatory agency registration documents (e.g., FDA form 1572, ICFs, and IRB/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 two 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 US FDA in accordance with the US 21 CFR 312.68 or other national or foreign regulatory authorities in accordance with regulatory requirements.

10.6 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.

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

10.7 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.

10.8 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).

10.9 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.

10.10 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.

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12. APPENDICES

12.1 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.....

12.2 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 ☐ 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	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**.	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? **IF YES**, how many times? _____ **IF YES**, when was the last suicide attempt?	NO	YES	4

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 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:	NO	YES	6

How often? How strong were the thoughts?

Occasionally	☐	Mild	☐
Often	☐	Moderate	☐
Very often	☐	Severe	☐

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**?	NO	YES	NO	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**?				
	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 ☐

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	YES ↳ **Q13**
		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**. ➡ NO YES

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: _____

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? IF **W2** IS **YES,** THEN **W2** SUMMARY IS **NO.** IF **W2** IS **NO,** THEN **W2** SUMMARY IS **YES.** OTHERWISE IT IS **UNCERTAIN.**	☐ No	☐ Yes	☐ 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

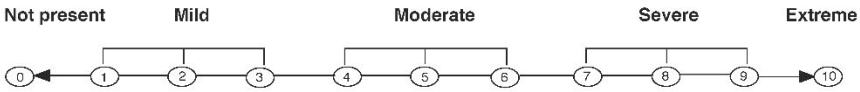
	Current	Past
Other Specified Bipolar and Related Disorder	☐	☐

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:



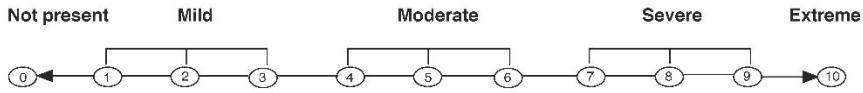
Assessment of Symptoms That Cut Across Disorders

	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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International Advisory Committee for MINI Kid version 2.0

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Naomi Breslau	Stephan Renou
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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)

12.3 Clinical Global Impression (CGI) Scale

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	☐ (4) Moderately ill
	☐ (2) Borderline mentally ill	☐ (5) Markedly ill
	☐ (3) Mildly 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 3/ Baseline, how much has the subject's *impulsive aggression* changed?

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

12.4 Columbia-Suicide Severity Rating Scales (C-SSRS)

12.4.1 C-SSRS, Lifetime/Recent

COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Lifetime Recent - 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.	**Lifetime: Time He/She Felt Most Suicidal**	**Past 1 month**
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 ☐	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 ☐	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 ☐	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 ☐	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 ☐	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). Ask about time he/she was feeling the most suicidal. Lifetime - ***Most Severe Ideation:*** _____ (*Type # (1-5)*) _____ (*Description of Ideation*) Recent - ***Most Severe Ideation:*** _____ (*Type # (1-5)*) _____ (*Description of Ideation*)	Most Severe	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	____	____

12.4.2 **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

12.5 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

12.6 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.

12.7 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).	☐ 0 ☐ 1

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

12.8 Swanson, Nolan, Pelham Rating Scale-Revised (SNAP-IV)

THE MTA SNAP-IV TEACHER AND PARENT RATING SCALE
James M. Swanson, Ph.D., University of California, Irvine, CA 92715

For each item, check the column which best describes this child	Not At All	Just A Little	Pretty Much	Very Much
1. Fails to give close attention to details or makes careless mistakes in schoolwork or tasks	___	___	___	___
2. Has difficulty sustaining attention in tasks or play activities	___	___	___	___
3. Does not seem to listen when spoken to directly	___	___	___	___
4. Does not follow through on instructions and fails to finish schoolwork, chores, or duties	___	___	___	___
5. Has difficulty organizing tasks and activities	___	___	___	___
6. Avoids, dislikes, or reluctantly engages in tasks requiring sustained mental effort	___	___	___	___
7. Loses things necessary for activities (e.g., toys, school assignments, pencils, or books)	___	___	___	___
8. Is distracted by extraneous stimuli	___	___	___	___
9. Is forgetful in daily activities	___	___	___	___
10. Fidgets with hands or feet or squirms in seat	___	___	___	___
11. Leaves seat in classroom or in other situations in which remaining seated is expected	___	___	___	___
12. Runs about or climbs excessively in situations in which it is inappropriate	___	___	___	___
13. Has difficulty playing or engaging in leisure activities quietly	___	___	___	___
14. Is "on the go" or often acts as if "driven by a motor"	___	___	___	___
15. Talks excessively	___	___	___	___
16. Blurts out answers before questions have been completed	___	___	___	___
17. Has difficulty awaiting turn	___	___	___	___
18. Interrupts or intrudes on others (e.g., butts into conversations / games)	___	___	___	___
19. Loses temper	___	___	___	___
20. Argues with adults	___	___	___	___
21. Actively defies or refuses adult requests or rules	___	___	___	___
22. Deliberately does things that annoy other people	___	___	___	___
23. Blames others for his or her mistakes or misbehavior	___	___	___	___
24. Is touchy or easily annoyed by others	___	___	___	___
25. Is angry and resentful	___	___	___	___
26. Is spiteful or vindictive	___	___	___	___

Rater Initials: ___ ___ ___

12.9 Child Health Questionnaire Parent Form 28-item (CHQ-PF28)

CHILD HEALTH QUESTIONNAIRE (CHQ-PF28)

PARENT FORM – 28 ENGLISH (U.S.)

ID NUMBER

TODAY'S DATE

MONTH / DAY / YEAR

INSTRUCTIONS: This form asks about your child's health and well-being. Your responses will be treated confidentially. There are no right or wrong responses. If you are unsure how to respond to a question, give the best response you can. It is important that you fill in each question. Please use blue or black ink.

Correct Marks: ■ ☒ ☑

SECTION 1: YOUR CHILD'S GLOBAL HEALTH

	Excellent	Very good	Good	Fair	Poor
1.1. In general, would you say your child's health is:	☐	☐	☐	☐	☐

SECTION 2: YOUR CHILD'S PHYSICAL ACTIVITIES

The following questions ask about physical activities your child might do during a day.

2.1. During the past 4 weeks, has your child been limited in any of the following activities due to health problems?	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Doing things that take a lot of energy, such as playing soccer, or running?	☐	☐	☐	☐
b. Doing things that take some energy such as riding a bike or skating?	☐	☐	☐	☐
c. Bending, lifting or stooping?	☐	☐	☐	☐

SECTION 3: YOUR CHILD'S EVERYDAY ACTIVITIES

3.1. During the past 4 weeks, has your child been limited in the AMOUNT of time he/she could spend on schoolwork or activities with friends due to EMOTIONAL difficulties or problems with his/her BEHAVIOR?

Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
☐	☐	☐	☐

3.2. During the past 4 weeks, has your child been limited in the KIND of schoolwork or activities he/she could do with friends due to problems with his/her PHYSICAL health?

Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
☐	☐	☐	☐

1

SECTION 4: PAIN

4.1. During the past 4 weeks, how often has your child had bodily pain or discomfort?

None of the time	Once or twice	A few times	Fairly often	Very often	Every/almost every day
☐	☐	☐	☐	☐	☐

SECTION 5: BEHAVIOR
Below is a list of items that describe children's behavior or problems they sometimes have.

5.1. How often during the past 4 weeks did each of the following statements describe your child?

	Very often	Fairly often	Some times	Almost never	Never
a. Argued a lot?	☐	☐	☐	☐	☐
b. Had difficulty concentrating or paying attention?	☐	☐	☐	☐	☐
c. Lied or cheated?	☐	☐	☐	☐	☐

5.2. Compared to other children your child's age, in general would you say his/her behavior is:

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

SECTION 6: WELL-BEING
The following phrases are about children's moods.

6.1. During the past 4 weeks, how much of the time do you think your child:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Felt lonely?	☐	☐	☐	☐	☐
b. Acted nervous?	☐	☐	☐	☐	☐
c. Acted bothered or upset?	☐	☐	☐	☐	☐

SECTION 7: SELF-ESTEEM
The following ask about your child's satisfaction with self, school, and others. It may be helpful if you keep in mind how other children your child's age might feel about these areas.

7.1. During the past 4 weeks, how satisfied do you think your child has felt about:	Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
a. His/her school ability?	☐	☐	☐	☐	☐
b. His/her friendships?	☐	☐	☐	☐	☐
c. His/her life overall?	☐	☐	☐	☐	☐

SECTION 8: YOUR CHILD'S HEALTH
The following statements are about health in general.

8.1. How true or false is the statement for your child?	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My child seems to be less healthy than other children I know.	☐	☐	☐	☐	☐
b. My child has never been seriously ill.	☐	☐	☐	☐	☐
c. I worry more about my child's health than other people worry about their children's health.	☐	☐	☐	☐	☐

8.2. Compared to one year ago, how would you rate your child's health now:

Much better now than 1 year ago	Somewhat better now than 1 year ago	About the same now as 1 year ago	Somewhat worse now than 1 year ago	Much worse now than 1 year ago
☐	☐	☐	☐	☐

SECTION 9: YOU AND YOUR FAMILY

		None at all	A little bit	Some	Quite a bit	A lot
9.1.	During the past 4 weeks, how MUCH emotional worry or concern did each of the following cause YOU?					
	a. Your child's physical health	☐	☐	☐	☐	☐
	b. Your child's emotional well-being or behavior	☐	☐	☐	☐	☐

		Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
9.2.	During the past 4 weeks, were you LIMITED in the amount of time YOU had for your own needs because of:				
	a. Your child's physical health	☐	☐	☐	☐
	b. Your child's emotional well-being or behavior?	☐	☐	☐	☐

		Very often	Fairly often	Sometimes	Almost never	Never
9.3.	During the past 4 weeks, how often has your child's health or behavior:					
	a. limited the types of activities you could do as a family?	☐	☐	☐	☐	☐
	b. interrupted various everyday family activities (eating meals, watching tv)?	☐	☐	☐	☐	☐

9.4. Sometimes families may have difficulty getting along with one another. They do not always agree and they may get angry. In general, how would you rate your family's ability to get along with one another?

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

CHILD HEALTH QUESTIONNAIRE (CHQ-PF28)

PARENT FORM – 28 SPANISH (U.S.)

NÚMERO DE IDENTIFICACIÓN

LA FECHA DE HOY

MES / DÍA / AÑO

INSTRUCCIONES: Este cuestionario contiene preguntas sobre la salud y el bienestar de su hijo(a). Sus respuestas serán tratadas confidencialmente. No hay respuestas correctas ni incorrectas. Si no está seguro(a) de cómo responder a una pregunta, por favor dé la mejor respuesta posible. Es muy importante que responda todas las preguntas. Por favor use tinta azul o negra.

Marcas correctas: ■ ☒ ☑ ⬅

SECCIÓN 1: LA SALUD EN GENERAL DE SU HIJO(A)

	Excelente	Muy buena	Buena	Regular	Mala
1.1. En general, ¿diría que la salud de su hijo(a) es ...?	☐	☐	☐	☐	☐

SECCIÓN 2: LAS ACTIVIDADES FÍSICAS DE SU HIJO(A)

Las siguientes preguntas se refieren a actividades físicas que su hijo(a) podría hacer en un día típico.

2.1. Durante las últimas 4 semanas, ¿ha estado su hijo(a) limitado(a) en alguna de las siguientes actividades a causa de problemas de salud?	Sí, muy limitado(a)	Sí, algo limitado(a)	Sí, un poquito limitado(a)	No, nada limitado(a)
a. Hacer cosas que requieren mucha energía, como jugar al fútbol o correr	☐	☐	☐	☐
b. Hacer cosas que requieren cierta energía, como andar en bicicleta o patinar	☐	☐	☐	☐
c. Inclinarse, levantar algo o agacharse	☐	☐	☐	☐

SECCIÓN 3: LAS ACTIVIDADES DIARIAS DE SU HIJO(A)

3.1. Durante las últimas 4 semanas, ¿ha estado su hijo(a) limitado(a) en cuanto a la CANTIDAD de tiempo que podría dedicar al trabajo escolar o a las actividades con amigos, a causa de dificultades EMOCIONALES o problemas relacionados con su COMPORTAMIENTO?

Sí, muy limitado(a)	Sí, algo limitado(a)	Sí, un poquito limitado(a)	No, nada limitado(a)
☐	☐	☐	☐

3.2. Durante las últimas 4 semanas, ¿ha estado su hijo(a) limitado(a) en cuanto a la CLASE de trabajo escolar o actividades con amigos que podría hacer, a causa de problemas relacionados con su salud FÍSICA?

Sí, muy limitado(a)	Sí, algo limitado(a)	Sí, un poquito limitado(a)	No, nada limitado(a)
☐	☐	☐	☐

SECCIÓN 4: DOLOR

4.1 Durante las últimas 4 semanas, ¿con qué frecuencia ha tenido su hijo(a) dolor físico o molestia?

Nunca	Una o dos veces	Algunas veces	Con cierta frecuencia	Con mucha frecuencia	Todos los días o casi todos los días
☐	☐	☐	☐	☐	☐

SECCIÓN 5: COMPORTAMIENTO

A continuación hay una lista de frases que describen el comportamiento de los niños o los problemas que a veces tienen.

5.1 ¿Con qué frecuencia durante las últimas 4 semanas ha hecho su hijo(a) lo que se indica en cada frase?	Con mucha frecuencia	Con cierta frecuencia	Algunas veces	Casi nunca	Nunca
a. Discutió mucho	☐	☐	☐	☐	☐
b. Tuvo dificultad para concentrarse o prestar atención	☐	☐	☐	☐	☐
c. Mintió o engañó	☐	☐	☐	☐	☐

5.2 En comparación con otros niños de su edad, ¿diría usted que el comportamiento en general de su hijo(a) es...?

Excelente	Muy bueno	Bueno	Regular	Malo
☐	☐	☐	☐	☐

SECCIÓN 6: BIENESTAR GENERAL
Las siguientes frases se refieren al estado de ánimo de los niños.

6.1 Durante las últimas 4 semanas, ¿cuánto tiempo cree usted que su hijo(a)...	Siempre	Casi siempre	Algunas veces	Casi nunca	Nunca
a. Se ha sentido solo(a)?	☐	☐	☐	☐	☐
b. Ha estado nervioso(a)?	☐	☐	☐	☐	☐
c. Ha estado molesto(a) o disgustado(a)?	☐	☐	☐	☐	☐

SECCIÓN 7: AUTOESTIMA
Las siguientes preguntas se refieren a lo satisfecho(a) que se siente su hijo(a) consigo mismo(a), con la escuela y con los demás. Sería útil si usted tuviera en cuenta cómo se sienten en estos aspectos otros niños de la misma edad que su hijo(a).

7.1. Durante las últimas 4 semanas, ¿qué tan satisfecho(a) le parece que se ha sentido su hijo(a) con:	Muy satisfecho(a)	Algo satisfecho(a)	Ni satisfecho(a) ni insatisfecho(a)	Algo insatisfecho(a)	Muy insatisfecho(a)
a. Su capacidad escolar?	☐	☐	☐	☐	☐
b. Sus amistades?	☐	☐	☐	☐	☐
c. Su vida en general?	☐	☐	☐	☐	☐

SECCIÓN 8: LA SALUD DE SU HIJO(A)
Las siguientes afirmaciones se refieren a la salud en general.

8.1 ¿Qué tan cierta o falsa es cada afirmación en el caso de su hijo(a)?	Absolutamente cierta	Bastante cierta	No sé	Bastante falsa	Absolutamente falsa
a. Parece que mi hijo(a) es menos sano(a) que otros niños que conozco.	☐	☐	☐	☐	☐
b. Mi hijo(a) no ha estado nunca gravemente enfermo(a).	☐	☐	☐	☐	☐
c. Me preocupo por la salud de mi hijo(a) más de lo que otras personas se preocupan por la salud de sus hijos(as).	☐	☐	☐	☐	☐

8.2 Comparando la salud presente de su hijo(a) con la de hace un año, ¿cómo la calificaría en general ahora?

Mucho mejor ahora que hace un año	Algo mejor ahora que hace un año	Más o menos igual ahora que hace un año	Algo peor ahora que hace un año	Mucho peor ahora que hace un año
☐	☐	☐	☐	☐

SECCIÓN 9: USTED Y SU FAMILIA

		Nada en absoluto	Un poco	Algo	Bastante	Mucho
9.1	Durante las últimas 4 semanas, ¿CUÁNTO sufrimiento emocional o preocupación le ha causado a USTED lo siguiente?					
	a. La salud física de su hijo(a)	☐	☐	☐	☐	☐
	b. El bienestar emocional o el comportamiento de su hijo(a)	☐	☐	☐	☐	☐

		Sí, muy limitado(a)	Sí, algo limitado(a)	Sí, un poquito limitado(a)	No, nada limitado(a)
9.2	Durante las últimas 4 semanas, ¿ha estado USTED LIMITADO(A) en cuanto a la cantidad de tiempo de que disponía para sus propias necesidades personales a causa de lo siguiente?				
	a. La salud física de su hijo(a)	☐	☐	☐	☐
	b. El bienestar emocional o el comportamiento de su hijo(a)	☐	☐	☐	☐

		Con mucha frecuencia	Con cierta frecuencia	Algunas veces	Casi nunca	Nunca
9.3	Durante las últimas 4 semanas, ¿con qué frecuencia los problemas de salud o comportamiento de su hijo(a):					
	a. Han limitado las clases de actividades que ustedes podrían hacer como familia?	☐	☐	☐	☐	☐
	b. Han interrumpido las actividades diarias de la familia (comer, ver la televisión)?	☐	☐	☐	☐	☐

9.4 A veces los miembros de las familias pueden tener dificultades para llevarse bien unos con otros. Éstos no siempre se ponen de acuerdo y pueden enojarse. En general, ¿cómo calificaría la capacidad de los miembros de su familia para llevarse bien unos con otros?

Excelente	Muy buena	Buena	Regular	Mala
☐	☐	☐	☐	☐

12.10 Stress Index for Parents of Adolescents (SIPA)

SIPA™

Answer Sheet

Peter L. Sheras, PhD, and
Richard R. Abidin, EdD

Name ______________ Relationship to Child ______________ Gender ______ Date of Birth ______ Ethnic group ______ Marital status ____

Child's name ______________ Child's gender ______ Child's date of birth ______ Today's date ______

SD = Strongly Disagree **D** = Disagree **NS** = Not Sure **A** = Agree **SA** = Strongly Agree

1. SD D NS A SA	**6.** SD D NS A SA	**11.** SD D NS A SA	**16.** SD D NS A SA	**21.** SD D NS A SA	**26.** SD D NS A SA	**31.** SD D NS A SA	**36.** SD D NS A SA	**41.** SD D NS A SA	**46.** SD D NS A SA
2. SD D NS A SA	**7.** SD D NS A SA	**12.** SD D NS A SA	**17.** SD D NS A SA	**22.** SD D NS A SA	**27.** SD D NS A SA	**32.** SD D NS A SA	**37.** SD D NS A SA	**42.** SD D NS A SA	**47.** SD D NS A SA
3. SD D NS A SA	**8.** SD D NS A SA	**13.** SD D NS A SA	**18.** SD D NS A SA	**23.** SD D NS A SA	**28.** SD D NS A SA	**33.** SD D NS A SA	**38.** SD D NS A SA	**43.** SD D NS A SA	**48.** SD D NS A SA
4. SD D NS A SA	**9.** SD D NS A SA	**14.** SD D NS A SA	**19.** SD D NS A SA	**24.** SD D NS A SA	**29.** SD D NS A SA	**34.** SD D NS A SA	**39.** SD D NS A SA	**44.** SD D NS A SA	**49.** SD D NS A SA
5. SD D NS A SA	**10.** SD D NS A SA	**15.** SD D NS A SA	**20.** SD D NS A SA	**25.** SD D NS A SA	**30.** SD D NS A SA	**35.** SD D NS A SA	**40.** SD D NS A SA	**45.** SD D NS A SA	**50.** SD D NS A SA
51. SD D NS A SA	**55.** SD D NS A SA	**59.** SD D NS A SA	**63.** SD D NS A SA	**67.** SD D NS A SA	**71.** SD D NS A SA	**75.** SD D NS A SA	**79.** SD D NS A SA	**83.** SD D NS A SA	**87.** SD D NS A SA
52. SD D NS A SA	**56.** SD D NS A SA	**60.** SD D NS A SA	**64.** SD D NS A SA	**68.** SD D NS A SA	**72.** SD D NS A SA	**76.** SD D NS A SA	**80.** SD D NS A SA	**84.** SD D NS A SA	**88.** SD D NS A SA
53. SD D NS A SA	**57.** SD D NS A SA	**61.** SD D NS A SA	**65.** SD D NS A SA	**69.** SD D NS A SA	**73.** SD D NS A SA	**77.** SD D NS A SA	**81.** SD D NS A SA	**85.** SD D NS A SA	**89.** SD D NS A SA
54. SD D NS A SA	**58.** SD D NS A SA	**62.** SD D NS A SA	**66.** SD D NS A SA	**70.** SD D NS A SA	**74.** SD D NS A SA	**78.** SD D NS A SA	**82.** SD D NS A SA	**86.** SD D NS A SA	**90.** SD D NS A SA

91. Y N	**93.** Y N	**95.** Y N	**97.** Y N	**99.** Y N	**101.** Y N	**103.** Y N	**105.** Y N	**107.** Y N	**109.** Y N	**111.** Y N
92. Y N	**94.** Y N	**96.** Y N	**98.** Y N	**100.** Y N	**102.** Y N	**104.** Y N	**106.** Y N	**108.** Y N	**110.** Y N	**112.** Y N

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