

**Safety and Tolerability of Initiating Aripiprazole Lauroxil in  
Subjects with Schizophrenia who are Inadequately Treated  
with Paliperidone Palmitate or Risperidone Long Acting  
Injection**

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## CLINICAL STUDY PROTOCOL

**ALK9072-A401**

Study Title	Safety and Tolerability of Initiating Aripiprazole Lauroxil in Subjects with Schizophrenia who are Inadequately Treated with Paliperidone Palmitate or Risperidone Long Acting Injection
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Sponsor	Alkermes, Inc. 852 Winter Street Waltham, MA 02451 USA

### CONFIDENTIAL

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**1. SYNOPSIS**

<b>Name of Sponsor/Company:</b> Alkermes, Inc.	
<b>Name of Product:</b> Aripiprazole lauroxil	
<b>Name of Active Ingredient:</b> Aripiprazole	
<b>Title of study:</b> Safety and Tolerability of Initiating Aripiprazole Lauroxil in Subjects with Schizophrenia who are Inadequately Treated with Paliperidone Palmitate or Risperidone Long Acting Injection	
<b>Study Center</b> Multicenter study (United States [US])	
<b>Study Period:</b> Estimated date of first subject's consent: Q4 2015 Estimated date of last subject's last visit: Q3 2017	<b>Phase of Study:</b> 4
<b>Objectives:</b> <b>Primary:</b> <ul style="list-style-type: none"> <li>To evaluate the safety, tolerability, and efficacy of aripiprazole lauroxil in subjects with schizophrenia who are inadequately treated with paliperidone palmitate or risperidone long acting injection</li> </ul> <b>Secondary:</b> <ul style="list-style-type: none"> <li>To evaluate quality of life, including daily and social functioning, after treatment with aripiprazole lauroxil</li> <li>To characterize the caregiver and healthcare burden</li> </ul>	
<b>Methodology:</b> <p>This is an open-label study in subjects who are switched to aripiprazole lauroxil from paliperidone palmitate or risperidone long acting injection. Subjects will participate for approximately 7 months, including a screening period of up to 30 days, and will be administered 4 to 6 doses of intramuscular (IM) aripiprazole lauroxil. Dosing may occur in monthly (441 mg, 662 mg, or 882 mg) or 6-week (882 mg only) intervals. The dose and frequency of dosing will be at the discretion of the investigator, based on the dose selected, and on dosing instructions.</p> <p>Potential subjects will be evaluated for eligibility according to the inclusion and exclusion criteria at a screening visit and again on Day 1. The first dose of aripiprazole lauroxil will be administered on Day 1. Subjects will receive their first dose of aripiprazole lauroxil no earlier than one week and not later than 6 weeks following their previous injection of paliperidone palmitate or risperidone long acting injection.</p> <p>For subjects who have never taken aripiprazole, two test doses of oral aripiprazole 5 mg will be administered during the screening period. Only subjects who exhibit tolerability to oral aripiprazole (either following test doses or by past experience) are eligible to enroll in the study.</p> <p>On Day 1, qualified subjects will be administered a single IM injection of aripiprazole lauroxil into the gluteal (441 mg, 662 mg, or 882 mg) or deltoid (441 mg only) muscle, according to the dosing instructions. Following the first injection, subjects will return to the study site monthly or every 6 weeks for IM aripiprazole lauroxil administration and outpatient assessments. Additional outpatient assessments may be scheduled at the discretion of the investigator.</p> <p>If a subject must withdraw from the study early, an early termination (ET) visit should be completed</p>	

using the assessments scheduled for Day 169.

**Number of Subjects Planned:**

This study will enroll approximately 50 subjects.

**Main Criteria for Inclusion:**

Men and women 18 through 65 years of age (inclusive) with a diagnosis of schizophrenia at screening and who have been taking paliperidone palmitate or risperidone long acting injection with inadequate results for at least 3 doses prior to screening may be eligible for this study.

**Product, Dosage, Duration and Mode of Administration:**

Aripiprazole lauroxil in doses of 441 mg (via deltoid or gluteal muscle), 662 mg (via gluteal muscle), or 882 mg IM (via gluteal muscle) will be administered monthly or every 6 weeks (882 mg only). The dose and frequency of dosing will be at the discretion of the investigator, based on the dose selected, and on dosing instructions (as depicted in the table below).

Dose	Dosing Frequency	Site of Intramuscular Injection
441 mg	Monthly	Deltoid or Gluteal
662 mg	Monthly	Gluteal
882 mg	Monthly or every 6 weeks	Gluteal

**Reference Therapy, Dosage, Duration and Mode of administration:**

Not applicable.

**Duration of Study:**

Approximately 7 months.

**Criteria for Evaluation:**

**Efficacy:**

The following scales will be used to assess efficacy:

- CGI-S and BPRS

**Safety and Tolerability:**

The following safety and tolerability measures will be assessed:

- AEs
- Injection site reactions
- Vital signs (blood pressure, heart rate, respiratory rate, and body temperature), weight, and waist circumference
- Clinical laboratory parameters (chemistry [including prolactin], hematology, and urinalysis)
- C-SSRS responses
- ESRS-A scores

**Quality of Life, Daily and Social Functioning**

The following assessments will be conducted to characterize any change in quality of life, including daily and social functioning:

- Quality of Life Scale (QLS)
- Negative Symptom Assessment-16 (NSA-16)

- Sexual functioning subscale from UKU Side Effect Rating Scale and CSFQ-14 scores
- Personal and Social Performance scale (PSP)
- Total and individual items scores of the Modified -MSQ

#### **Other Assessments**

The following assessments will be collected to explore potential changes in healthcare burden, cognition, insight, and psychosocial care needs:

- Health economics
  - Total healthcare costs as measured by Treatment Services Review (TSR-6) (Modified for Mental Health)
- Functional Assessment
  - Birchwood Insight Scale (BIS)
- Family Measures
  - Caregiver Quality of Life – Burden Dimensions (CarerQOL–7D) and VAS
  - Burden Assessment Scale
- Investigator- and Caregiver-Rated Cognition
  - Respective New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT) subscales
- Substance Use
  - Mini International Neuropsychiatric Interview (M.I.N.I.) Module I (alcohol use disorder)
  - Mini International Neuropsychiatric Interview (M.I.N.I.) Module J (substance use disorder)

#### **Statistical Methods:**

The safety population will include all subjects who received at least one dose of aripiprazole lauroxil injection. All analyses will be carried out using the safety population.

#### **Efficacy:**

The change from baseline in CGI-S and BPRS scores at each post-baseline visit will be summarized.

#### **Safety and Tolerability:**

The number and percentage of treatment emergent adverse events (TEAEs) will be summarized by treatment group and overall by system organ class, and preferred terms within each system organ class. Serious adverse events (SAEs) and AEs resulting in treatment discontinuation will also be summarized.

Observed values and change from baseline in vital signs, clinical laboratory data, and ESRS scores will be summarized

Shift tables and potential clinical significance tables, along with supporting listings, will be provided for selected parameters.

#### **Analyses of Other Assessments**

Data on quality of life and functional domains including personal, social, and family measures will be summarized using the safety population.

**Sample Size Considerations:**

No formal sample size calculations have been performed. The sample size is based on clinical considerations.

**2. TABLE OF CONTENTS**

TITLE PAGE .....	1
CONTACT INFORMATION.....	2
1. SYNOPSIS .....	3
2. TABLE OF CONTENTS .....	7
3. LIST OF ABBREVIATIONS.....	12
4. INTRODUCTION .....	14
5. OBJECTIVES .....	15
5.1. Primary Objective .....	15
5.2. Secondary Objectives .....	15
6. SELECTION AND WITHDRAWAL OF SUBJECTS.....	16
6.1. Subject Inclusion Criteria .....	16
6.2. Subject Exclusion Criteria .....	17
6.3. Subject Withdrawal .....	18
6.4. Replacement of Subjects.....	19
7. STUDY DESIGN .....	20
7.1. Overall Study Design and Plan.....	20
7.2. Schedule of Visits and Assessments.....	21
7.3. Study Procedures Descriptions .....	26
7.3.1. Informed Consent .....	26
7.3.2. Eligibility Review .....	26
7.3.3. Demographics and Medical History .....	26
7.3.4. Concomitant Medication Review .....	26
7.3.5. Vital Signs, Weight, and Waist Circumference.....	26
7.3.6. Physical Examination .....	26
7.3.7. 12-Lead Electrocardiogram .....	26
7.3.8. Columbia Suicide Severity Rating Scale .....	27
7.3.9. Extrapyramidal Symptom Rating Scale – Abbreviated.....	27
7.3.10. Laboratory Assessments .....	27
7.3.10.1. Drug Testing .....	27
7.3.10.2. Hematology, Biochemistry, and Urinalysis.....	27



7.3.10.3.	Pregnancy Testing .....	28
7.3.11.	Drug Dispensation and Reconciliation .....	28
7.3.12.	Adverse Event Monitoring .....	28
7.3.13.	Efficacy Assessments .....	29
7.3.13.1.	Clinical Global Impressions-Severity .....	29
7.3.13.2.	Brief Psychiatric Rating Scale .....	29
7.3.14.	Quality of Life, Daily, and Social Functioning Assessments .....	29
7.3.14.1.	Sexual Functioning Subscale from Udvalg for Kliniske Undersøgelser Side Effect Rating Scale .....	29
7.3.14.2.	Changes in Sexual Functioning Questionnaire Short Form .....	29
7.3.14.3.	Personal and Social Performance Scale .....	29
7.3.14.4.	Heinrichs-Carpenter Quality of Life Scale .....	29
7.3.14.5.	Negative Symptom Assessment-16 .....	30
7.3.14.6.	Modified Medication Satisfaction Questionnaire .....	30
7.3.15.	Other Assessments .....	30
7.3.15.1.	Sixth edition of the Treatment Services Review (TSR-6)-Modified for Mental Health .....	30
7.3.15.2.	Caregiver Quality of Life – Burden Dimensions (7D) and Visual Analog Scale .....	30
7.3.15.3.	Burden Assessment Scale .....	30
7.3.15.4.	Birchwood Insight Scale (BIS) .....	31
7.3.15.5.	New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment subscales .....	31
7.3.15.6.	MINI International Neuropsychiatric Interview – Modules I and J .....	31
7.4.	Study Requirements and Restrictions .....	31
7.4.1.	Prohibited Medications .....	31
7.4.2.	Contraception and Pregnancy .....	31
8.	TREATMENT OF SUBJECTS .....	33
8.1.	Study Drug Dose and Administration .....	33
8.2.	Missed Doses .....	34
8.3.	Early Dosing .....	34
8.4.	Dose Adjustments for CYP450 Considerations .....	35
8.5.	Oral Aripiprazole Test Doses .....	36

8.6.	Treatment Adherence.....	36
8.7.	Blinding .....	36
9.	STUDY DRUG MATERIALS AND MANAGEMENT .....	37
9.1.	Study Drugs .....	37
9.2.	Accountability.....	37
9.3.	Handling and Disposal.....	37
10.	ASSESSMENT OF EFFICACY .....	38
11.	QUALITY OF LIFE, DAILY AND SOCIAL FUNCTIONING .....	39
12.	OTHER ASSESSMENTS .....	40
13.	ASSESSMENT OF SAFETY AND TOLERABILITY .....	41
13.1.	Definition of Adverse Event.....	41
13.2.	Definition of Serious Adverse Event.....	41
13.3.	Relationship to Study Drug .....	42
13.4.	Monitoring and Recording of Adverse Events .....	43
13.5.	Reporting of Serious Adverse Events.....	44
14.	STATISTICS .....	45
14.1.	Sample Size Considerations .....	45
14.2.	General Statistical Methodology .....	45
14.2.1.	Study Population.....	45
14.3.	Demographics and Baseline Data.....	45
14.4.	Efficacy Analyses .....	45
14.5.	Safety and Tolerability Analysis .....	45
14.6.	Analyses of Other Assessments.....	46
15.	DIRECT ACCESS TO SOURCE DATA/DOCUMENTS.....	47
15.1.	Study Monitoring.....	47
15.2.	Audits and Inspections.....	47
15.3.	Institutional Review Board/ Independent Ethics Committee .....	47
16.	QUALITY CONTROL AND QUALITY ASSURANCE .....	48
16.1.	Case Report Forms .....	48
16.2.	Confidentiality of Data .....	48
17.	ETHICAL CONSIDERATIONS.....	49
17.1.	Ethics Review .....	49

17.2.	Ethical Conduct of the Study .....	49
17.3.	Written Informed Consent .....	49
18.	DATA HANDLING AND RECORDKEEPING .....	51
18.1.	Data Capture .....	51
18.2.	Inspection of Records .....	51
18.3.	Retention of Records .....	51
18.4.	Use of Information and Publication Policy .....	52
19.	REFERENCES .....	53

### LIST OF TABLES

Table 1:	Schedule of Visits and Assessments.....	22
Table 2:	Clinical Laboratory Assessments .....	28
Table 3:	Aripiprazole Lauroxil Dosing Frequency and Site of Injection .....	33
Table 4:	Aripiprazole Lauroxil Doses Based on Oral Aripiprazole Total Daily Dose .....	34
Table 5:	Recommendation for Concomitant Oral Aripiprazole Supplementation Following Missed Doses <sup>a</sup> .....	34
Table 6:	Aripiprazole Lauroxil Dose Adjustments with Concomitant CYP450 Modulator Use .....	35
Table 7:	Adverse Event Causality Guidelines .....	43

### LIST OF FIGURES

Figure 1:	Study Design (ALK9072-A401).....	20
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**LIST OF APPENDICES**

Appendix A.	Columbia Suicide Severity Rating Scale (Sample)
Appendix B.	Extrapyramidal Symptom Rating Scale – Abbreviated (ESRS-A) (Sample)
Appendix C.	Clinical Global Impressions-Severity (CGI-S) (Sample)
Appendix D.	Brief Psychiatric Rating Scale (BPRS) (Sample)
Appendix E.	Sexual Functioning Subscale from Udvalg for Kliniske Undersøgelser (UKU) Side Effect Rating Scale (Sample)
Appendix F.	Changes in Sexual Functioning Questionnaire (Sample)
Appendix G.	Personal and Social Performance Scale (PSP) (Sample)
Appendix H.	Heinrichs-Carpenter Quality of Life Scale (QLS) (Sample)
Appendix I.	Negative Symptom Assessment-16 (NSA-16) (Sample)
Appendix J.	Modified Medication Satisfaction Questionnaire (Modified MSQ) (Sample)
Appendix K.	Sixth Edition of the Treatment Services Review (TSR-6) (Sample)
Appendix L.	Caregiver Quality of Life (CarerQOL) – Burden Dimensions (7D) [Brouwer WBF, 2006] and Visual Analog Scale (VAS) (Sample)
Appendix M.	Burden Assessment Scale (Sample)
Appendix N.	Birchwood Insight Scale (BIS) (Sample)
Appendix O.	New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT) Subscales (Sample)
Appendix P.	Mini International Neuropsychiatric Interview (M.I.N.I.) – Modules I and J (Sample)
Appendix Q.	List of Potent Cytochrome P450 3A4 (CYP3A4) Inducers and Moderate-to-Strong Inhibitors of 3A4 or 2D6

### 3. LIST OF ABBREVIATIONS

The following abbreviations are used in this study protocol.

Abbreviation or Term	Explanation or Definition
AE	adverse event
ALK-P	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical [classification system]
BIS	Birchwood Insight Scale
BPRS	Brief Psychiatric Rating Scale
CarerQOL-7D	Caregiver Quality of Life – Burden Dimensions
CGI-S	Clinical Global Impressions-Severity
CPK	creatine phosphokinase
CSA	Clinical Study Agreement
CSFQ-14	Changes in Sexual Functioning Questionnaire Short Form
CRO	contract research organization
C-SSRS	Columbia Suicide Severity Rating Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition
EC	Ethics Committee
ECG	electrocardiogram
eCRF	electronic case report form
EPS	Extrapyramidal symptoms
ESRS-A	Extrapyramidal Symptom Rating Scale - Abbreviated
ET	early termination
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGP	gamma-glutamyl transferase
HIV	human immunodeficiency virus
HR	heart rate
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

<b>Abbreviation or Term</b>	<b>Explanation or Definition</b>
IRB	Institutional Review Board
ISR	injection site reaction
LAI	long acting injectable antipsychotic
LDH	lactic dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
M.I.N.I.	Mini International Neuropsychiatric Interview
NSA-16	Negative Symptom Assessment-16
NY-AACENT	New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment
PANSS	Positive and Negative Syndrome Scale
PK	pharmacokinetics
QLS	Quality of Life Scale
RR	respiratory rate
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
TEAE	treatment-emergent adverse event
TSR-6	Sixth edition of the Treatment Services Review
UKU	Udvalg for Kliniske Undersøgelser
ULN	upper limit of normal
VAS	Visual Analog Scale
WHO	World Health Organization

#### 4. INTRODUCTION

Aripiprazole lauroxil is a covalently bonded, non-ester modification of aripiprazole, a second generation atypical antipsychotic agent, to form *N*-lauroyloxymethyl aripiprazole. It is formulated as an extended-release suspension to be administered via intramuscular (IM) injection into the gluteal or deltoid muscle. Conversion of aripiprazole lauroxil to aripiprazole is governed by dissolution of the aripiprazole lauroxil drug crystal from the injection site and subsequent enzyme-mediated cleavage, generating lauric acid and *N*-hydroxymethyl aripiprazole; the covalently bonded hydroxymethyl group *N*-hydroxymethyl aripiprazole dissociates, releasing aripiprazole and formaldehyde.

In clinical trials, treatment with aripiprazole lauroxil demonstrated statistically significant reductions from baseline in Positive and Negative Syndrome Scale (PANSS) total scores at Week 12, compared with placebo. Aripiprazole lauroxil was generally well tolerated for patients with schizophrenia at monthly IM dosing of 441 mg and 882 mg with the most common adverse events being insomnia, akathisia, and headache. This study is designed to demonstrate that 1) the transition from treatment with other long acting injectable antipsychotics (LAIs) to aripiprazole lauroxil is clinically feasible, and that 2) comparative assessments of the safety and tolerability profiles of the respective treatments is clinically important.

Paliperidone palmitate (Invega<sup>®</sup> Sustenna<sup>®</sup>) or risperidone long acting injection (Risperdal<sup>®</sup> Consta<sup>®</sup>) are commonly prescribed long-acting injectable antipsychotics. Paliperidone palmitate is a prodrug of paliperidone (9-hydroxy risperidone), the active metabolite of risperidone. As potent D2 antagonists, risperidone and paliperidone are pharmacologically distinct from aripiprazole's hypothesized principal mechanism of antipsychotic action, one of high affinity, partial dopamine agonism.

This study is an open label, 7-month prospective evaluation of the safety, tolerability, and efficacy of aripiprazole lauroxil in subjects with schizophrenia inadequately treated with risperidone long acting injection or paliperidone palmitate.

## **5. OBJECTIVES**

### **5.1. Primary Objective**

The primary objective of this study is to evaluate the safety, tolerability, and efficacy of aripiprazole lauroxil in subjects with schizophrenia who are inadequately treated with paliperidone palmitate or risperidone long acting injection.

### **5.2. Secondary Objectives**

The secondary objectives of this study are to:

- Evaluate quality of life, including daily and social functioning, after treatment with aripiprazole lauroxil
- Characterize the caregiver and healthcare burden



## 6. SELECTION AND WITHDRAWAL OF SUBJECTS

Each subject must meet all of the eligibility criteria to be qualified to participate in this study.

### 6.1. Subject Inclusion Criteria

Each subject must meet all of the following inclusion criteria to be qualified to participate in this study.

1. Is willing and able to provide informed consent
2. Is between 18 and 65 years of age, inclusive, at screening
3. Meets either of the following aripiprazole tolerability criteria:
  - Has demonstrated tolerability to test doses of oral aripiprazole during screening; OR
  - Has a history of tolerated use of aripiprazole
4. Has a diagnosis of schizophrenia as defined by Diagnostic and Statistical Manual of Mental Disorders, 5th Edition [DSM-5] ([American Psychiatric Association 2013](#)) criteria at screening
5. Is clinically stable as evidenced by no hospitalizations for acute psychiatric exacerbations within the 2 months prior to screening and prior to initiation on Day 1. Social hospitalizations are not applicable and should not disqualify subjects
6. Has a BPRS score of  $\geq 30$  and  $\leq 45$  at screening
7. Has received at least 3 doses of risperidone long acting injection (Risperdal Consta<sup>®</sup>) or paliperidone palmitate (Invega Sustenna<sup>®</sup>) prior to screening (may include the 'loading' dose). Has no antipsychotic medication regimen change for 4 weeks prior to Day 1 (medication or dose level, unless due to tolerability).
8. In the judgment of the investigator, is inadequately responding to or not tolerating long acting injectable (risperidone or paliperidone), and is likely to benefit from a transition to aripiprazole lauroxil
9. Agrees to abide by the contraceptive requirements of the protocol (as defined in [Section 7.4.2](#))
10. Has an identified reliable informant (caregiver), in the opinion of the investigator
11. Resides in a stable living situation, in the opinion of the investigator
12. Is fluent (oral and written) in the language in which standardized tests will be administered, and can be reliably rated

## 6.2. Subject Exclusion Criteria

Each subject must not have any of the following conditions to be qualified to participate in this study.

1. Is currently pregnant or breastfeeding, or is planning to become pregnant during the study
2. Has received Invega Trinza<sup>®</sup> (3-month formulation of paliperidone palmitate), aripiprazole lauroxil or IM depot aripiprazole within 6 months of screening
3. Has a history of poor or inadequate response to oral or injectable aripiprazole
4. Has participated in a clinical trial involving any investigational product (ie, drug, device, biologic) within the past 3 months, or is currently participating in a clinical trial involving an investigational product
5. Has a history of psychopathology other than schizophrenia as indicated by any of the following:
  - Has a DSM-5 ([American Psychiatric Association 2013](#)) diagnosis of moderate to severe substance use disorder (except tobacco use disorder), within the 12 months prior to screening
  - Has any primary DSM-5 diagnosis other than schizophrenia within the 12 months prior to screening or upon admission (depression, schizoaffective disorder, bipolar disorder, or neurocognitive disorder)
6. In the opinion of the investigator, the subject is a danger to himself/herself or others at screening or upon admission or meets one of the following criteria for elevated suicidal ideation or behavior:
  - At screening (using “Baseline” version of the C-SSRS):
    - Answers “Yes” to items 4 or 5 of the C-SSRS “Suicidal Ideation” section with the most recent episode occurring within the 6 months prior to screening
    - Answers “Yes” to any of the 5 items C-SSRS “Suicidal Behavior” with an episode occurring within the 1 year prior to screening
  - Upon entry (on Day 1) (using “Since Last Visit” version of the C-SSRS):
    - Answers “Yes” to items 4 or 5 of the C-SSRS “Suicidal Ideation”
    - Answers “Yes” to any of the 5 items of the C-SSRS “Suicidal Behavior”
7. Has a history or current evidence of a clinically significant condition or abnormality (including clinical laboratory test results or ECG findings) that in the investigator’s opinion could preclude safe participation in this study, or prevent, limit, or confound protocol specified assessments
8. Has any of the following conditions or abnormalities at screening:
  - In the opinion of the investigator or sponsor has uncontrolled diabetes, heart disease or stroke

- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels  $\geq 3$  times the upper limit of the laboratory reference range at screening
  - An absolute neutrophil count  $\leq 1.5 \times 10^3 \mu\text{L}$  (or for black patients with history of “benign neutropenia”, a sustained count of  $\leq 1 \times 10^3 \mu\text{L}$ )
  - A platelet count  $\leq 100 \times 10^3 \mu\text{L}$
  - Has a QT interval (corrected using the Fridericia formula; QTcF)  $> 450$  milliseconds for men or  $> 470$  milliseconds for women at screening
9. Has a history of neuroleptic malignant syndrome or clinically significant tardive dyskinesia
10. Is taking both strong CYP2D6 and strong CYP3A4 inhibitors. In addition, patients who are known CYP2D6 poor metabolizers taking strong CYP3A4 inhibitors are excluded
11. Has a positive urine drug test for illicit use of amphetamines, barbiturates, cocaine, methadone, opiates, phencyclidine, at screening. Repeat testing may be performed if positive results cannot be confirmed by a history of presumed active substance use, or use of prescribed medications which may account for the positive urine drug test results
12. Is employed by Alkermes, PPD the investigator, the study center (includes permanent or temporary contract workers and designees responsible for the conduct of the study), or a third-party agent of this study or is immediate family of an employee of Alkermes, PPD the investigator, the study center, or other third-party agent
- Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.

### 6.3. Subject Withdrawal

A subject may be discontinued from the study at any time if the subject, investigator, or sponsor determines that it is not in the best interest of the subject to continue participation. Reasons for discontinuation include:

- AE
- Lost to follow-up
- Lack of Efficacy
- Withdrawal by subject
- Non-compliance with study drug
- Other
- Pregnancy
- Protocol deviation
- Study terminated by sponsor

Subjects completing all visits up to and including Day 169 will be considered completers.

If a subject withdraws from the study for any reason, any ongoing AEs will be followed until resolution, until deemed stable by the investigator, or until the subject is deemed by the investigator to be lost to follow-up. If, in the opinion of the investigator, it is necessary to monitor a subject beyond the final study visit, the study period may be extended as necessary. In such instances, the sponsor and the investigator will agree to an acceptable schedule.

In the event that a subject chooses to withdraw from the study, the investigator should make a reasonable effort to ascertain the reason(s) for withdrawal, while fully respecting the subject's rights. Subjects are to be asked to return to the clinic for an ET visit. If the subject fails or refuses to return to the study center, an attempt must be made to contact the subject by telephone in order to assess as many safety and efficacy parameters as possible. All data collected over the telephone must be documented and kept in the subject's record.

The investigator must maintain a record of all subjects who fail to complete the study. The reason for study discontinuation will be made on the appropriate electronic case report form (eCRF). If a subject is lost to follow-up, a reasonable attempt to contact the subject must be made and documented.

#### **6.4. Replacement of Subjects**

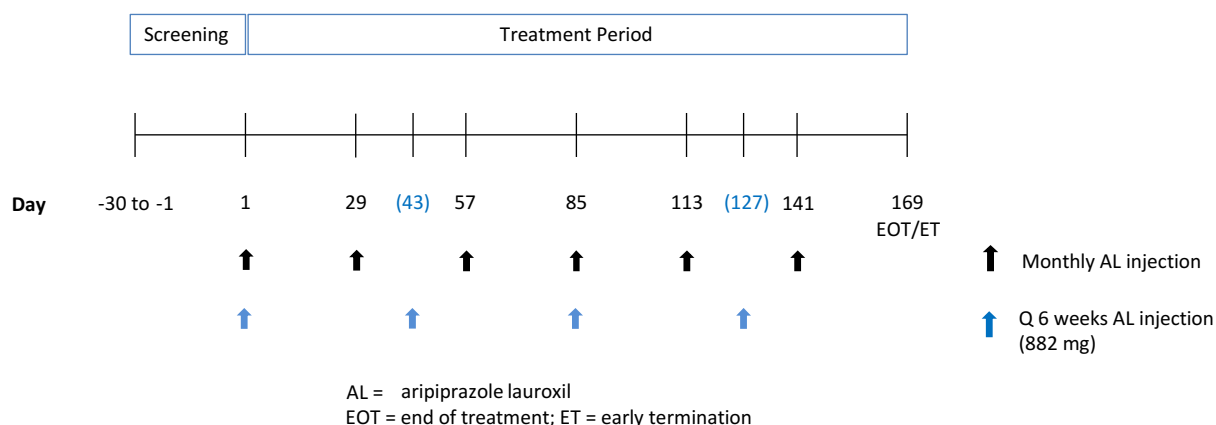
Subjects who withdraw before completion of the study will not be replaced.

## 7. STUDY DESIGN

### 7.1. Overall Study Design and Plan

This is an open-label study in approximately 50 subjects who are switched to aripiprazole lauroxil from long acting injectable risperidone or paliperidone palmitate. In total, subjects will participate for approximately 7 months, including a screening period of up to 30 days, and will be administered 4 to 6 doses of IM aripiprazole lauroxil (Figure 1). Dosing may occur in monthly (441 mg, 662 mg, or 882 mg) or 6-week (882 mg only) intervals. The dose and frequency of dosing will be at the discretion of the investigator, based on the subject's history, dose selected, and on dosing instructions (Section 8.1).

**Figure 1: Study Design (ALK9072-A401)**



Potential subjects will be evaluated for eligibility according to the inclusion and exclusion criteria at a screening visit and again on Day 1. The first dose of aripiprazole lauroxil will be administered on Day 1. Subjects will receive their first dose of aripiprazole lauroxil no earlier than one week and not later than six weeks following their previous injection of paliperidone palmitate or risperidone. The cross-tapering from risperidone or paliperidone to aripiprazole lauroxil is facilitated by the gradual disappearance of plasma risperidone/paliperidone while aripiprazole is concomitantly released from the initial IM aripiprazole lauroxil injection.

For subjects who have never taken aripiprazole, two test doses of oral aripiprazole 5 mg will be administered during the screening period. Only subjects who exhibit tolerability to oral aripiprazole (either following test doses or by past experience) are eligible to enroll in the study.

On Day 1, qualified subjects will be administered a single IM injection of aripiprazole lauroxil into the gluteal (441, 662 or 882 mg) or deltoid muscle (441 mg), according to the dosing instructions (Section 8.1). Following the first injection, subjects will return to the study site monthly or every 6 weeks (882 mg, gluteal IM only) for IM aripiprazole lauroxil administration and outpatient assessments. Additional outpatient assessments may be scheduled at the discretion of the investigator.

Efficacy will be evaluated based on Clinical Global Impressions-Severity (CGI-S) and Brief Psychiatric Rating Scale (BPRS) responses.

Safety and tolerability will be evaluated based on adverse events (AEs), injection site reactions (ISRs), clinical laboratory data, vital sign data, Columbia Suicide Severity Rating Scale (C-SSRS) responses, and Abbreviated Extrapyramidal Symptom Rating Scale (ESRS-A) scores. Potential changes in informant-rated cognition, insight, treatment satisfaction, quality of life, daily and social functioning, caregiver and healthcare burden, and psychosocial care needs following a transition to aripiprazole lauroxil will be examined. Total healthcare costs as measured by TSR-6-(Modified for Mental Health) survey will also be evaluated.

## **7.2. Schedule of Visits and Assessments**

The schedules of visits and assessments are shown in [Table 1](#).

For a missed visit, the site should attempt to contact the subject to reschedule.

Premature discontinuation procedures are provided in [Section 6.3](#).

**Table 1: Schedule of Visits and Assessments**

	Screening	Treatment Period <sup>1)</sup>						
		Day 1	Month 1	Month 2	Month 3 <sup>2)</sup>	Month 4	Month 5	Month 6 EOT/ET
	V1	V2	V3	V4	V5	V6	V7	V8
Visit windows (days)		Day 1	22-36	37-64	65-92	93-120	121-148	149-183
4 week dosing target day		1	29	57	85	113	141	169
6 week dosing target day		1	May skip Visit <sup>3)</sup>	43	85	May skip Visit <sup>3)</sup>	127	169
Study Drug Administration		Injections are to be given monthly (6 total injections) or every 6 weeks (4 total injections) based on the dosing regimen selected; After Day 1, subsequent injections will occur 28 or 42 days following the previous injection						
Informed Consent	X							
Eligibility Criteria Review <sup>4)</sup>	X	X						
Oral Aripiprazole Test Dose Administration <sup>5)</sup>	X							
Drug Screen <sup>6)</sup>	X							
12-Lead ECG	X							
Demographics and Medical History	X							
Reason for switching paliperidone/risperidone	X							
MINI (Modules I & J)	X							X
Height	X							
Pregnancy Testing <sup>7)</sup>	X	X						

**Table 1: Schedule of Visits and Assessments (Continued)**

	Screening	Treatment Period <sup>1)</sup>						
		Day 1	Month 1	Month 2	Month 3 <sup>2)</sup>	Month 4	Month 5	Month 6 EOT/ET
	V1	V2	V3	V4	V5	V6	V7	V8
Visit windows (days)		Day 1	22-36	37-64	65-92	93-120	121-148	149-183
Physical Exam <sup>8)</sup>	X	X						
Adverse Event Monitoring	X	X	X	X	X	X	X	X
Concomitant Medication Review	X	X	X	X	X	X	X	X
Vital Signs, Weight, Waist Circumference <sup>9)</sup>	X	X	X	X	X	X	X	X
ESRS-A		X			X			X
Clinical Lab Tests <sup>10)</sup>	X	X	X <sup>11)</sup>	X <sup>11)</sup>	X <sup>11)</sup>			X
Modified MSQ	X <sup>12)</sup>							X <sup>12)</sup>
Modified UKU	X	X						X
CSFQ-14	X	X						X
Injection Site Evaluation <sup>13)</sup>		X	X	X	X	X	X	X
C-SSRS <sup>14)</sup>	X	X	X	X	X	X	X	X
TSR-6-Modified	X	X	X	X	X	X	X	X
CGI-S	X	X	X	X	X	X	X	X
BPRS	X	X	X	X	X	X	X	X
QLS	X				X			X
NSA-16	X				X			X
NY-AACENT	X							X



**Table 1: Schedule of Visits and Assessments (Continued)**

	Screening	Treatment Period <sup>1)</sup>						
		Day 1	Month 1	Month 2	Month 3 <sup>2)</sup>	Month 4	Month 5	Month 6 EOT/ET
	V1	V2	V3	V4	V5	V6	V7	V8
Visit windows (days)		Day 1	22-36	37-64	65-92	93-120	121-148	149-183
PSP	X				X			X
BIS	X							X
Burden Assessment Scale	X							X
CarerQOL-7D+VAS	X							X

EOT= end of treatment; ET= early termination; ECG= electrocardiogram; MINI = Mini International Neuropsychiatric Interview; ESRs-A=Abbreviated Extrapyramidal Symptom Rating Scale; MSQ= Medication Satisfaction Questionnaire; UKU= Udvalg for Kliniske Undersøgelser Side Effect Rating Scale; CSFQ-14=Changes in Sexual Functioning Questionnaire Short Form; C-SSRS= Columbia Suicide Severity Rating Scale; TSR-6= Sixth edition of the Treatment Services Review; CGI-S= Clinical Global Impressions-Severity; BPRS= Brief Psychiatric Rating Scale; QLS = Quality of Life Scale; NSA-16 = Negative Symptom Assessment-16; NY-AACENT= New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment; PSP= Personal and Social Performance scale; BIS= Birchwood Insight Scale; CarerQOL-7D+VAS= Caregiver Quality of Life – burden dimensions and visual analog scale

<sup>1)</sup> For all visits other than Screening and Day 1, the visit will be anchored to the previous visit (based on dosing regimen schedule)

<sup>2)</sup> In the event the Month 3 visit is missed or skipped, the additional assessments required at the Month 3 visit (ESRS-A, prolactin, QLS, NSA-16, PSP) should be conducted (via unscheduled assessment) at the subject's next visit

<sup>3)</sup> Visits may be skipped for subjects on a 6 week dosing regimen

<sup>4)</sup> Eligibility Review Form must be reviewed by **PPD** Clinical Surveillance Team (CST) prior to enrolling a subject on Day 1

<sup>5)</sup> Only for prospective subjects who have never received aripiprazole. The oral aripiprazole test doses will consist of 5 mg/day for 2 consecutive days during the screening period. The first test dose should be administered at the clinic.

<sup>6)</sup> Urine drug screen via dipstick at screening. The urine drug screen includes amphetamines, barbiturates, cocaine, methadone, opiates, and phencyclidine. Rescreening may be performed if positive results cannot be confirmed by a history of presumed active substance use or use of prescribed medications, which may account for the positive urine drug test results.

<sup>7)</sup> Urine pregnancy testing will be completed for ALL women. At screening, pregnancy test should be completed prior to the administration of the first oral aripiprazole test dose, where applicable. On Day 1, testing will be performed before dosing.

<sup>8)</sup> Full physical examination at screening; brief physical examination on Day 1; symptom directed physical exams may be performed as needed at the Investigator's discretion.

<sup>9)</sup> Vital signs include blood pressure, heart rate, respiratory rate, and body temperature,

<sup>10)</sup> Includes biochemistry (including prolactin), hematology, and urinalysis.

<sup>11)</sup> Prolactin only will be measured at Month 1, Month 2 and Month 3.

<sup>12)</sup>Modified MSQ question #1 only at screening; the entire modified MSQ will be completed at Visit 8 (EOT)

<sup>13)</sup>The injection site and surrounding area will be evaluated following each injection and monitored so long as there are reactions to be monitored; if there are no observed reactions, continuing evaluation is not necessary

<sup>14)</sup>“Baseline” version used at screening; “since last visit” used at all subsequent visits

### **7.3. Study Procedures Descriptions**

Details of the study procedures are described below. The overall schedules of assessments are provided in [Table 1](#).

#### **7.3.1. Informed Consent**

The nature of the study and its risks and benefits will be explained to the subject and caregiver by the principal investigator or designated study personnel as outlined in [Section 17.3](#).

Prior to the administration of any study-specific procedures, authorized study personnel will obtain written informed consent from each potential subject and caregiver.

#### **7.3.2. Eligibility Review**

An eligibility review will be conducted by the investigator at the visits specified in [Table 1](#) using the subject inclusion criteria in [Section 6.1](#) and exclusion criteria in [Section 6.2](#).

#### **7.3.3. Demographics and Medical History**

Subject's demographic data and medical history will be reviewed and documented at the time point(s) specified in [Table 1](#).

#### **7.3.4. Concomitant Medication Review**

At the time point(s) specified in [Table 1](#), prospective subjects will be asked about the medications they have taken since the last visit and are currently taking, including prescription and nonprescription medications, vitamins, and supplements.

The investigator will record the following data on all medications used by the subject: name, dose, regimen, route of administration, start and stop dates, and the indication for use.

#### **7.3.5. Vital Signs, Weight, and Waist Circumference**

Vital signs (blood pressure, heart rate, respiratory rate, and body temperature), waist circumference, and weight will be assessed at the time point(s) specified in [Table 1](#). Blood pressure, heart rate, and respiratory rate will be measured after the subject has been resting in a seated or supine position for at least 5 minutes.

#### **7.3.6. Physical Examination**

A full physical examination will be performed at screening and a brief physical exam performed on Day 1. Symptom-directed physical exams may be performed as needed at the Investigator's discretion.

#### **7.3.7. 12-Lead Electrocardiogram**

A 12-lead electrocardiogram (ECG) will be conducted at screening only.

**7.3.8. Columbia Suicide Severity Rating Scale**

The PI or designee will administer the C-SSRS ([Appendix A](#)) according to the schedule in [Table 1](#). At screening, the “Baseline” version will be administered ([Posner, Brent et al. 2009](#)), and at all other visits, the “Since Last Visit” version will be administered ([Posner, Brent et al. 2009](#)). For “Since Last Visit” versions, subjects should be asked to report on ideation and behavior since the last scheduled C-SSRS assessment. The C-SSRS should be administered by a clinician trained to assess and manage suicidal ideation and behavior.

**7.3.9. Extrapyramidal Symptom Rating Scale – Abbreviated**

The ESRS-A is a questionnaire that assesses the severity and/or frequency of drug induced movement disorders (eg. Parkinsonism, dystonia, dyskinesia, and akathisia) ([Chouinard and Margolese 2005](#)). The investigator or designee will administer the ESRS-A scale at time points specified in [Table 1](#). A sample of the ESRS-A can be found in [Appendix B](#).

**7.3.10. Laboratory Assessments****7.3.10.1. Drug Testing**

Subjects will complete a urine drug test for illicit amphetamines, barbiturates, cocaine, methadone, opiates, phencyclidine, at screening. A positive drug test will exclude the subject from the study. Repeat testing may be performed if positive results cannot be confirmed by a history of presumed active substance use or use of prescribed medications which account for the positive urine drug test results.

**7.3.10.2. Hematology, Biochemistry, and Urinalysis**

Blood and urine samples will be collected at the time points specified in [Table 1](#) for specific hematology, biochemistry, and urinalysis assessments that are listed in [Table 2](#). Samples will be analyzed by a central laboratory. Laboratory assessments may be repeated at the investigator’s discretion.

**Table 2: Clinical Laboratory Assessments**

Hematology	Biochemistry	Urinalysis
<ul style="list-style-type: none"> <li>• Hematocrit</li> <li>• Hemoglobin</li> <li>• Platelets</li> <li>• Red blood cell count</li> <li>• Total and differential (absolute) white blood cell count</li> </ul>	<ul style="list-style-type: none"> <li>• Albumin</li> <li>• Creatine phosphokinase(CPK)</li> <li>• Glucose</li> <li>• Lactic dehydrogenase (LDH)</li> <li>• Potassium</li> <li>• Sodium</li> <li>• Total protein</li> <li>• Alanine aminotransferase(ALT)</li> <li>• Alkaline phosphatase(ALK-P)</li> <li>• Aspartate aminotransferase(AST)</li> <li>• Gamma-glutamyl transferase (GGT)</li> <li>• Total bilirubin</li> <li>• Prolactin</li> <li>• Blood urea nitrogen</li> <li>• Creatinine</li> <li>• HbA1c</li> <li>• Total cholesterol</li> <li>• LDL</li> <li>• HDL</li> <li>• Triglycerides</li> <li>• TSH, <i>at screening only</i></li> </ul>	<ul style="list-style-type: none"> <li>• Bilirubin</li> <li>• Color and appearance</li> <li>• Glucose</li> <li>• Nitrite</li> <li>• Occult blood</li> <li>• pH</li> <li>• Protein</li> <li>• Specific gravity</li> <li>• Urobilinogen</li> </ul>

**7.3.10.3. Pregnancy Testing**

Urine pregnancy testing will be completed for all women at the time points specified in [Table 1](#). Pregnancy testing will be performed before administration of the first 5 mg aripiprazole test dose (where required) at Screening and before dosing on Day 1.

Results must be negative for initial study eligibility and continued participation.

**7.3.11. Drug Dispensation and Reconciliation**

[Section 8](#) provides information related to drug dispensing procedures. Study drug will be administered at the time point(s) specified in [Table 1](#) and reviewed with the subject.

**7.3.12. Adverse Event Monitoring**

AEs will be monitored continuously from the time a subject signs the informed consent document until the completion of the final study visit (see [Table 1](#)). AEs and serious adverse

events (SAEs) are defined in [Section 13.1](#) and [13.2](#), respectively. [Section 13.4](#) provides guidance on the monitoring and reporting requirements for AEs. [Section 13.5](#) provides guidance on the reporting requirements for SAEs.

### **7.3.13. Efficacy Assessments**

#### **7.3.13.1. Clinical Global Impressions-Severity**

The investigator or designee will complete the Clinical Global Impression – Severity (CGI-S) ([Appendix C](#)) scale ([Guy 2000](#)) at screening and at every time point as identified in [Table 1](#).

#### **7.3.13.2. Brief Psychiatric Rating Scale**

The investigator or designee will complete the Brief Psychiatric Rating Scale (BPRS) ([Appendix D](#)) at screening and at every time point as identified in [Table 1](#).

### **7.3.14. Quality of Life, Daily, and Social Functioning Assessments**

#### **7.3.14.1. Sexual Functioning Subscale from Udvalg for Kliniske Undersøgelser Side Effect Rating Scale**

The sexual functioning subscale from the UKU Side Effect Rating Scale ([Appendix E](#)) contains 7 items for males and 9 items for females ([Lingjaerde, Ahlfors et al. 1987](#), [Lindstrom, Lewander et al. 2001](#)). Each item is rated on a 4-point scale (0 = none or doubtful, 1 = present to a mild degree, 2 = present to a moderate degree, and 3 = present to a severe degree). This scale will be completed by the patient at the time points specified in [Table 1](#).

#### **7.3.14.2. Changes in Sexual Functioning Questionnaire Short Form**

The CSFQ-14 ([Appendix F](#)) is a 14-item rating scale that evaluates sexual functioning in each domain of the sexual response cycle ([Keller, McGarvey et al. 2006](#)). The subjects rate their sexual functioning on a 5-point Likert scale. Higher scores indicate more sexual dysfunction. The CSFQ will be completed by the patient at the time points specified in [Table 1](#).

#### **7.3.14.3. Personal and Social Performance Scale**

The investigator or designee will complete the 5-point Personal and Social Performance (PSP) ([Appendix G](#)) scale ([Patrick, Burns et al. 2009](#)) at the time points identified in [Table 1](#).

#### **7.3.14.4. Heinrichs-Carpenter Quality of Life Scale**

The QLS is a clinician-rated scale that is used to assess health-related quality of life and functioning in patients with schizophrenia during the preceding 4 weeks ([Heinrichs, Hanlon et al. 1984](#)) ([Appendix H](#)). The QLS consists of 21 items in 4 major domains (Intrapsychic Foundations, Interpersonal Relations, Instrumental Role, and Common Objects and Activities). Following a semi-structured interview, each item is rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). The QLS will be completed at the time points specified in [Table 1](#).

**7.3.14.5. Negative Symptom Assessment-16**

The Negative Symptom Assessment is a clinician-rated scale that is used to evaluate the presence, severity, and range of the negative symptoms that often impact the quality of life of those with schizophrenia (Axelrod, Goldman et al. 1993) (Appendix I). The NSA-16 consists of 16 items with 5 domains (Communication, Emotion/Affect, Social Involvement, Motivation, and Retardation). Each item is rated on a 6-point scale that ranges from 1 to 6 with higher scores indicating more severe pathology. The NSA-16 will be completed at the time points specified in Table 1.

**7.3.14.6. Modified Medication Satisfaction Questionnaire**

The Modified MSQ (Appendix J) is a 3-item self-report patient satisfaction questionnaire which assesses the level of patient satisfaction with medication. Subjects rate their satisfaction with their current medication, their preference for their current medication versus the one taken prior to the study, and their opinion on the side effects of their current medication versus the one taken prior to the study. Ratings are on a 5-point Likert scale. The Modified MSQ will be collected at the time points identified in Table 1.

**7.3.15. Other Assessments****7.3.15.1. Sixth edition of the Treatment Services Review (TSR-6)-Modified for Mental Health**

The modified TSR-6 (Appendix K) is a brief structured interview to assess specific services provided to patients; this version was modified for use in a patient population for chronic mental illness. The modified TSR-6 focuses on services for five potential problem areas: medical condition, employment and support, legal status, family/social relations, and psychiatric function. Patients are asked about the services that they received in the past 28-42 days. The modified TSR-6 consists of 22 items; it will be administered at the time points identified in Table 1.

**7.3.15.2. Caregiver Quality of Life – Burden Dimensions (7D) and Visual Analog Scale**

The CarerQOL-7D and VAS (Brouwer, van Exel et al. 2006) (Appendix L) measures care-related quality of life in informal caregivers. The burden component utilizes 7 items to assess burden, and the valuation component uses a VAS to ascertain level of happiness. The burden items require caregivers to indicate whether they have ‘no’, ‘some’ or ‘a lot’ of problems or fulfillment/ support regarding the given dimension. For problem-related items, ‘no’, ‘some’ and ‘a lot’ are scored 3, 2, and 1, respectively. For fulfillment/support items, reverse scoring applies, so a high score indicates a high level of burden. The valuation component allows for the calculation of a score from 0 (completely unhappy) to 10 (completely happy). The CarerQOL-7D and VAS will be completed by the designated caregiver at the time points identified in Table 1.

**7.3.15.3. Burden Assessment Scale**

The Burden Assessment Scale (Appendix M) is a 19-item scale completed by the caregiver that focuses on specific subjective and objective consequences of families caring for individuals with severe mental disorders (Reinhard, Gubman et al. 1994). Respondents are required to indicate

whether they have experienced each of the types of burden - 'Not at all', 'A little', 'Some' or 'A lot' - in the past four weeks. These are scored 1, 2, 3, and 4 respectively. A higher score indicates more perceived burden. The Burden Assessment Scale will be completed by the designated caregiver at the time points identified in [Table 1](#).

#### **7.3.15.4. Birchwood Insight Scale (BIS)**

The BIS ([Appendix N](#)) is an 8-item self-report measure addressing the three components of insight: awareness of illness, relabeling of symptoms (ie, attribution of one's symptoms as part of one's disorder), and need for treatment ([Birchwood, Smith et al. 1994](#)). Possible responses of "agree," "unsure," or "disagree" are scored on a Likert-type scale ranging from 0 to 2. The total score will be summed for a BIS total score (range = 0-16), with higher scores indicating greater insight. The BIS will be completed by the subject at the time points identified in [Table 1](#).

#### **7.3.15.5. New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment subscales**

The NY-AACENT subscales ([Appendix O](#)) are used to detect changes in cognitive function subsequent to pharmacological or similar treatments for neurological or psychiatric problems ([Opler, Antonius et al. 2015](#)). It is comprised of seven items for the patient, seven items for the caregiver, and seven items for the clinician derived from these seven domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. The NY-AACENT will be administered at the time points identified in [Table 1](#).

#### **7.3.15.6. MINI International Neuropsychiatric Interview – Modules I and J**

The MINI is a short, clinician-administered, structured diagnostic interview for making DSM-5 diagnoses ([Appendix P](#)). The MINI has been validated against the much longer Structured Clinical Interview for DSM diagnoses (SCID-5). Modules I (Alcohol Use Disorder) and J (Substance Use Disorder) from the MINI will be administered as shown in [Table 1](#).

### **7.4. Study Requirements and Restrictions**

#### **7.4.1. Prohibited Medications**

Concomitant use of potent oral CYP3A4 inhibitors **and** CYP2D6 inhibitors is to be avoided. In addition, subjects with known CYP2D6 poor metabolism should not receive strong oral CYP3A4 inhibitors during the study. During the study, dose adjustment may be necessary in the event of potent oral CYP2D6 inhibitor, or a CYP3A4 inhibitor or inducer, use. For example, the use of CYP3A4 inducers may require dose escalation. Investigators should consult the Medical Monitor for questions regarding any such dose adjustments. A list of common CYP3A4 inducers or inhibitors and CYP2D6 inhibitors is provided in [Appendix Q](#).

#### **7.4.2. Contraception and Pregnancy**

All male and female subjects must agree to use an acceptable method of contraception for the duration of the study unless they are surgically sterile or post-menopausal (see below). The following are considered acceptable methods of contraception:



1. Double-barrier protection (eg, a condom with spermicide or a diaphragm with spermicide)
2. Intrauterine device (IUD)
3. Oral contraceptive pills or other hormonal methods (eg, a vaginal ring, contraceptive patch, contraceptive implant)

Subjects who are abstinent are eligible, provided they agree to use an acceptable contraceptive method should they become sexually active.

Subjects who are surgically sterile are exempt from the requirement to use contraception. Women who have undergone a hysterectomy, bilateral tubal ligation, or bilateral salpingo-oophorectomy are considered surgically sterile. Men who have undergone a vasectomy or bilateral orchiectomy are considered surgically sterile. Partner vasectomy is not considered an approved acceptable method of contraception for a female subject.

Women who are postmenopausal are also exempt from the requirement to use contraception. For the purpose of this study, postmenopausal is defined as the permanent cessation of menstruation for at least 12 months prior to screening in women who are 45 years of age or older.

If a subject becomes pregnant while participating in the study, she will be discontinued from study drug immediately. Pregnancy is not considered an AE, however pregnancy, whether a female study subject or the partner of a male study subject, must be immediately documented on a Pregnancy Form and faxed to <sup>PPD</sup> [REDACTED] at the SAE reporting fax number ([Section 13.5](#)) within 24 hours of the investigator becoming aware of the pregnancy. Additional follow-up may be required.

## 8. TREATMENT OF SUBJECTS

### 8.1. Study Drug Dose and Administration

The initial dose of aripiprazole lauroxil will be selected according to the investigator's judgment and will be prepared and administered in accordance with the Directions for Use.

Depending on individual patient's needs, treatment with aripiprazole lauroxil can be initiated at a dose of 441 mg, 662 mg or 882 mg administered monthly, which corresponds to 300 mg, 450 mg and 600 mg of aripiprazole, respectively. Treatment may also be initiated with the 882 mg dose every 6 weeks.

Subjects will receive their first dose of aripiprazole lauroxil no earlier than one week and not later than 6 weeks following their previous dose of injectable risperidone or paliperidone. Due to safety concerns and the potential for rapid emergence of adverse events including akathisia, dystonia and EPS, oral aripiprazole dosing for 21 days after the initial dose of aripiprazole lauroxil is not recommended. Cross-tapering patients from long acting injectable risperidone or paliperidone palmitate to aripiprazole lauroxil is facilitated by the gradual disappearance of plasma risperidone/paliperidone while aripiprazole is concomitantly released from the initial IM aripiprazole lauroxil injection.

Administer aripiprazole lauroxil either in the deltoid muscle (441 mg dose only) or gluteal muscle (441 mg, 662 mg or 882 mg). See Table 3.

**Table 3: Aripiprazole Lauroxil Dosing Frequency and Site of Injection**

Dose	Dosing Frequency	Site of Intramuscular Injection
441 mg	Monthly	Deltoid or Gluteal
662 mg	Monthly	Gluteal
882 mg	Monthly or every 6 weeks	Gluteal

During the course of the study, the PI may adjust the dose of aripiprazole lauroxil. Stepwise dose decreases will be allowed for tolerability, accounting for the slow and prolonged release of aripiprazole lauroxil. Increased dose or frequency (e.g. to monthly from every 6 weeks) may be considered for inadequate efficacy. To allow for the gradual stepwise increase in aripiprazole levels with initial injections, dose increases may be performed after the second injection. Schedule changes, from monthly to every 6 weeks (or the reverse) will also be allowed after the second injection. Dose changes due to the medical need to initiate concomitant CYP modulators may be performed at any time if the concomitant medication is necessary for more than 2 weeks.

After the first change, further dose or schedule changes should be made in consultation with the PPD Medical Monitor and must account for the gradual increase in plasma aripiprazole levels following the initial monthly doses.

Table 4 outlines the recommended starting dose for subjects who have been historically stabilized on oral aripiprazole:

**Table 4: Aripiprazole Lauroxil Doses Based on Oral Aripiprazole Total Daily Dose**

Oral Aripiprazole Dose	Intramuscular Aripiprazole Lauroxil Dose
10 mg	441 mg
15 mg	662 mg
20 mg or higher	882 mg

## 8.2. Missed Doses

When a dose is missed, administer the next injection of aripiprazole lauroxil as soon as possible. If the time elapsed since the last aripiprazole lauroxil injection exceeds the length of time noted in Table 5, use oral aripiprazole supplementation with the next aripiprazole lauroxil injection as recommended below.

**Table 5: Recommendation for Concomitant Oral Aripiprazole Supplementation Following Missed Doses<sup>a</sup>**

Dose of Patient's Last Aripiprazole Lauroxil Injection	Length of Time Since Last Injection		
	No Oral Supplementation Required	Supplement with 7 Days Oral Aripiprazole	Supplement with 21 Days Oral Aripiprazole
Monthly 441 mg	≤ 6 weeks	> 6 and ≤ 7 weeks	> 7 weeks
Monthly 662 mg	≤ 8 weeks	> 8 and ≤ 12 weeks	> 12 weeks
Monthly 882 mg	≤ 8 weeks	> 8 and ≤ 12 weeks	> 12 weeks
882 mg every 6 weeks	≤ 8 weeks	> 8 and ≤ 12 weeks	> 12 weeks

<sup>a</sup> Oral aripiprazole supplementation dosage may be per Table 4.

## 8.3. Early Dosing

The aripiprazole lauroxil injection should not be given earlier than 14 days after the previous injection.

#### 8.4. Dose Adjustments for CYP450 Considerations

In subjects taking strong CYP2D6 or CYP3A4 modulators the initial and subsequent dose of aripiprazole lauroxil should be selected based upon the recommendations of Table 6 below.

Once stabilized on aripiprazole lauroxil, refer to the dosing recommendations below for patients taking CYP2D6 inhibitors, CYP3A4 inhibitors, or CYP3A4 inducers:

- No dosage changes recommended for aripiprazole lauroxil, if CYP450 modulators are added for less than 2 weeks.
- Make dose changes to aripiprazole lauroxil if CYP450 modulators are added for greater than 2 weeks (see Table 6).

**Table 6: Aripiprazole Lauroxil Dose Adjustments with Concomitant CYP450 Modulator Use**

Concomitant Medicine	Dose Change for ARIPIPRAZOLE LAUROXIL <sup>a</sup>
Strong CYP3A4 Inhibitor	Reduce the dose of ARIPIPRAZOLE LAUROXIL to the next lower strength. No dosage adjustment is necessary in patients taking 441 mg ARIPIPRAZOLE LAUROXIL, if tolerated. <i>For patients known to be poor metabolizers of CYP2D6:</i> Reduce dose to 441 mg from both higher doses. No dosage adjustment is necessary in patients taking 441 mg ARIPIPRAZOLE LAUROXIL, if tolerated.
Strong CYP2D6 Inhibitor	Reduce the dose of ARIPIPRAZOLE LAUROXIL to the next lower strength. No dosage adjustment is necessary in patients taking 441 mg ARIPIPRAZOLE LAUROXIL, if tolerated. <i>For patients known to be poor metabolizers of CYP2D6:</i> No dose adjustment required.
Both Strong CYP3A4 Inhibitor and Strong CYP2D6 Inhibitor	Avoid use for patients at 662 mg or 882 mg dose. No dosage adjustment is necessary in patients taking 441 mg ARIPIPRAZOLE LAUROXIL, if tolerated. <i>For patients known to be poor metabolizers of CYP2D6:</i> Same as for extensive metabolizers.
CYP3A4 Inducers	No dose adjustment for 662 mg and 882 mg dose, increase the 441 mg dose to 662 mg. <i>For patients known to be poor metabolizers of CYP2D6:</i> Same as for extensive metabolizers.

<sup>a</sup> For the 882 mg dose administered every 6 weeks, the next lower strength should be 441 mg administered every 4 weeks.

Augmentation with oral antipsychotics is permitted per clinical judgment and should be recorded as a concomitant medication separately from other concomitant medications.

Sites must have written procedures in place detailing the healthcare personnel required to be on site during subject dosing, the availability of equipment and medications necessary to treat an emergency (should it occur), and the process for transferring a subject to a medical facility if necessary.

**8.5. Oral Aripiprazole Test Doses**

Oral aripiprazole for use as test doses during screening is an approved antipsychotic marketed under the trade name Abilify® (Bristol-Myers Squibb 2016). The first test dose will be administered in the clinic.

Oral test doses of aripiprazole are in 5 mg tablet form. Oral aripiprazole tablets must be kept in a locked storage area before dosing and must be stored in accordance with the full prescribing information for Abilify.

Aripiprazole for use as oral aripiprazole test doses will be commercially available Abilify® 5 mg tablets (Bristol-Myers Squibb 2016) or aripiprazole obtained from a local commercial source, provided in commercial packaging provided to the site by Alkermes.

**8.6. Treatment Adherence**

All study drug injections will be directly administered by clinical study staff. Study staff will address non-adherence with the subject as needed.

**8.7. Blinding**

Not applicable. The study is open-label.

## **9. STUDY DRUG MATERIALS AND MANAGEMENT**

### **9.1. Study Drugs**

The product in this study is aripiprazole lauroxil, a covalently bonded modification of aripiprazole to form *N*-lauroyloxymethyl aripiprazole.

Detailed information about aripiprazole lauroxil can be found in the Aripiprazole Lauroxil [Investigator's Brochure](#) (IB).

### **9.2. Accountability**

The clinical site is required to maintain current drug dispensation and accountability logs throughout the study. All unused supplies will be checked against the drug movement records during the study and/or at the end of the study.

### **9.3. Handling and Disposal**

Following completion and verification of accountability logs, all unused and used packages must be destroyed. Packages may be destroyed on site according to Good Clinical Practice (GCP) and site practice. Alternatively, the sponsor may arrange for destruction with a third party vendor operating in accordance with GCP and/or Good Manufacturing Practice (GMP), as applicable.

## **10. ASSESSMENT OF EFFICACY**

Efficacy will be evaluated based on Clinical Global Impressions-Severity (CGI-S) and Brief Psychiatric Rating Scale (BPRS) responses.

## **11. QUALITY OF LIFE, DAILY AND SOCIAL FUNCTIONING**

The following assessments will be collected to characterize any change in quality of life, including daily and social functioning, after treatment with aripiprazole lauroxil:

- Heinrichs-Carpenter Quality of Life Scale (QLS)
- Negative Symptom Assessment-16 (NSA-16)
- Sexual functioning subscale from UKU Side Effect Rating Scale and CSFQ scores
- Personal and Social Performance scale (PSP)
- Total and individual items scores of the Modified MSQ



## 12. OTHER ASSESSMENTS

The following assessments will be collected to explore potential changes in healthcare burden, cognition, insight, and psychosocial care needs following a transition to aripiprazole lauroxil:

- Health economics
  - Total healthcare costs as measured by TSR-6-Modified for Mental Health
- Functional Assessment
  - BIS
- Family Measures
  - CarerQOL-7D and VAS
  - Burden Assessment Scale
- Investigator- and Caregiver-Rated Cognition
  - Respective NY-AACENT subscales
- Substance Use
  - M.I.N.I. Module I (alcohol use disorder)
  - M.I.N.I. Module J (substance use disorder)

### 13. ASSESSMENT OF SAFETY AND TOLERABILITY

The following safety and tolerability measures will be assessed throughout the study and summarized:

- AEs
- Injection site reactions
- Vital signs (blood pressure, heart rate, respiratory rate, and body temperature), and waist circumference and weight
- Clinical laboratory parameters (chemistry [including prolactin], hematology, and urinalysis) ([Table 2](#))
- C-SSRS responses
- ESRS-A scores

#### 13.1. Definition of Adverse Event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product. The occurrence, which may or may not have a causal relationship with the treatment, may include any clinical or laboratory change that does not commonly occur in that subject and is considered clinically significant.

Illnesses present prior to the subject signing the informed consent form (ICF) are considered to be pre-existing conditions and are documented on the medical history eCRF. Pre-existing conditions that worsen during the study are entered on the AE eCRF.

All out-of-range laboratory values will be deemed as clinically significant or not clinically significant by the investigator. Clinically significant values will be considered AEs and recorded as such on the eCRFs.

Pregnancy alone is not considered an AE, although a female subject will be withdrawn from study drug treatment if a pregnancy occurs. If a pregnancy occurs in the partner of a male subject, it is not required that the male be withdrawn from study drug; however, contraceptive requirements should be revisited. As described in [Section 7.4.2](#), the pregnancy must be reported to Alkermes and additional follow-up may be required.

#### 13.2. Definition of Serious Adverse Event

An SAE is any AE, occurring at any dose and regardless of causality that:

- Results in death
- Is life-threatening. The subject is at immediate risk of death from the reaction as it occurs. This does not include reaction that, had it occurred in a more severe form, might have caused death.

- Requires inpatient hospitalization or prolongation of existing hospitalization. Hospital admission for elective surgery scheduled prior to study entry is not considered an SAE.
- Results in disability/incapacity (eg, a substantial disruption of a person's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect

Important medical events that may not result in death, be immediately life threatening, or require hospitalization may be considered to be SAEs when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require intervention to prevent one of the other outcomes listed above.

### **13.3. Relationship to Study Drug**

The assessment of study drug relationship to each AE will be reported on the appropriate source document (and SAE form, in the event of an SAE) by the investigator (or designated sub-investigator) according to his/her best clinical judgment. The criteria listed in [Table 7](#) should be used to guide this assessment. Please note that not all criteria must be present to be indicative of a particular drug relationship. All study drugs are considered "test drugs" for the purposes of the definitions listed in the table.

**Table 7: Adverse Event Causality Guidelines**

<b>Relationship</b>	<b>Criteria for assessment</b>
<b>Definitely related</b>	<p>There is evidence of exposure to the test drug.</p> <p>AND</p> <p>The temporal sequence of the AE onset relative to administration of the test drug is reasonable.</p> <p>The AE is more likely explained by the test drug than by another cause.</p> <p>Dechallenge (if performed) is positive.</p> <p>Rechallenge (if feasible) is positive.</p> <p>The AE shows a pattern consistent with previous knowledge of the test drug or test drug class.</p>
<b>Probably related</b>	<p>There is evidence of exposure to the test drug.</p> <p>AND</p> <p>The temporal sequence of the AE onset relative to administration of the test drug is reasonable.</p> <p>The AE is more likely explained by the test drug than by another cause.</p> <p>Dechallenge (if performed) is positive.</p>
<b>Possibly related</b>	<p>There is evidence of exposure to the test drug.</p> <p>AND</p> <p>The temporal sequence of the AE onset relative to administration of the test drug is reasonable.</p> <p>The AE could have been due to another equally likely cause.</p> <p>Dechallenge (if performed) is positive.</p>
<b>Probably not related</b>	<p>There is evidence of exposure to the test drug.</p> <p>AND</p> <p>There is another more likely cause of the AE.</p> <p>Dechallenge (if performed) is negative or ambiguous.</p> <p>Rechallenge (if performed) is negative or ambiguous.</p>
<b>Definitely not related</b>	<p>The subject did not receive the test drug.</p> <p>OR</p> <p>Temporal sequence of the AE onset relative to administration of the test drug is not reasonable.</p> <p>OR</p> <p>There is another obvious cause of the AE.</p>

### 13.4. Monitoring and Recording of Adverse Events

AE data collection will begin after a subject signs the ICF and will continue until completion of the End of Treatment/Early Termination visit (Day 169). Any AE or SAE having an onset after the End of Treatment/Early Termination visit will not be collected or reported unless the investigator feels that the event may be related to the study drug.

Subjects will be instructed by the investigator or designee to report the occurrence of any AE. All volunteered, elicited, and observed AEs are to be recorded on the AE eCRFs.

The investigator will assess all AEs regarding any causal relationship to the study drug (see [Section 13.3](#)), the intensity (severity) of the event, action taken, and subject outcome.

The following criteria should be used to guide the assessment of intensity (severity):

- **Mild:** Causes awareness of sign or symptom, but is easily tolerated; does not interfere with usual activities
- **Moderate:** Causes discomfort enough to interfere with usual activities
- **Severe:** Is incapacitating; results in inability to work or perform usual activities

All AEs will be followed until resolution, until deemed stable by the investigator, or until the subject is deemed by the investigator to be lost to follow-up.

For clinical study safety reporting purposes, the most recent version of the Investigator's Brochure will be used as the reference document to designate event expectedness.

Withdrawal from the study as a result of an AE and any therapeutic measures that are taken shall be at the discretion of the investigator. If a subject withdraws from the study for any reason, any ongoing AEs will be followed until resolution, until deemed stable by the investigator, or until the subject is deemed by the investigator to be lost to follow-up.

### 13.5. Reporting of Serious Adverse Events

All SAEs must be reported to Alkermes, via PPD within 1 business day of discovery, by faxing the report to the following:

Attention: PPD Drug Safety

PHONE Number: PPD

FAX Number: PPD

FAX Number: PPD

PPD

The written report should be submitted on the SAE form provided for this purpose. The report must include the investigator's opinion as to whether the event is study drug-related. If this relationship is determined to be possibly, probably, or definitely related to study drug, evidence to support this assessment must also be provided.

## **14. STATISTICS**

### **14.1. Sample Size Considerations**

No formal sample size calculations have been performed. The sample size is based on clinical considerations.

### **14.2. General Statistical Methodology**

In general, summary statistics (n, mean, standard deviation, median, minimum and maximum values for continuous variables, and number and percentage of subjects in each category for categorical variables) will be provided for evaluated variables. All individual subject level data will be presented as data listings.

#### **14.2.1. Study Population**

The safety population will include all subjects who received at least one dose of aripiprazole lauroxil injection. All analyses will be carried out using the safety population.

### **14.3. Demographics and Baseline Data**

Demographics and baseline characteristics such as gender, age, race, weight, height, and BMI will be summarized using descriptive statistics. Medical history will be summarized using the number of observations and percentage of subjects reporting each category.

### **14.4. Efficacy Analyses**

The change from baseline in CGI-S and BPRS scores at each post-baseline visit will be summarized.

### **14.5. Safety and Tolerability Analysis**

The safety analysis will be carried out using the safety population. Reported AE terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

The number and percentage of TEAEs will be summarized by treatment group and overall by system organ class, and preferred terms within each system organ class. Serious adverse events (SAEs) and AEs resulting in treatment discontinuation will also be summarized.

Observed values and change from baseline in vital signs, clinical laboratory data, and ESRs scores will be summarized

Shift tables and potential clinical significance tables, along with supporting listings, will be provided for selected parameters.

Prior and concomitant medication use will be summarized by World Health Organization Drug Dictionary Anatomical Therapeutic Class code and treatment group.

Listings will be provided for all safety endpoints.

Additional details on the safety analysis will be provided in the Statistical Analysis Plan.

#### **14.6. Analyses of Other Assessments**

Data on quality of life, social functioning, functional assessment, and family measures will be summarized using the safety population.

## **15. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS**

### **15.1. Study Monitoring**

Monitoring of the study site (including, but not limited to, reviewing eCRFs for accuracy and completeness) will be performed by an Alkermes monitor or designee.

### **15.2. Audits and Inspections**

By signing the protocol, the investigator agrees that, within local regulatory restrictions and institutional and ethical considerations, authorized representatives of Alkermes, a regulatory authority, and/or an institutional review board (IRB)/independent ethics committee (IEC) may visit the site to perform audits or inspections, including the drug storage area, study drug stocks, drug accountability records, subject charts and source documents, and other records relative to study conduct. The purpose of an Alkermes audit or inspection is to systematically and independently examine all study-related activities and documents (eg, laboratory reports, x-rays, workbooks, subjects' medical records) to determine whether these activities were conducted, and data recorded, analyzed, and accurately reported according to the protocol, GCP guidelines of the International Conference on Harmonisation (ICH), and any applicable regulatory requirements.

The investigator should contact Alkermes immediately if contacted by a regulatory agency regarding an inspection.

### **15.3. Institutional Review Board/ Independent Ethics Committee**

The investigator must obtain IRB/IEC approval for the investigation. Initial IRB/IEC approval as well as all materials approved by the IRB/IEC for this study, including the subject consent form and recruitment materials, must be maintained by the investigator and made available for inspection.



## **16. QUALITY CONTROL AND QUALITY ASSURANCE**

This study will be conducted under GCP and all applicable regulatory requirements. To ensure data accuracy, completeness and compliance, the study site should have processes in place for data review and quality control. Alkermes may also conduct a quality assurance audit. Please see [Section 15.2](#) for details regarding the audit process.

### **16.1. Case Report Forms**

This study will use eCRFs. All eCRF data must be based on source documents or approved to be the original data (ie, data directly reported on the eCRF). All eCRFs will be completed by the clinic staff prior to review by the Alkermes monitor or designated representative.

The Alkermes monitor or designated representative will review all source records on-site and compare them to the data collected on the eCRF.

### **16.2. Confidentiality of Data**

By signing this protocol, the investigator affirms to Alkermes that he or she will maintain in confidence information furnished to him or her by Alkermes and will divulge such information to his or her respective IRB or IEC under an appropriate understanding of confidentiality with such board. All data will be considered the sole property of Alkermes. Please refer to the Clinical Study Agreement (CSA) for details.

## **17. ETHICAL CONSIDERATIONS**

### **17.1. Ethics Review**

The clinical site's IRB/IEC must meet all relevant regulatory requirements. The study protocol and ICF will be reviewed by the IRB/IEC prior to enrolling subjects into the study; written approval from the committee must be received by Alkermes before drug will be released to the investigator. The protocol must be re-approved by the IRB/IEC upon receipt of amendments and annually, as local regulatory requirements require.

The investigator is responsible for submitting all protocol changes and SAE reports to the IRB/IEC according to local procedures. At a minimum, all SAEs requiring a drug safety report must be immediately reported. For this study, submissions to the central IRB will be completed on behalf of the sites by <sup>PPD</sup> as outlined in the study-specific regulatory and safety management plans.

All relevant correspondence from the IRB/IEC will be filed at the site and collected by the Alkermes monitor or designated representative for inclusion in the Trial Master File (TMF) in a timely fashion.

### **17.2. Ethical Conduct of the Study**

This study will be conducted in accordance with the protocol, the ICH Guideline E6, and all applicable local regulatory requirements. GCP is an international ethical and scientific quality standard used for designing, conducting, recording, and reporting studies involving the participation of human subjects. Alkermes is committed to complying with this standard to provide assurance that the rights, safety, and well-being of study subjects will be protected, consistent with the principles having their origin in the Declaration of Helsinki.

### **17.3. Written Informed Consent**

The investigator (or authorized designee) at each center will ensure that the subject (or the subject's legal representative) and reliable informant is given full and adequate oral and written information about the nature, purpose, potential and possible risks and benefits of the study. Each prospective subject and informant will receive an IRB-approved informed consent form (ICF) that summarizes the pertinent study information and will be given ample time to read the form and ask questions about the study. All information is to be provided in a language understandable to the subject and informant and must not include any language that waives the subject's/informant's legal rights. Prospective subjects/informants must also be informed of their right to withdraw consent without prejudice at any time during the study. If the subject/informant chooses to participate, he/she must sign the ICF before any study-specific procedures are conducted.

All subjects/informants will be informed of their rights to privacy and will be made aware that the study data will be submitted to Alkermes, the IRB, the contract research organization (CRO) if applicable, and to regulatory authorities for review and evaluation for the duration of the study and until the project has been approved for marketing, or is withdrawn from investigation. They

will also be informed that the study monitor may inspect their medical records to verify the accuracy and completeness of the study records and results.

Significant changes to the protocol or product safety information may require a revision of the ICF, which must be reviewed and approved by the IRB, and then signed by all applicable study participants.

The time that informed consent is obtained must be documented. The investigator must maintain the original, signed ICF in the subject's source documents. A copy of the signed ICF must be given to the subject/informant.

## **18. DATA HANDLING AND RECORDKEEPING**

An overview of study data handling and recordkeeping procedures and restrictions is provided in the subsequent sections; please refer to the CSA for further details.

### **18.1. Data Capture**

As stated in [Section 16.1](#), this study will use eCRFs for capturing data. All entries, corrections, and alterations will be made by the investigator or other authorized study personnel. All data entries will be verified for accuracy and correctness by independent monitors. The electronic data capture system maintains a full audit trail.

A paper copy of all laboratory reports will remain with the source documents at the study site. All out of range laboratory values will be deemed as clinically significant or not clinically significant by the investigator. Clinically significant values will be considered AEs and recorded as such on the eCRFs.

AEs will be coded using MedDRA. Concomitant medications will be categorized using the WHO-ATC classification system.

### **18.2. Inspection of Records**

Alkermes or its representative will be allowed to conduct site visits to the investigational facilities for the purpose of monitoring any aspect of the study. The investigator agrees to allow the monitor to inspect the drug storage area, study drug stocks, drug accountability records, subject charts and source documents, and other records relative to study conduct.

### **18.3. Retention of Records**

Retention and storage of essential clinical study documents (eg, worksheets, drug accountability forms, and other administrative documentation) shall be governed by the terms and conditions of the site's CSA. If the CSA does not state specific document retention terms, then the site shall keep essential clinical study documentation for the longer of:

- Ten years after discontinuation of the study, or
- Two years following the date a marketing application is approved for the study drug for the indication for which it is being investigated pursuant to the study, or
- If no application is to be filed or if the application is not approved for such indication, until 2 years after the date the study is terminated.

Subjects' medical files should be retained in accordance with the applicable legislation and in accordance with the maximum period of time permitted by the hospital, institution, or private practice.

#### **18.4. Use of Information and Publication Policy**

Data generated in this study are proprietary information that is the sole property of Alkermes. Results of the study are to be held in confidence by both the investigators and the sponsor.

Please refer to the CSA for details on the procedures for publishing and presenting data.

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## APPENDICES

- Appendix A. Columbia Suicide Severity Rating Scale (Sample)
- Appendix B. Extrapyramidal Symptom Rating Scale – Abbreviated (ESRS-A) (Sample)
- Appendix C. Clinical Global Impressions-Severity (CGI-S) (Sample)
- Appendix D. Brief Psychiatric Rating Scale (BPRS) (Sample)
- Appendix E. Sexual Functioning Subscale from Udvalg for Kliniske Undersøgelser (UKU) Side Effect Rating Scale (Sample)
- Appendix F. Changes in Sexual Functioning Questionnaire (Sample)
- Appendix G. Personal and Social Performance Scale (PSP) (Sample)
- Appendix H. Heinrichs-Carpenter Quality of Life Scale (QLS) (Sample)
- Appendix I. Negative Symptom Assessment-16 (NSA-16) (Sample)
- Appendix J. Modified Medication Satisfaction Questionnaire (Modified MSQ) (Sample)
- Appendix K. Sixth Edition of the Treatment Services Review (TSR-6) (Sample)
- Appendix L. Caregiver Quality of Life (CarerQOL) – Burden Dimensions (7D) [Brouwer WBF, 2006] and Visual Analog Scale (VAS) (Sample)
- Appendix M. Burden Assessment Scale (Sample)
- Appendix N. Birchwood Insight Scale (BIS) (Sample)
- Appendix O. New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT) Subscales (Sample)
- Appendix P. Mini International Neuropsychiatric Interview (M.I.N.I.) – Modules I and J (Sample)
- Appendix Q. List of Potent Cytochrome P450 3A4 (CYP3A4) Inducers and Moderate-to-Strong Inhibitors of 3A4 or 2D6



**APPENDIX A. COLUMBIA SUICIDE SEVERITY RATING SCALE  
(SAMPLE)**

# COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Baseline

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 PPD New York State Psychiatric Institute, 1051 Riverside Drive, New York, New York, 10032; inquiries and training requirements contact PPD

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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
<b>1. Wish to be Dead</b> Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. <b>Have you wished you were dead or wished you could go to sleep and not wake up?</b>  If yes, describe:	Yes    No <input type="checkbox"/> <input type="checkbox"/>
<b>2. Non-Specific Active Suicidal Thoughts</b> 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. <b>Have you actually had any thoughts of killing yourself?</b>  If yes, describe:	Yes    No <input type="checkbox"/> <b>K</b>
<b>3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act</b> 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." <b>Have you been thinking about how you might do this?</b>  If yes, describe:	Yes    No <input type="checkbox"/> <b>K</b>
<b>4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan</b> Active suicidal thoughts of killing oneself and subject reports having <u>some intent to act on such thoughts</u> , as opposed to "I have the thoughts but I definitely will not do anything about them." <b>Have you had these thoughts and had some intention of acting on them?</b>  If yes, describe:	Yes    No <input type="checkbox"/> <b>K</b>
<b>5. Active Suicidal Ideation with Specific Plan and Intent</b> Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. <b>Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?</b>  If yes, describe:	Yes    No <input type="checkbox"/> <b>K</b>
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.  <b>Most Severe Ideation:</b> _____ <div style="display: flex; justify-content: space-between;"> <span>Type # (1-5)</span> <span>Description of Ideation</span> </div>	Most Severe
<b>Frequency</b> <b>How many times have you had these thoughts?</b> (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	_____
<b>Duration</b> <b>When you have the thoughts, how long do they last?</b> (1) Fleeting - few seconds or minutes    (4) 4-8 hours/most of day (2) Less than 1 hour/some of the time    (5) More than 8 hours/persistent or continuous (3) 1-4 hours/a lot of time	_____
<b>Controllability</b> <b>Could/can you stop thinking about killing yourself or wanting to die if you want to?</b> (1) Easily able to control thoughts    (4) Can control thoughts with a lot of difficulty (2) Can control thoughts with little difficulty    (5) Unable to control thoughts (3) Can control thoughts with some difficulty    (0) Does not attempt to control thoughts	_____
<b>Deterrents</b> <b>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?</b> (1) Deterrents definitely stopped you from attempting suicide    (4) Deterrents most likely did not stop you (2) Deterrents probably stopped you    (5) Deterrents definitely did not stop you (3) Uncertain that deterrents stopped you    (0) Does not apply	_____
<b>Reasons for Ideation</b> <b>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?</b> (1) Completely to get attention, revenge or a reaction from others    (4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (2) Mostly to get attention, revenge or a reaction from others    (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain.    (0) Does not apply	_____



# COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Since Last Visit

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 PPD New York State Psychiatric Institute, 1051 Riverside Drive, New York, New York, 10032; inquiries and training requirements contact PPD*

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<b>SUICIDAL BEHAVIOR</b> (Check all that apply, so long as these are separate events; must ask about all types)		Since Last Visit
<b>Actual Attempt:</b> A potentially self-injurious act committed with at least some wish to die, <i>as a result of act</i> . Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is <b>any</b> intent/desire to die associated with the act, then it can be considered an actual suicide attempt. <b><i>There does not have to be any injury or harm</i></b> , 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. <b>Have you made a suicide attempt?</b> <b>Have you done anything to harm yourself?</b> <b>Have you done anything dangerous where you could have died?</b> <i>What did you do?</i> <i>Did you _____ as a way to end your life?</i> <i>Did you want to die (even a little) when you _____?</i> <i>Were you trying to end your life when you _____?</i> <i>Or did you think it was possible you could have died from _____?</i> <b>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)?</b> (Self-Injurious Behavior without suicidal intent) If yes, describe:		Yes No <input type="checkbox"/> <input type="checkbox"/>  Total # of Attempts _____  Yes No <input type="checkbox"/> <input type="checkbox"/>
<b>Has subject engaged in Non-Suicidal Self-Injurious Behavior?</b>		<input type="checkbox"/> <input type="checkbox"/>
<b>Interrupted Attempt:</b> When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act ( <i>if not for that, actual attempt would have occurred</i> ). 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. <b>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?</b> If yes, describe:		Yes No <input type="checkbox"/> <input type="checkbox"/>  Total # of interrupted _____
<b>Aborted Attempt:</b> 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. <b>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?</b> If yes, describe:		Yes No <input type="checkbox"/> <input type="checkbox"/>  Total # of aborted _____
<b>Preparatory Acts or Behavior:</b> 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). <b>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)?</b> If yes, describe:		Yes No <input type="checkbox"/> <input type="checkbox"/>
<b>Suicidal Behavior:</b> Suicidal behavior was present during the assessment period?		Yes No <input type="checkbox"/> <input type="checkbox"/>
<b>Suicide:</b>		Yes No <input type="checkbox"/> <input type="checkbox"/>
<b>Answer for Actual Attempts Only</b>		Most Lethal Attempt Date:
<b>Actual Lethality/Medical Damage:</b> 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; <i>medical</i> 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; <i>medical</i> 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 _____
<b>Potential Lethality: Only Answer if Actual Lethality=0</b> 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 _____

**APPENDIX B. EXTRAPYRAMIDAL SYMPTOM RATING SCALE –  
ABBREVIATED (ESRS-A) (SAMPLE)**



# Extrapyramidal Symptom Rating Scale-Abbreviated

## Scoring Sheet-Long Form (NOT FOR COMPLETION)

### Parkinsonism

#### Rigidity

##### Upper limbs

- 0 No rigidity
- 1 Minimal *Very mild, barely perceptible*
- 2 Mild *Some resistance to passive movements*
- 3 Moderate *Definite resistance to passive movements, still easy to move limb, full range motion achieved*
- 4 Severe *Marked resistance to passive movements, difficulty to move limb with full range of motion*
- 5 Extreme *Lead pipe rigidity, limb nearly frozen; motion achieved with difficulty*

##### Lower limbs

- 0 No rigidity
- 1 Minimal *Very mild, barely perceptible*
- 2 Mild *Some resistance to passive movements*
- 3 Moderate *Definite resistance to passive movements, still easy to move limb, full range motion achieved*
- 4 Severe *Marked resistance to passive movements, difficulty to move limb with full range of motion*
- 5 Extreme *Lead pipe rigidity, limb nearly frozen; motion achieved with difficulty*

##### Neck

- 0 No rigidity
- 1 Minimal *Very mild, barely perceptible*
- 2 Mild *Some resistance to passive movements*
- 3 Moderate *Definite resistance to passive movements, still easy to move neck, full range motion achieved*
- 4 Severe *Marked resistance to passive movements, difficulty to move neck within full range of motion*
- 5 Extreme *Lead pipe rigidity, neck nearly frozen; motion achieved with difficulty*

#### Tremor

##### Face, jaw/chin, lips, head

- 0 No tremor *Absent at rest and during action/posture*
- 1 Minimal *Tremor with action/posture. Absent at rest; rare (<10% of the time)*
- 2 Mild *Small amplitude tremor with action/posture; occasional (<50% of the time). Absent at rest*
- 3 Moderate *Moderate amplitude tremor with action/posture; noticeable (>50% of the time). May be absent at rest*
- 4 Severe *Large amplitude tremor at rest or during action/posture; occasional (<50% of the time)*
- 5 Extreme *Large amplitude tremor at rest and during action/posture; noticeable (>50% of the time)*

##### Upper limbs/hands

- 0 No tremor *Absent at rest and during action/posture*
- 1 Minimal *Tremor with action/posture. Absent at rest; rare (<10% of the time)*
- 2 Mild *Small amplitude tremor with action/posture; occasional (<50% of the time) Absent at rest*
- 3 Moderate *Moderate amplitude tremor with action/posture; noticeable (>50% of the time). May be absent at rest*
- 4 Severe *Large amplitude tremor at rest or during action/posture; occasional (<50% of the time)*
- 5 Extreme *Large amplitude tremor at rest and during action/posture; noticeable (>50% of the time)*

##### Lower limbs/feet

- 0 No tremor *Absent at rest and during action/posture*
- 1 Minimal *Tremor with action/posture. Absent at rest; rare (<10% of the time)*
- 2 Mild *Small amplitude tremor with action/posture (<50% of the time); absent at rest*
- 3 Moderate *Moderate amplitude tremor with action/posture; noticeable (>50% of the time); may be absent at rest*
- 4 Severe *Large amplitude tremor at rest or during action/posture; occasional (<50% of the time)*
- 5 Extreme *Large amplitude tremor at rest and during action/posture; noticeable (>50% of the time)*

## Parkinsonism (continued)

### Reduced facial expression/speech

- 0 Normal
- 1 Minimal *Very mild decrease in facial expressiveness*
- 2 Mild *Mild decrease in facial expressiveness; hypomania*
- 3 Moderate *Rare spontaneous smile, decreased blinking, voice monotonous*
- 4 Severe *Difficulty to frown, slurred speech, staring gaze*
- 5 Extreme *Unable to frown, unintelligible speech, fixed facial expression, lips parted*

### Impaired Gait/Posture

- 0 Normal
- 1 Minimal *Very mild decreased pendular arm movement, not quite erect normally: stooped posture*
- 2 Mild *Mild decrease of pendular arm movement, mildly stooped posture*
- 3 Moderate *No pendular arm movement, head flexed, can be leaning to one side*
- 4 Severe *Small step (shuffling gait), stiff posture (neck, back), moderate leaning to one side*
- 5 Extreme *Festination/freezing on turning, barely able to walk, triple flexion: posture extreme abnormal*

### Postural Instability

- 0 No postural instability
- 1 Minimal *Hesitation when suddenly pushed or pulled but no latero, antero nor retropulsion*
- 2 Mild *Latero, antero or retropulsion but recovers unaided*
- 3 Moderate *Absence of postural response, would fall if not caught*
- 4 Severe *Unstable while standing, even without pushing*
- 5 Extreme *Unable to stand without assistance*

### Bradykinesia/ Hypokinesia

- 0 No slowness of movement
- 1 Minimal *Minimally/questionably slowed movements, hesitancy*
- 2 Mild *Mildly slowed movements, mild poverty of movements*
- 3 Moderate *Moderate difficulty in initiating or stopping movements*
- 4 Severe *Rare voluntary movements, small amplitude movements*
- 5 Extreme *Almost completely immobile*

## Dystonia

### Tongue

- |   |          |  |
|---|----------|--|
| 0 | None     | No contraction at rest or during action  |
| 1 | Minimal  | Very mild contraction partial tongue protrusion; rare (<10% of the time)                   |
| 2 | Mild     | Mild contraction partial tongue protrusion; occasional (<50% of the time)                  |
| 3 | Moderate | Sustained min effort contraction partial tongue protrusion; noticeable (>50% of the time)  |
| 4 | Severe   | Forceful effort contraction near complete tongue protrusion; occasional (<50% of the time) |
| 5 | Extreme  | Forceful effort near complete tongue protrusion; noticeable (>50% of the time)             |

### Jaw

- |   |          |  |
|---|----------|--|
| 0 | None     | No contractions at rest or during action   |
| 1 | Minimal  | Very mild contraction partial jaw opening or clenching; rare (<10% of the time)          |
| 2 | Mild     | Mild contraction partial jaw opening or clenching; occasional (<50% of the time)         |
| 3 | Moderate | Sustained min effort partial jaw opening or clenching; noticeable (>50% of the time)     |
| 4 | Severe   | Forceful effort complete jaw opening or clenching/bruxism; occasional (<50% of the time) |
| 5 | Extreme  | Forceful effort complete jaw opening or clenching/bruxism; noticeable (>50% of the time) |

### Eyes, upper face, lower face, larynx

- |   |          |  |
|---|----------|--|
| 0 | None     | No contractions at rest or during action   |
| 1 | Minimal  | Very mild blepharospasm, oculogyration, choked voice or grimacing; rare (<10% of the time)                   |
| 2 | Mild     | Mild blepharospasm, oculogyration, choked voice or grimacing; occasional (<50% of the time)                  |
| 3 | Moderate | Sustained min effort blepharospasm, oculogyration, choked voice or grimacing; predominant (>50% of the time) |
| 4 | Severe   | Forceful effort blepharospasm, oculogyration, choked voice or grimacing; occasional (<50% of the time)       |
| 5 | Extreme  | Forceful effort blepharospasm, oculogyration, choked voice or grimacing; noticeable (>50% of the time)       |

### Shoulders, upper limbs, hands

- |   |          |   |
|---|----------|---|
| 0 | None     | No contraction at rest or during action   |
| 1 | Minimal  | Very mild contraction of shoulder, upper limb or hand; rare (<10% of the time)                  |
| 2 | Mild     | Mild contraction of shoulder, upper limb or hand; occasional (<50% of the time)                 |
| 3 | Moderate | Sustained min effort contraction of shoulder, upper limb or hand; noticeable (>50% of the time) |
| 4 | Severe   | Forceful effort contraction of shoulder, upper limb or hand; occasional (<50% of the time)      |
| 5 | Extreme  | Forceful effort contraction of shoulder, upper limb or hand; noticeable (>50% of the time)      |

### Hips, lower limbs, feet

- |   |          |  |
|---|----------|--|
| 0 | None     | No contraction at rest or during action  |
| 1 | Minimal  | Very mild contraction of hip, lower limb or foot; rare (<10% of the time)                  |
| 2 | Mild     | Mild contraction of hip, lower limb or foot; occasional (<50% of the time)                 |
| 3 | Moderate | Sustained min effort contraction of hip, lower limb or foot; noticeable (>50% of the time) |
| 4 | Severe   | Forceful effort contraction of hip, lower limb or foot; occasional (<50% of the time)      |
| 5 | Extreme  | Forceful effort contraction of hip, lower limb or foot; noticeable (>50% of the time)      |

### Trunk, neck

- |   |          |  |
|---|----------|--|
| 0 | None     | No contraction at rest or during action  |
| 1 | Minimal  | Very mild contraction trunk bending or head turning; rare (<10% of the time)             |
| 2 | Mild     | Mild contraction trunk bending or head turning; occasional (<50% of the time)            |
| 3 | Moderate | Sustained min effort trunk bending or head turning; noticeable (>50% of the time)        |
| 4 | Severe   | Forceful effort contraction trunk bending or head turning; occasional (<50% of the time) |
| 5 | Extreme  | Forceful effort contraction trunk bending or head turning; noticeable (>50% of the time) |

## Dyskinesia

### Tongue

- |          |                 |  |
|----------|-----------------|--|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>  |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic lateral or torsion movement of tongue; rare (&lt;10% of the time)</i>      |
| <b>2</b> | <b>Mild</b>     | <i>Lateral or torsion tongue dyskinesia within oral cavity; occasional (&lt;50% of the time)</i>   |
| <b>3</b> | <b>Moderate</b> | <i>Lateral or torsion tongue dyskinesia within oral cavity; noticeable (&gt;50% of the time)</i>   |
| <b>4</b> | <b>Severe</b>   | <i>Near complete tongue protrusion dyskinesia (fly catching); occasional (&lt;50% of the time)</i> |
| <b>5</b> | <b>Extreme</b>  | <i>Near complete tongue protrusion dyskinesia (fly catching); noticeable (&gt;50% of the time)</i> |

### Jaw

- |          |                 |  |
|----------|-----------------|--|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>  |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic lateral, chewing or biting jaw movement; rare (&lt;10% of the time)</i>    |
| <b>2</b> | <b>Mild</b>     | <i>Lateral, chewing or biting dyskinesia without jaw opening; occasional (&lt;50% of the time)</i> |
| <b>3</b> | <b>Moderate</b> | <i>Lateral, chewing or biting dyskinesia without jaw opening; noticeable (&gt;50% of the time)</i> |
| <b>4</b> | <b>Severe</b>   | <i>Near complete jaw opening dyskinesia; occasional (&lt;50% of the time)</i>                      |
| <b>5</b> | <b>Extreme</b>  | <i>Near complete jaw opening dyskinesia; noticeable (&gt;50% of the time)</i>                      |

### Eyes, upper face, lower face

- |          |                 |   |
|----------|-----------------|---|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>                                   |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic blinking, or pouting; rare (&lt;10% of the time)</i>    |
| <b>2</b> | <b>Mild</b>     | <i>Blinking, or pouting dyskinesia; occasional (&lt;50% of the time)</i>        |
| <b>3</b> | <b>Moderate</b> | <i>Blinking, or pouting dyskinesia; noticeable (&gt;50% of the time)</i>        |
| <b>4</b> | <b>Severe</b>   | <i>Marked blinking, or pouting dyskinesia; occasional (&lt;50% of the time)</i> |
| <b>5</b> | <b>Extreme</b>  | <i>Marked blinking, or pouting dyskinesia noticeable (&gt;50% of the time)</i>  |

### Shoulders, upper limbs, hands

- |          |                 |  |
|----------|-----------------|--|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>  |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic shoulder, limb or hand movement; rare (&lt;10% of the time)</i>  |
| <b>2</b> | <b>Mild</b>     | <i>Unilateral dyskinesia of shoulder, limb or hand; occasional (&lt;50% of the time)</i> |
| <b>3</b> | <b>Moderate</b> | <i>Unilateral dyskinesia of shoulder, limb or hand; noticeable (&gt;50% of the time)</i> |
| <b>4</b> | <b>Severe</b>   | <i>Bilateral dyskinesia of shoulder, limb or hand; occasional (&lt;50% of the time)</i>  |
| <b>5</b> | <b>Extreme</b>  | <i>Bilateral dyskinesia of shoulder, limb or hand; noticeable (&gt;50% of the time)</i>  |

### Hips, lower limbs, feet

- |          |                 |   |
|----------|-----------------|---|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>                                       |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic hip, limb or foot movement; rare (&lt;10% of the time)</i>  |
| <b>2</b> | <b>Mild</b>     | <i>Unilateral dyskinesia of hip, limb or foot; occasional (&lt;50% of the time)</i> |
| <b>3</b> | <b>Moderate</b> | <i>Unilateral dyskinesia of hip, limb or foot; noticeable (&gt;50% of the time)</i> |
| <b>4</b> | <b>Severe</b>   | <i>Bilateral dyskinesia of hip, limb or foot; occasional (&lt;50% of the time)</i>  |
| <b>5</b> | <b>Extreme</b>  | <i>Bilateral dyskinesia of hip, limb or foot; noticeable (&gt;50% of the time)</i>  |

### Trunk, neck

- |          |                 |  |
|----------|-----------------|--|
| <b>0</b> | <b>Absent</b>   | <i>No dyskinesia at rest or during action</i>  |
| <b>1</b> | <b>Minimal</b>  | <i>Very mild dyskinetic trunk bending or head turning; rare (&lt;10% of the time)</i>      |
| <b>2</b> | <b>Mild</b>     | <i>Mild trunk bending or head turning dyskinesia; occasional (&lt;50% of the time)</i>     |
| <b>3</b> | <b>Moderate</b> | <i>Moderate trunk bending or head turning dyskinesia; noticeable (&gt;50% of the time)</i> |
| <b>4</b> | <b>Severe</b>   | <i>Marked trunk bending or head turning dyskinesia; occasional (&lt;50% of the time)</i>   |
| <b>5</b> | <b>Extreme</b>  | <i>Marked trunk bending or head turning dyskinesia; noticeable (&gt;50% of the time)</i>   |

## Akathisia

### Subjective (reported by the patient)

**0** None

*No feelings of restlessness/urge to move, nor distress reported.*

**1** Minimal

*Slight vague feelings of restlessness/urge to move, minimally aware or distressed.  
Rare (<10% of the time)*

**2** Mild

*Clearly identifiable feelings of restlessness/urge to move that are manageable, do not require treatment, mildly aware or distressed. No impact on daily activities. Occasional (<50% of the time)*

**3** Moderate

*Feelings of restlessness/urge to move require effort to manage, interfere with some daily activities, moderately aware or distressed. Patient may seek treatment. Noticeable (>50% of the time)*

**4** Severe

*Feelings of restlessness/urge to move with significant impact on daily activities, intensely aware or distressed. Medications may not completely control symptoms. Occasional (<50% of the time)*

**5** Extreme

*Feelings of restlessness/urge to move with severe impact on all daily activities, extremely aware or distressed. Medications have minimal effects. Noticeable (>50% of the time)*

### Objective (observed during patient examination)

**0** None

*No overt signs of restlessness or fidgeting.*

**1** Minimal

*Slight restless movements, fidgeting or crossing-uncrossing of leg. Rare (<10% of the time)*

**2** Mild

*Mild restless movements. Need to move at least one extremity, fidgets in his/her chair, rocks or crosses and uncrosses his/her legs. Occasional (<50% of the time)*

**3** Moderate

*Noticeable restless movements, but can remain seated. Need to move one extremity or to change position, fidgets in his/her chair, may rock back and forth, may need to stand up and walk. Noticeable (>50% of the time)*

**4** Severe

*Evident restless movements, unable to sit down for more than a short period of time.  
Rocking, need to get up and leave his/her seat, or to pace back and forth, or shift from foot to foot when standing. Occasional (<50% of the time)*

**5** Extreme

*Unremitting severe restless movements, moves or walks constantly with no apparent control. Rocks uncontrollably, cannot sit still, paces back and forth, marches in place. Noticeable (>50% of the time)*

## Clinical Global Impression of Movement Severity (CGI-S)

### Parkinsonism

- 0 Absent
- 1 Minimal
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Extreme

### Dystonia

- 0 Absent
- 1 Minimal
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Extreme

### Dyskinesia

- 0 Absent
- 1 Minimal
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Extreme

### Akathisia

- 0 Absent
- 1 Minimal
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Extreme

For Review Only

**APPENDIX C. CLINICAL GLOBAL IMPRESSIONS-SEVERITY (CGI-S)  
(SAMPLE)**

### Clinical Global Impression – Severity (CGI-S) Scale

Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?

- ☐ 1 = Normal, not at all ill
- ☐ 2 = Borderline mentally ill
- ☐ 3 = Mildly ill
- ☐ 4 = Moderately ill
- ☐ 5 = Markedly ill
- ☐ 6 = Severely ill
- ☐ 7 = Among the most extremely ill patients

**Rater Signature:** \_\_\_\_\_

Busner, J., Targum, S. (2007), as adapted from Kay, Stanley R., Positive and Negative Symptoms in Schizophrenia: Assessment and Research. Clinical and Experimental Psychiatry, Monograph No. 5. Brunner/Mazel, 1991.

Modified from Guy W. Clinical Global Impressions: In ECDEU Assessment Manual for Psychopharmacology. 1976; 218-222. Revised DHEW Pub. (ADM) Rockville, MD: National Institute for Mental Health



## CGI-S Scoring Guidelines

1	Normal, not at all ill	Symptoms of disorder have not been present in the past seven days
2	Borderline mentally ill	Subtle or suspected pathology present within the past seven days
3	Mildly ill	Clearly established symptoms causing minimal, if any, distress for the subject or difficulty in social and occupational function
4	Moderately ill	Overt symptoms causing noticeable, but modest, functional impairment or distress for the subject; Some symptoms may warrant adjustment of medication
5	Markedly ill	Intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress for the subject; There is overt behavioral or social dysfunction that is obvious to others
6	Severely ill	Disruptive pathology; behavior and function are frequently influenced by symptoms;  Extent of overt dysfunction may require intervention from others
7	Among the most extremely ill patients	Pathology drastically interferes in many life functions; patient may be hospitalized

**Rater Signature:** \_\_\_\_\_

Busner, J., Targum, S. (2007), as adapted from Kay, Stanley R., Positive and Negative Symptoms in Schizophrenia: Assessment and Research. Clinical and Experimental Psychiatry, Monograph No. 5. Brunner/Mazel, 1991.

Modified from Guy W. Clinical Global Impressions: In ECDEU Assessment Manual for Psychopharmacology. 1976; 218-222.  
Revised DHEW Pub. (ADM) Rockville, MD: National Institute for Mental Health

**APPENDIX D. BRIEF PSYCHIATRIC RATING SCALE (BPRS)  
(SAMPLE)**

**BPRS-A (Brief Psychiatric Rating Scale - Anchored)**



**NORTH SHORE -  
LONG ISLAND JEWISH  
HEALTH SYSTEM**  
Department of Psychiatry Research

The starred items (Items 3, 4, 6, 7, 13, 14, 16, 17 and 18) should be rated on the basis of observations made during the interview. For these items, 1 = Not observed. The remaining items should be rated on the basis of reported (i.e., subjective) information pertaining to the past week. For these items, 1 = Not reported.

1. **SOMATIC CONCERN**: Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not. Do not rate mere reporting of somatic symptoms. Rate only concern for (or worrying about) physical problems (real or imagined). Rate on the basis of reported (i.e., subjective) information pertaining to the past week.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or Not assessed

1 = Not Reported

2 = Very Mild: occasionally is somewhat concerned about body, symptoms or physical illness

3 = Mild: occasionally is moderately concerned, or often is somewhat concerned

4 = Moderate: occasionally is very concerned, or often is moderately concerned

5 = Moderately Severe: often is very concerned

6 = Severe: is very concerned most of the time

7 = Very Severe: is very concerned nearly all of the time

- During the past week how has your physical health been?
- Do you feel you are physically ill in any way? (What do you think is wrong?) (How serious is it?)
- Have you worried about your health recently?

2. **ANXIETY**: Worry, fear or overly concerned for present or future. Rate solely on the basis of verbal report of patient's own subjective experiences. Do not infer anxiety from physical sign or from neurotic defense mechanisms. Do not rate if restricted to somatic concern.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or Not assessed

1 = Not Reported

2 = Very Mild: occasionally feels somewhat anxious

3 = Mild: occasionally feels moderately anxious, or often feels somewhat anxious

4 = Moderate: occasionally feels very anxious, or often feels moderately anxious

5 = Moderately Severe: often feels very anxious

6 = Severe: feels very anxious most of the time

7 = Very Severe: feels very anxious nearly all of the time

- During the past week have you felt very frightened or anxious?
- Have you worried a lot? (What do you worry about?)
- Have you had the feeling that something terrible might happen?

\*3. **EMOTIONAL WITHDRAWAL**: Deficiency in relating to the interviewer and to the interview situation. Overt manifestations of this deficiency include poor/absence of eye contact, failure to orient oneself physically toward the interviewer, and a general lack of involvement or engagement in the interview. Distinguish from BLUNTED AFFECT, in which deficits in facial expression, body gesture, and voice pattern are scored.

- 7 = Cannot be assessed (e.g., scored from audio tape)
- 1 = Not observed
- 2 = Very Mild: e.g., occasionally exhibits poor eye contact
- 3 = Mild: e.g., as above, but more frequent
- 4 = Moderate: e.g., exhibits little eye contact, but still seems engaged in the interview and is appropriately responsive to all questions
- 5 = Moderately Severe: e.g., stares at floor or orients self away from interviewer, but still seems moderately engaged
- 6 = Severe: e.g., as above, but more persistent or pervasive
- 7 = Very Severe: e.g., appears "spacey" or "out of it" (total absence of emotional relatedness), and is disproportionately uninvolved or unengaged in the interview

\*4. **CONCEPTUAL DISORGANIZATION**: Degree of speech incomprehensibility. Include any type of formal thought disorder (e.g., loose associations, incoherence, flight of ideas, neologisms). DO NOT include mere circumstantiality or pressured speech, even if marked. DO NOT rate on the basis of the patient's subjective impressions (e.g., "my thoughts are racing. I can't hold a thought," "my thinking gets all mixed up."). Rate *ONLY* on the basis of observations made during the interview.

- 7 = Not assessed
- 1 = Not observed
- 2 = Very Mild: e.g., somewhat vague, but of doubtful clinical significance
- 3 = Mild: e.g., frequently vague, but the interview is able to progress smoothly
- 4 = Moderate: e.g., occasional irrelevant statements, infrequent use of neologisms, or moderate loosening of associations
- 5 = Moderately Severe: as above, but more frequent
- 6 = Severe: formal thought disorder is present for most of the interview, and the interview is severely strained
- 7 = Very Severe: very little coherent information can be obtained

**5. GUILT FEELINGS:** Overly concerned or remorseful for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report. Do not infer guilt feelings from depression, anxiety or neurotic defenses.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or Not assessed

1 = Not Reported

2 = Very Mild: occasionally feels somewhat guilty

3 = Mild: occasionally feels moderately guilty, or often feels somewhat guilty

4 = Moderate: occasionally feels very guilty, or often feels moderately guilty

5 = Moderately Severe: often feels very guilty

6 = Severe: feels very guilty most of the time, or encapsulated delusion of guilt

7 = Very Severe: agonizing constant feelings of guilt, or pervasive delusions of guilt

- During the past week have you been blaming yourself for anything?
- Have you been feeling guilty? (Do you feel that you deserve punishment?) (Have you been thinking about this a lot?)

**\*6. TENSION:** Rate motor restlessness (agitation) observed during the interview. DO NOT rate on the basis of subjective experiences reported by the patient. Disregard suspected pathogenesis (e.g., tardive dyskinesia).

-7 = Cannot be assessed (e.g., scored from audiotape)

1 = Not observed

2 = Very Mild: e.g., occasionally fidgets

3 = Mild: e.g., frequently fidgets

4 = Moderate: e.g., constantly fidgets, or frequently fidgets, wrings hands and pulls clothing

5 = Moderately Severe: e.g., constantly fidgets, wrings hands and pulls clothing

6 = Severe: e.g., cannot remain seated (i.e., must pace)

7 = Very Severe: e.g., paces in a frantic manner

**\*7. MANNERISMS AND POSTURING:** Unusual and unnatural motor behavior. Rate only abnormality of movements; do not rate simple heightened motor activity here. Consider frequency, duration, and degree of bizarreness. Disregard suspected pathogenesis.

-7 = Cannot be assessed (e.g., scored from audiotape)

1 = Not observed

2 = Very Mild: odd behavior but of doubtful clinical significance, e.g. occasional unprompted smiling, infrequent lip movements

3 = Mild: strange behavior but not obviously bizarre, e.g., infrequent head-tilting (side to side) in a rhythmic fashion, intermittent abnormal finger movements

4 = Moderate: e.g., assumes yoga position for a brief period of time, infrequent tongue protrusions, rocking

5 = Moderately Severe: e.g., assumes and maintains yoga positions throughout interview, unusual movements in several body areas

6 = Severe: as above, but more frequent, intense, or pervasive

7 = Very Severe: e.g., bizarre posturing throughout most of the interview, continuous abnormal movements in several body areas

**8. GRANDIOSITY:** Inflated self-esteem (self-confidence), or inflated appraisal of one's talents, powers, abilities, accomplishments, knowledge, importance, or identity. Do not score mere grandiose quality of claims (e.g., "I'm the worst sinner in the world," "The entire country is trying to kill me") unless the guilt/persecution is related to some special, exaggerated attributes of the individual. Also, the patient must claim exaggerated attributes: e.g., if patient denies talents, powers, etc., even if he or she states that others indicate that he/she has these attributes, this item should not be scored.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: e.g., is more confident than most people, but of only possible clinical significance

3 = Mild: e.g., definitely inflated self-esteem or exaggerates talents somewhat out of proportion to the circumstances

4 = Moderate: e.g., inflated self-esteem clearly out of proportion to the circumstances, or suspected grandiose delusion(s)

5 = Moderately Severe: e.g., a single (definite) encapsulated grandiose delusion, or multiple (definite) fragmentary grandiose delusions

6 = Severe: e.g., a single (definite) grandiose delusion/delusional system, or multiple (definite) grandiose delusions that the patient seems preoccupied with

7 = Very Severe: e.g., as above, but nearly all conversation is directed toward the patient's grandiose delusion(s)

- During the past week have you felt more self-confident than usual?
- Do you have any special abilities or talents?
- Do you feel there is a special purpose or mission to your life? (Have you thought you might be somebody rich or famous?)

**9. DEPRESSIVE MOOD:** Subjective report of feeling depressed, blue, "down in the dumps," etc. Rate only degree of reported depression. Do not rate on the basis of inferences concerning depression based upon general retardation and somatic complaints.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: occasionally feels somewhat depressed

3 = Mild: occasionally feels moderately depressed, or often feels somewhat depressed

4 = Moderate: occasionally feels very depressed, or often feels moderately depressed

5 = Moderately Severe: often feels very depressed

6 = Severe: feels very depressed most of the time

7 = Very Severe: feels very depressed nearly all of the time

- In the past week have you had less interest in your usual activities?
- Have you felt sad or depressed? (Have you cried at all?) (How bad is the feeling?) (How long does it last?)

10. **HOSTILITY:** Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others during the week. Do not infer hostility from neurotic defenses, anxiety or somatic complaints.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: occasionally feels somewhat angry

3 = Mild: often feels somewhat angry, or occasionally feels moderately angry

4 = Moderate: occasionally feels very angry, or often feels moderately angry or occasionally yells at others

5 = Moderately Severe: often feels very angry; often yells at others or occasionally threatens to harm others

6 = Severe: has acted on his anger by becoming physically abusive on one or two occasions or makes frequent threats to harm other

7 = Very Severe: has been physically aggressive and/or has required intervention to prevent assaultiveness on several occasions; or any serious assaultive act.

- During the past week have you been feeling irritable?
- How have you been getting along with other people? (Have you gotten in any arguments or fights?)
- Have you been easily annoyed or angered? (How strongly have you felt this way?) (How much of the time?)

11. **SUSPICIOUSNESS:** Belief (delusional or otherwise) that others have now, or have had in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions that are currently held whether they concern past or present circumstances.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: rare instances of suspiciousness that may or may not be warranted by the situation

3 = Mild: occasional instances of suspiciousness that are definitely not warranted by the situation

4 = Moderate: more frequent suspiciousness, or transient ideas of reference

5 = Moderately Severe: pervasive suspiciousness, or frequent ideas of reference

6 = Severe: definite, delusion(s) of reference or persecution that is (are) not wholly pervasive (e.g., an encapsulated delusion)

7 = Very Severe: as above, but more widespread, frequent or intense

- How did you get along with people in general, during the past week?
- Do you feel that you have to be on guard with people?
- Has anyone been giving you a hard time, or accusing you of things?
- Has anyone deliberately tried to annoy you?
- Tried to harm you?

**12. HALLUCINATORY BEHAVIOR:** Perceptions (in any sensory modality) in the absence of an identifiable external stimulus. Rate only those experiences that have occurred during the last week. DO NOT rate “voices in my head,” or “visions in my mind” unless the patient can differentiate between these experiences and his or her thoughts.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: suspected hallucinations only

3 = Mild: definite hallucinations, but insignificant, infrequent, or transient (e.g., occasional formless visual hallucinations, a voice calling the patient’s name)

4 = Moderate: as above, but more frequent or extensive (e.g., frequently sees the devil’s face, two voices carry on lengthy conversations)

5 = Moderately Severe: hallucinations are experienced nearly every day, or are a source of extreme distress

6 = Severe: as above, and has had a moderate impact on the patient’s behavior (e.g., concentration difficulties leading to impaired work functioning)

7 = Very Severe: as above, and has had a severe impact (e.g., attempts suicide in response to command hallucinations)

- Have you had any unusual experiences during the past week?
- Do you seem to hear noises or voices when there’s no one around and nothing else to explain it?
- Have you had visions, or seen things that others couldn’t see?
- Is there anything unusual about the way things feel, or taste, or smell?
- How often do you [hear voices]? (Do the voices make it hard to concentrate?) (Do they tell you to do things?)

**\*13. MOTOR RETARDATION:** Reduction in energy level evidenced in slowed movements. Rate on the basis of observed behavior of the patient only; do not rate on the basis of the patient’s subjective impression of his or her own energy level.

-7 = Cannot be assessed (e.g., scored from audiotape)

1 = Not observed

2 = Very Mild and of doubtful clinical significance

3 = Mild: e.g. conversation is somewhat retarded, movements somewhat slowed

4 = Moderate: e.g., conversation is noticeably retarded, but not strained

5 = Moderately Severe: e.g., conversation is strained, moves very slowly

6 = Severe: e.g., conversation is difficult to maintain, hardly moves at all

7 = Very Severe: e.g., conversation is almost impossible, does not move at all throughout the interview



**\*14. UNCOOPERATIVENESS:** Evidence of resistance, unfriendliness, resentment, and lack of readiness to cooperate with the interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation; do not rate on the basis of reported resentment or uncooperativeness outside the interview situation.

-7 = Not assessed

1 = Not observed

2 = Very Mild: e.g., does not seem motivated

3 = Mild: e.g., seems evasive in certain areas

4 = Moderate: e.g., monosyllabic, fails to elaborate spontaneously

5 = Moderately Severe: e.g., expresses resentment and is unfriendly throughout the interview

6 = Severe: e.g., refuses to answer a number of questions

7 = Very Severe: e.g., refuses to answer most questions

**15. UNUSUAL THOUGHT CONTENT:** Severity of delusions of any type – consider conviction, and effect on actions. Assume full conviction if patient has acted on his or her beliefs. Rate on the basis of reported (i.e., subjective) information pertaining to the past week.

-7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed

1 = Not reported

2 = Very Mild: delusion(s) suspected or likely

3 = Mild: at times, patient questions his or her belief(s) (partial delusion)

4 = Moderate: full delusional conviction, but delusion(s) has little or no influence on behavior

5 = Moderately Severe: full delusional conviction, but delusion(s) has only occasional impact on behavior

6 = Severe: delusion(s) has significant effect, e.g. neglects responsibilities because of preoccupations with belief the he/she is God

7 = Very Severe: delusion(s) has major impact, e.g., stops eating because believes food is poisoned

- Have you had any difficulty with your thinking in the past week?
- Do certain things have special meaning for you? (Give me an example.)
- Is there any interference with your thoughts?
- Is there anything controlling your thoughts or movements?
- Do you see references to yourself in surprising places, like on TV?

**\*16. BLUNTED AFFECT:** Diminished affected responsivity, as characterized by deficits in facial expression, body gesture, and voice pattern. Distinguish from EMOTIONAL WITHDRAWAL, in which the focus is on the interpersonal impairment rather than affect. Consider degree and consistency of impairment.

- 7 = Cannot be assessed (e.g., scored from audiotape)
- 1 = Not observed
- 2 = Very Mild: e.g., occasionally seems indifferent to material that is usually accompanied by some show of emotion
- 3 = Mild: e.g., somewhat diminished facial expression, or somewhat monotonous voice or somewhat restricted gestures
- 4 = Moderate: e.g., as above, but more intense, prolonged or frequent
- 5 = Moderately Severe: e.g., flattening of affect, including at least two of the three features: severe lack of facial expression, monotonous voice, or restricted body gestures
- 6 = Severe: e.g., profound flattening of affect
- 7 = Very Severe: e.g., totally monotonous voice, and total lack of expressive gestures throughout the evaluation

**\*17. EXCITEMENT:** Heightened emotional tone, including irritability and expansiveness (hypomanic affect). Do not infer affect from statement of grandiose delusions.

- 7 = Not assessed
- 1 = Not observed
- 2 = Very Mild and of doubtful clinical significance
- 3 = Mild: e.g., irritable or expansive at times
- 4 = Moderate: e.g., frequently irritable or expansive
- 5 = Moderately Severe: e.g., constantly irritable or expansive; or, at times, enraged or euphoric
- 6 = Severe: e.g., enraged or euphoric throughout most of the interview
- 7 = Very Severe: e.g., as above, but to such a degree that the interview must be terminated prematurely

**\*18. DISORIENTATION:** Confusion or lack of proper association for person, place or time.

- 7 = Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness, or Not assessed
  - 1 = Not observed
  - 2 = Very Mild: e.g., seems somewhat confused
  - 3 = Mild: e.g., indicates 2000 when, in fact, it is 2001
  - 4 = Moderate: e.g. indicates 1998
  - 5 = Moderately Severe: e.g., is unsure where he/she is
  - 6 = Severe: e.g., has no idea where he/she is
  - 7 = Very Severe: e.g., does not know who he/she is
- Now I want to ask you some standard questions that we usually ask at this point. What is today's date? (What day of the week is it? What month? What day of the month? What year?)
  - Where are we now?

**APPENDIX E. SEXUAL FUNCTIONING SUBSCALE FROM UDVALG  
FOR KLINISKE UNDERSØGELSER (UKU) SIDE  
EFFECT RATING SCALE**

### **The UKU Side Effect Rating Scale, Self-rating version Modified**

- 4.9 Have you noticed milk from your nipples?
- ☐ Not at all
  - ☐ Some
  - ☐ Yes, but not troublesome
  - ☐ Much, stains my underwear
- 4.10 Have you experienced tension or swelling in your breasts?
- ☐ Not at all
  - ☐ Some tension and swelling
  - ☐ Breasts are tense and larger than normal
  - ☐ Breasts clearly enlarged
- 4.11 Have you experienced increased sexual interest or increased sexual desire?
- ☐ Not at all
  - ☐ Somewhat more than normal
  - ☐ More than normal
  - ☐ Much more than normal
- 4.12 Have you experienced decreased sexual interest or decreased sexual desire?
- ☐ Not at all
  - ☐ A little less than normal
  - ☐ Less than normal
  - ☐ Much less than normal

***Females only***

4.7a Have you noticed more discharge/bleeding when menstruating?

- ☐ Not at all
- ☐ Somewhat more than normally
- ☐ More than normally
- ☐ Profuse discharge/bleeding

4.7b Have you noticed discharge/bleeding between periods?

- ☐ Not at all
- ☐ Occasional discharge/bleeding
- ☐ Substantial discharge/bleeding, occasionally
- ☐ Frequent discharge/bleeding between periods

4.8 Have you noticed less discharge/bleeding when menstruating?

- ☐ Not at all
- ☐ Slightly less than normal
- ☐ Less than normal
- ☐ Menstruation has not occurred

4.15 Have you experienced difficulty in reaching orgasm?

- ☐ Not at all
- ☐ Some difficulty
- ☐ More difficult than normal
- ☐ Rarely have orgasm

4.16 Do you have problems with a dry vagina during intercourse?

- ☐ Not at all
- ☐ Some dryness
- ☐ More problems than normal
- ☐ Severe problems, must use lubrication

***Males only***

4.13 Have you experienced difficulty in reaching erection?

- ☐ Not at all
- ☐ Slightly more difficult than normal
- ☐ More difficult than normal
- ☐ Cannot get erection

4.14a Have you experienced difficulties in ejaculation?

- ☐ Not at all
- ☐ Ejaculation slightly delayed
- ☐ Ejaculation delayed
- ☐ Cannot ejaculate

4.14b Have you experienced early (premature) ejaculation?

- ☐ Not at all
- ☐ Ejaculation slightly early
- ☐ Ejaculation early
- ☐ Spontaneous ejaculations

For Review Only

**APPENDIX F. CHANGES IN SEXUAL FUNCTIONING  
QUESTIONNAIRE**

## CHANGES IN SEXUAL FUNCTIONING QUESTIONNAIRE (CSFQ-F-C)

Patient Name \_\_\_\_\_

Today's Date \_\_\_\_\_

**NOTE: This is a questionnaire about sexual activity and sexual function. By sexual activity, we mean sexual intercourse, masturbation, sexual fantasies and other activity.**

1. Compared with the most enjoyable it has ever been, how enjoyable or pleasurable is your sexual life right now?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

2. How frequently do you engage in sexual activity (sexual intercourse, masturbation, etc.) now?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

3. How often do you desire to engage in sexual activity?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

4. How frequently do you engage in sexual thoughts (thinking about sex, sexual fantasies) now?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

5. Do you enjoy books, movies, music or artwork with sexual content?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

6. How much pleasure or enjoyment do you get from thinking about and fantasizing about sex?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

7. How often do you become sexually aroused?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

8. Are you easily aroused?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

9. Do you have adequate vaginal lubrication during sexual activity?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

10. How often do you become aroused and then lose interest?

- ☐ 5-Never
- ☐ 4-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 2-Often (much more than half the time)
- ☐ 1-Always

11. How often do you experience an orgasm?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

12. Are you able to have an orgasm when you want to?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

13. How much pleasure or enjoyment do you get from your orgasms?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

14. How often do you have painful orgasm?

- ☐ 5-Never
- ☐ 4-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 2-Often (more than twice a week)
- ☐ 1-Every day

\_\_\_\_ = Pleasure (Item 1)  
\_\_\_\_ = Desire/Frequency (Item 2 + Item 3)  
\_\_\_\_ = Desire/Interest (Item 4 + Item 5 + Item 6)  
\_\_\_\_ = Arousal/Excitement (Item 7 + Item 8 + Item 9)  
\_\_\_\_ = Orgasm/Completion (Item 11 + Item 12 + Item 13)  
\_\_\_\_ = **Total CSFQ Score** (Items 1 to 14)



## CHANGES IN SEXUAL FUNCTIONING QUESTIONNAIRE (CSFQ-M-C)

Patient Name \_\_\_\_\_

Today's Date \_\_\_\_\_

**NOTE:** This is a questionnaire about sexual activity and sexual function. By sexual activity, we mean sexual intercourse, masturbation, sexual fantasies and other activity.

1. Compared with the most enjoyable it has ever been, how enjoyable or pleasurable is your sexual life right now?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

2. How frequently do you engage in sexual activity (sexual intercourse, masturbation, etc.) now?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

3. How often do you desire to engage in sexual activity?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

4. How frequently do you engage in sexual thoughts (thinking about sex, sexual fantasies) now?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

5. Do you enjoy books, movies, music or artwork with sexual content?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

6. How much pleasure or enjoyment do you get from thinking about and fantasizing about sex?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

7. How often do you have an erection related or unrelated to sexual activity?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

8. Do you get an erection easily?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

9. Are you able to maintain an erection?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

10. How often do you experience painful, prolonged erections?

- ☐ 5-Never
- ☐ 4-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 2-Often (more than twice a week)
- ☐ 1-Every day

11. How often do you have an ejaculation?

- ☐ 1-Never
- ☐ 2-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 4-Often (more than twice a week)
- ☐ 5-Every day

12. Are you able to ejaculate when you want to?

- ☐ 1-Never
- ☐ 2-Rarely (much less than half the time)
- ☐ 3-Sometimes (about half the time)
- ☐ 4-Often (much more than half the time)
- ☐ 5-Always

13. How much pleasure or enjoyment do you get from your orgasms?

- ☐ 1-No enjoyment or pleasure
- ☐ 2-Little enjoyment or pleasure
- ☐ 3-Some enjoyment or pleasure
- ☐ 4-Much enjoyment or pleasure
- ☐ 5-Great enjoyment or pleasure

14. How often do you have painful orgasm?

- ☐ 5-Never
- ☐ 4-Rarely (once a month or less)
- ☐ 3-Sometimes (more than once a month, up to twice a week)
- ☐ 2-Often (more than twice a week)
- ☐ 1-Every day

\_\_\_\_\_ = Pleasure (Item 1)

\_\_\_\_\_ = Desire/Frequency (Item 2 + Item 3)

\_\_\_\_\_ = Desire/Interest (Item 4 + Item 5 + Item 6)

\_\_\_\_\_ = Arousal/Erection (Item 7 + Item 8 + Item 9)

\_\_\_\_\_ = Orgasm/Ejaculation (Item 11 + Item 12 + Item 13)

\_\_\_\_\_ = **Total CSFQ Score** (Items 1 to 14)

**APPENDIX G. PERSONAL AND SOCIAL PERFORMANCE SCALE  
(PSP) (SAMPLE)**

## Personal and Social Performance Scale (PSP) – Worksheet

The rating is based on four main areas: (a) socially useful activities, including work and study; (b) personal and social relationships; (c) self-care; and (d) disturbing and aggressive behaviors.

Data will be captured in the following format using the PSP descriptions provided below:

	Absent	Mild	Manifest	Marked	Severe	Very Severe
a. Socially useful activities, including work and study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Personal and social relationships	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Self-care	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Disturbing and aggressive behaviors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

The levels of functioning in other areas should be taken into account to adjust the rating inside the decimal level (for instance, from 31 to 40). Suicidal risk is not included in the scale.

### 10-point intervals

### PSP descriptions

100-91	Excellent functioning in all four main areas*. He/she is held in high consideration for his/her good qualities, copes adequately with life problems, is involved in a wide range of interests and activities
90-81	Good functioning in all four main areas, presence of only common problems or difficulties
80-71	Mild difficulties in 1 or more of areas a-c
70-61	Manifest, but not marked difficulties in 1 or more areas a-c, <i>or</i> mild difficulties in d
60-51	Marked difficulties in 1 of areas a-c, <i>or</i> manifest difficulties in d
50-41	Marked difficulties in 2 or more, <i>or</i> severe difficulties in 1 of areas a-c, with or without manifest difficulties in d
40-31	Severe difficulties in 1 <i>and</i> marked difficulties in at least 1 of areas a-c, <i>or</i> marked difficulties in d
30-21	Severe difficulties in 2 of areas a-c, <i>or</i> severe difficulties in d, with or without impairment in areas a-c
20-11	Severe difficulties in all areas a-d, <i>or</i> very severe in d with or without impairment in general areas a-c. If the person reacts to external prompts the suggested scores are 20-16; if not, the suggested scores are 15-11.
10-1	Lack of autonomy in basic functioning with extreme behaviors but without survival risk (ratings 6-10) or with survival risk, eg, death risk due to malnutrition, dehydration, infections, inability to recognize situation of manifest danger (ratings 5-1).

**Overall score** |\_\_\_|\_\_\_|\_\_\_|

For main areas a-c, the degrees of severity are:

Absent	
Mild	Not manifest difficulties, known only to someone who is very familiar with the person
Manifest, but not marked	Difficulties clearly noticeable by everyone, but not interfering substantially with the person's ability to perform his/her role in that area, given the person's socio-cultural context, age, sex and educational levels
Marked	Difficulties heavily interfering with role performance in that area; however, the person is still able to do something without professional or social help, although inadequately and/or occasionally; if helped by someone, he/she may be able to reach the previous level of functioning
Severe	Difficulties that make the person unable to any role performance in that area, if not professionally helped, or lead the person to a destructive role; however, there are no survival risks.
Very severe	Impairments and difficulties of such intensity to endanger person's survival.

For general area d, the degrees of severity are:	
Absent	
Mild	Mild rudeness, unsociability or whingeing
Manifest, but not marked	Speaking too loudly or speaking to others in a too-familiar manner, or eating in a socially unacceptable manner
Marked	Insulting other in public, breaking or wrecking objects, acting frequently in a socially inappropriate but not dangerous way (eg, stripping in public or urinating in public).
Severe	Frequent verbal threats or frequent physical assaults, without intention or possibility of severe injuries.
Very severe	Frequent aggressive acts, aimed at or likely to cause severe injuries.

Occasional is defined as occurring three or more times in the reference period or occurring even less than three times but in circumstances and/or with such a previous history to convince the rater that there is a risk of recurrence in the near future. If the aggressive behavior has been present occasionally, the rating may be decreased by one degree, eg, from severe to marked.

\* Main areas: a=socially useful activities, including work and study; b=personal and social relationships; c=self-care; d=disturbing and aggressive behaviors.

#### **Guidelines for PSP Total Score**

Ratings from 71-100 reflect only mild difficulties.

Ratings from 31-70 reflect manifest disabilities of various degrees.

Ratings from 1-30 reflect functioning so poor that intensive support or supervision is needed.

Morosini, P.L., Magliano, L., Brambilla, L., Ugolini, S., Pioli, R. (2000). Development, reliability, and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatrica Scandinavica* 101(4), 323-329.

Rater Signature: \_\_\_\_\_

Date: \_\_\_\_\_

## **APPENDIX H. HEINRICHS-CARPENTER QUALITY OF LIFE SCALE (QLS) (SAMPLE)**

April 10, 1992

### QUALITY OF LIFE SCALE

This instrument is designed to evaluate the current functioning of nonhospitalized schizophrenic persons apart from the presence or absence of florid psychotic symptomatology or need for hospitalization. It assesses the richness of their personal experience, the quality of their interpersonal relations, and their productivity in occupational roles.

It is intended to be administered as a semi-structured interview. Each item consists of three parts. First, a brief statement is provided to help the interviewer understand and focus on the parameter to be assessed. Second, a number of suggested questions are provided that may help the interviewer begin his exploration with the subject. Finally, a seven-point scale is provided for each item, with a brief description at four points to help the interviewer make his judgment and unlabeled points.

The questions provided are just suggestions. They are to be altered or supplemented as needed. Each item should be explored as much as required to allow the rater to make a good clinical judgment. The intent of the schedule is to assess limitations due to psychopathology or personality deficits. Adjustments should be made by the rater when extraneous factors are clearly and unambiguously involved (e.g., decreased social contact due to serious physical illness).

All items should be rated. Circle the appropriate number on each item scale.

---

SCORING: Mean scores of the following subscales and total (prorate items 1 and 12 for missing data as indicated in the manual).

Subscale Scores:

I. Interpersonal Relations (1-8): \_\_\_\_\_

II. Instrumental Role (9-12): \_\_\_\_\_

III. Intrapsychic Foundations (13-17,20,21): \_\_\_\_\_

IV. Common Objects and Activities (18,19): \_\_\_\_\_

III plus IV (13 thru 20): \_\_\_\_\_

Total Score (Items 1-21): \_\_\_\_\_

## 1. RATE INTIMATE RELATIONSHIPS WITH HOUSEHOLD MEMBERS

This item is to rate close relationships with significant mutual caring and sharing with immediate family or members of the subject's current household.

### Suggested questions:

Are you especially close with any of the people you currently live with or your immediate family?

0 - Virtually no intimacy

Can you discuss personal matters with them?

1 -

How much have you talked with them?

2 - Only sparse and intermittent intimate interactions

What are these relationships like?

3 -

Can they discuss personal matters with you?

4 - Some consistent intimate interactions but reduced in extent or intensity; or intimacy only present erratically

What sorts of things have you done together?

5 -

When at home, have you spent much time around your family or were you generally alone?

6 - Adequate involvement in intimate relations with household members or immediate family

---

9 - Score here if lives alone and no immediate family nearby

Note: (For Factor and Total Scores, prorate this item on the basis of Items 2 through 8.)

## 2. RATE INTIMATE RELATIONSHIPS

This item is to rate close relationships with significant mutual caring and sharing, with people other than immediate family or household members. Exclude relationships with mental health workers.

### Suggested questions:

Do you have friends with whom you are especially close other than your immediate family or the people you live with?	0 - Virtually absent
	1 -
	2 - Only sparse intermittent relations
Can you discuss personal matters with them?	3 -
How many friends do you have?	4 - Some consistent intimate relations but reduced in number or intensity; or intimacy only present erratically
How often have you spoken with them recently, in person or by phone?	
What have these relationships been like?	5 -
Can they discuss personal matters with you?	6 - Adequate involvement with intimate relationships with more than one other person



### 3. RATE ACTIVE ACQUAINTANCES

This item is to rate relationships with people based on liking one another and sharing common activities or interests but without the intimate emotional investment of the above item. Exclude relationships with mental health workers and other household members.

#### Suggested questions:

Apart from close personal friends, are there people you know with whom you have enjoyed doing things?	0 - Virtually absent
How many?	1 -
How often have you gotten together with them?	2 - Few active acquaintances and only infrequent contact
What things have you done together?	3 -
Have you been with people as a part of clubs or organize activities?	4 - Some ongoing active acquaintance but reduced contact and limited shared activity
Have you had extra social contact with co-workers, such as going to lunch together or going out after work?	5 -
	6 - Adequate involvement with active acquaintances

#### 4. RATE LEVEL OF SOCIAL ACTIVITY

This item is to rate involvement in activities with other people done for enjoyment. Exclude social activity that is primarily instrumental for other goals, for example, work and school. Exclude psychotherapy.

##### Suggested questions:

How often have you done things for enjoyment that involve other people?

0 - Virtually absent

1 -

What sort of things?

2 - Occasional social activity but lack of regular pattern of such activity, or limited only to activity with immediate family or members of household

Have you participated in clubs or other organized social groups?

3 -

4 - Some regular social activity but reduced in frequency or diversity

5 -

6 - Adequate level of regular social activity

## 5. RATE INVOLVED SOCIAL NETWORK

This item is to rate the extent to which other people concern themselves with the person, care about his fortunes or know about his activities. Exclude mental health workers.

### Suggested questions:

- |   |   |
|---|---|
| Are there people who have been concerned about your happiness and well being?   | 0 - Virtually absent  |
| How many?   | 1 -   |
| How did they show it?   | 2 - Minimal in number or degree of involvement, and/or limited to immediate family          |
| If some important and exciting thing happened to you, who would you contact or inform?  | 3 -   |
| Are there people who often provided you emotional support or help in day-to-day matters such as food, transportation, and practical advice? | 4 - Presence of some involved social network but reduced in number or degree of involvement |
| Are there people you could turn to or depend on for help if anything happened?  | 5 -   |
|   | 6 - Adequate involved social network in both extent and in degree of involvement            |

## 6. RATE SOCIAL INITIATIVES

This item is to rate the degree to which the person is active in directing his social interactions - what, how much, and with whom.

### Suggested questions:

Have you often asked people to do something with you, or have you usually waited for others to ask you?

0 - Social activity almost completely dependent on initiatives of others

1 -

When you have had an idea for a good time, have you sometimes missed out because it's hard to ask others to participate?

2 - Occasional social initiative, but social life significantly impoverished due to his pattern of social passivity, or initiative limited to immediate family

Have you contacted people by phone?

3 -

Have you tended to seek people out?

4 - Evidence of some reduction of social initiative, but with only minimal adverse consequences on his social activity

Have you usually done things alone or with other people?

5 -

6 - Adequate social initiative

## 7. RATE SOCIAL WITHDRAWAL

This item is to rate the degree to which the person actively avoids social interaction due to his discomfort or disinterest.

### Suggested questions:

- |  |   |
|--|---|
| Have you felt uncomfortable with people?   | 0 - Active avoidance of virtually all social contact  |
| Have you turned down offers to do things with other people? Would you if you were asked? | 1 -   |
| Have you done this even when you have had nothing to do?                                 | 2 - Tolerates that social contact required for meeting other needs, but very little social contact for its own sake, or lack of withdrawal only with immediate family |
| Have you avoided answering the phone?  | 3 -   |
| How has this interfered with your life?  | 4 - Some satisfying and enjoyable social engagement, but reduced due to avoidance   |
| Have you dealt with people only when it's necessary to accomplish something you want?    | 5 -   |
| Have you stayed to yourself at home?   | 6 - No evidence of significant social withdrawal  |
| Have you preferred to be alone?  |   |

## 8. RATE SOCIOSEXUAL RELATIONS

This item is to rate the capacity for mature intimate relations with members of the opposite sex and satisfying sexual activity. The wording assumes a heterosexual preference. In clear cases of consistent homosexual preference, reword accordingly and rate these same capacities.

### Suggested questions if single:

- |  |  |
|--|--|
| Have your social activities involved women (men)?                      | 0 - No interest in opposite sex, or active avoidance   |
| Have you avoided them or found it too uncomfortable to deal with them? | 1 -  |
| Have you dated?  | 2 - Some limited contact with opposite sex but superficial with avoidance of intimacy; or sexual activity as just physical release without emotional involvement; or relationships marked by severe and chronic disruption, dissatisfaction or affective chaos |
| Did you have one or more girlfriends? (boyfriends?)                    |  |
| Have the relationships been satisfying?                                |  |
| Have emotionally involved were you?                                    | 3 -  |
| Were you in love?  | 4 - Relationships with some intimacy and emotional investment, predominantly satisfying, and perhaps some sexual expression or physical signs of affection   |
| Were you having sexual activity?                                       |  |
| Was it satisfying?   | 5 -  |
| Did you show physical signs of affection, such as hugging and kissing? | 6 - Usually has satisfying relationships, emotionally rich and intimate and appropriate sexual expression and physical signs of expression   |

Suggested questions if married or living with someone:

Were you happy in your relationship with your partner?	0 - No interest in opposite sex, or active avoidance
Have you done many things together?	1 -
Did you talk together much?	2 - Some limited contact with opposite sex but superficial with avoidance of intimacy; or sexual activity as just physical release without emotional involvement; or relationships marked by severe and chronic disruption, dissatisfaction or affective chaos
Did you discuss personal thoughts and feelings?	
Did you fight much?	
Has your sex life been satisfying?	
Did you show physical signs of affection such as hugging and kissing?	3 -
Did you feel close to her (him)?	4 - Relationships with some intimacy and emotional investment, predominantly satisfying, and perhaps some sexual expression or physical signs of affection
	5 -
	6 - Usually has satisfying relationships, emotionally rich and intimate and appropriate sexual expression and physical signs of expression

## 9. RATE OF EXTENT OF OCCUPATIONAL ROLE FUNCTIONING

This item is to rate the amount of role functioning the person is attempting, not how well nor how completely he is succeeding. For homemakers, consider whether for a person with normal efficiency the responsibilities would represent a full-time job seeking activity.

### Suggested questions:

Have you had a job? 0 – Virtually no role functioning

How many hours a week did you work? 1 -

Were you involved in school in addition to work? 2 – Less than half-time

3 -

### Suggested questions:

4 – Half-time or more, but less than full time

What sort of education program were you pursuing?

5 –

How many classes were you taking?

6 - Full-time or more

How much time did school take per week?

Were you also working, caring for children or responsible for housekeeping?

### Suggested questions for homemakers:

How much was involved in taking care of your home and family?

Were you raising children?

What were your responsibilities in the home?

How much did other people help with these responsibilities?



## 10. RATE LEVEL OF ACCOMPLISHMENT

This item is to rate the level of success and achievement in fulfilling the particular role the person has chosen to attempt.

Question the subject regarding salary and raises, the challenge and responsibility of the job, praise or reprimands from employer, adequacy of interaction with co-workers, absenteeism, promotions or demotions. For students, question regarding grades, the difficulty of the curriculum, praise or criticism from teachers, adequacy of interaction with other classmates, class attendance, completion of assigned work, and extracurricular activities. For homemakers, question regarding the adequate performance of required tasks such as cooking, shopping, washing dishes, cleaning, dusting, laundry, management of household budget, physical care of children, and meeting the emotional needs of children. Question further regarding praise or criticism by family members about either housekeeping or child raising.

0 - Attempting no role function or performing at level so poor as to imminently threaten the ability to continue in that role

1 -

2 - Functioning just well enough to keep position with very low level of accomplishment

3 -

4 - Generally adequate functioning

5 -

6 - Very good functioning with evidence of new or progressive accomplishments and/or very good functioning in some areas

## 11. RATE DEGREE OF UNDEREMPLOYMENT

This item is to rate the degree to which the existing extent of and accomplishment in occupational role functioning reflects full utilization of the potentiality and opportunities available to the person. Consider innate abilities, physical handicaps, education, economic and social culture factors. Obviously, limitations directly reflecting any mental illness or personality disorder should not be considered in estimating the person's potential.

### Suggested questions:

This item requires a complex judgment.

Ask any further questions needed to clarify the abilities and opportunities of this individual.

0 - Almost complete failure to actualize potentials

1 -

2 - Significant underemployment of abilities or unemployed but looking for work actively.

3 -

4 - Somewhat below the person's capacity

5 -

6 - Role functioning commensurate with person's abilities and opportunities

## 12. RATE SATISFACTION WITH OCCUPATIONAL ROLE FUNCTIONING

This item is to rate the extent to which the person is comfortable with his choice of role, the performance of it, and the situation in which he performs it. It also is to rate the extent to which it provides a sense of satisfaction, pleasure, and fulfillment to him.

### Suggested questions:

Did you like your work or schooling?

Would you have preferred to be doing something else?

Do you plan a change? Why?

Did you get good feelings from doing your work – pleasure, fulfillment, etc.

Did your work or school make you feel good about yourself?

Are you enthusiastic about your job?

Do you look forward to going to work?

0 - Pervasive unhappiness and dissatisfaction with occupational role

1 -

2 - Little or no definite evidence of unhappiness or dissatisfaction, but role does not provide any positive pleasure or fulfillment. Perhaps boredom is evident.

3 -

4 - Little or no discontent and some limited pleasure in work

5 -

6 - Rather consistent sense of fulfillment and satisfaction, perhaps in spite of some limited complaints

---

9 - Not applicable if patient not involved in any occupational role functioning

Note: (This item should be rated 2 if item #9 is rated less than 3. For Factor and Total scores, prorate this item on the basis if items 9 through 11.)

### 13. RATE SENSE OF PURPOSE

This item is to rate the degree to which the person posits realistic, integrated goals for his life. If the person's current life reflects such goals, it is not necessary that he (she) be planning a change in order to be judged to have a good sense of purpose.

#### Suggested questions:

What makes life worth living for you?

Do you think much about the future?

Have you set any goals for yourself?

What do you anticipate your living and working situation to be a few months from now?

What plans do you have for your life over the next year or so – personal as well as job related ones?

0 - No plans, or plans are bizarre, delusional, or grossly unrealistic

1 -

2 - Has plans, but they are vague, somewhat unrealistic, poorly integrated with one another, or of little consequence to the person's life

3 -

4 - Realistic and concise plans for next year or so but little integration into long-range life plan

5 -

6 - Realistic, concise, and integrated plans, both short- and long-range

#### 14. RATE DEGREE OF MOTIVATION

This item is to rate the extent to which the person is unable to initiate or sustain goal-directed activity due to inadequate drive.

##### Suggested questions:

How have you been going about accomplishing your goals?

0 - Lack of motivation significantly interferes with basic routine

What other things have you worked on or accomplished recently?

1 -

Have there been tasks in any area that you wanted to do but didn't because you somehow didn't get around to it?

2 - Able to meet basic maintenance demands of life, but lack of motivation significantly impairs any progress or new accomplishments

Has this experience of just not getting around to it interfered with your regular daily activities?

3 -

How motivated have you been?

4 - Able to meet routine demands of life and some new accomplishments, but lack of motivation results in significant underachievement in some areas

Have you had much enthusiasm, energy, and drive? .

5 -

Have you tended to get into a rut?

6 - No evidence of significant lack of motivation

Have you tended to put things off?

## 15. RATE CURIOSITY

This item is to rate the degree to which the person is interested in his surroundings and questions those things he doesn't understand. Exclude interest in hallucinations or delusions or other psychotic products. However, pathological preoccupation with psychotic products or other themes may limit curiosity or interest in other things.

### Suggested questions:

How often have you seen or heard about something that you wanted to know more about or understand better?

0 - Very little curiosity or interest in new topics or events

What sorts of things?

1 -

Have you done anything to learn more about them? Please specify.

2 - Some sporadic curiosity, but not pursued in thought or action

Have you read the newspapers, or listened to the news on TV or radio?

3 -

Were you interested in any issues in current events or sports?

4 - Some curiosity and time spent thinking about topics or interest and some actual effort to learn more about them

How curious about things have you been?

5 -

6 - Curiosity about a number of topics and some effort to learn more about some of them such as reading, asking questions and planned observation

## 16. RATE ANHEDONIA

This item is to rate the person's capacity to experience pleasure and humor. Do not rate anhedonia that presents as the result of a clear and observable depressive syndrome, e.g., agitation, crying, marked feelings of wickedness and worthlessness, etc. However, anhedonia accompanied by apathy and withdrawal from which depression may be inferred should be rated. Ask any questions necessary to determine the presence of depression and its effect on hedonic capacity. This is to be distinguished from the capacity to display affect, which is not rated here.

### Suggested questions:

Have you been able to enjoy yourself?

How often have you really enjoyed or gotten satisfaction from something you were doing?

How often did you choose to do something that struck you as amusing or made you feel like laughing?

Did you have trouble getting enjoyment from things that seemed like they should be fun? Do other people seem to get more enjoyment in things than you do?

Did you often spend the better part of the day bored or disinterested in things?

0 - Nearly complete inability to experience pleasure or humor

1 -

2 - Some sporadic and limited experiences of pleasure or humor but a predominant lacking of these capacities

3 -

4 - Some regular experiences of pleasure & humor but reduced in extent & intensity

5 -

6 - No evidence of anhedonia or can be explained completely by concurrent depression or anxiety

## 17. RATE TIME UTILIZATION

This item is to rate the amount of time passed in aimless inactivity -sleeping during the day, lying in bed, sitting around doing nothing or in front of the TV or radio when not particularly interested.

### Suggested questions:

Did you spend much time doing nothing  
Just sitting around or in bed?

0 - Spends the vast majority of his day in  
aimless activity

Did you spend much time watching TV or  
listening to music - were you really  
interested or just had nothing better to do?

1 -

2 - Spends about half of his days in aimless  
activity

Did you sleep much during the day?

How much of your days were spent in  
these ways?

3 -

4 - Some excessive aimless inactivity but  
less than half his day

How have you utilized your time?

Did you tend to waste time?

5 -

6 - No excessive aimless inactivity beyond  
the normal amount required for  
relaxation



## 18. RATE COMMONPLACE OBJECTS

This item assumes that basic participation in living in this culture nearly always requires a person to possess certain objects.

### Suggested questions:

For this question, inquire about each of the 12 items listed below.

Are you wearing or carrying the following?

- (1) a wallet or purse
- (2) keys
- (3) a driver's license
- (4) a watch
- (5) a credit card
- (6) a Social Security or Medical Assistance card

0 - Absence of nearly all commonplace objects (0 items)

1 -

2 - Major deficit of commonplace objects (3-4 items)

3 -

4 - Moderate deficit (7-8 items)

5 -

Do you have with you at your place of residence the following?

- (1) a map of the city or area
- (2) your own alarm clock
- (3) a comb or hair brush
- (4) an overnight bag
- (5) a library card
- (6) postage stamps

6 - Little or no deficit (11-12 items)

## 19. RATE COMMONPLACE ACTIVITIES

This item assumes that basic participation in living in this culture nearly always requires a person to engage in certain activities.

### Suggested questions:

For this item inquire about each of the 8 items listed below. Which of the following have you done in the past two weeks? (1) read a newspaper, (2) paid a bill, (3) wrote a letter, (4) gone to a movie or play, (5) driven a car or ridden public transportation alone, (6) shopped for food, (7) shopped for other than food, (8) eaten in a restaurant, (9) taken a book or record out of the library, (10) participated in a public gathering, (11) attended a sporting event, (12) visited a public park or other recreational facility.

0 - Absence of nearly all activities (0 items)

1 -

2 - Major deficit (3-4 items)

3 -

4 - Moderate deficit (7-8 items)

5 -

6 - Little or no deficit

## 20. RATE CAPACITY FOR EMPATHY

This item is to rate the person's capacity to regard and appreciate the other person's situation as different from his own - to appreciate different perspectives, affective states and points of view. It is reflected in the person's description of interactions with other people and how he views such interactions. Specific probing to elicit the person's description and assessment of relevant situations can be done at this time if sufficient data has not emerged thus far in the interview.

### Suggested questions:

Consider someone you are close to or spend a lot of time with. What about them irritates or annoys you? What about you irritates or annoys them? What things do they like? What things that you do please them? If they appear upset, how do you usually react? If you have an argument or difference of opinion with them, how do you handle it?

Are you usually sensitive to the feelings of others?

Are you affected very much by how other people feel?

0 - Shows no capacity to consider the views and feelings of others

1 -

2 - Shows little capacity to consider the views and feelings of others

3 -

4 - He can consider other people's views and feelings but tends to be caught up in his own world.

5 -

6 - He spontaneously considers the other person's situation in most instances, can intuit the other person's affective responses, and uses this knowledge to adjust his own responses.

## 21. RATE CAPACITY FOR ENGAGEMENT AND EMOTIONAL INTERACTION WITH INTERVIEWER

This item is to rate the person's ability to engage the interviewer, to make him feel affectively in touch and acknowledge him as a participant individual in the encounter, and to react in a give and take way.

This is a global judgment based on the entire interview.

- 0 - Interviewer feels virtually ignored with essentially no sense of engagement, with very little reactivity
- 1 -
- 2 - Very limited engagement
- 3 -
- 4 - Engagement somewhat limited or present erratically
- 5 -
- 6 - Consistently good engagement and reactivity

**APPENDIX I. NEGATIVE SYMPTOM ASSESSMENT-16 (NSA-16)  
(SAMPLE)**

## Negative Symptom Assessment-16 (NSA-16)—Long Form

1. **Prolonged time to respond.** After asking the subject a question, he/she pauses for inappropriately long periods before answering. Rate severity of the frequency of these pauses.
  1. No abnormal pauses before speaking
  2. Minimal evidence of inappropriate pauses, may be extreme of normal
  3. Occasionally pauses long enough before answering the question to cause you to wonder whether he/she heard it
  4. Long pauses occur frequently (20-40% of responses)
  5. Long pauses occur most of the time (40-80% of responses)
  6. Long pauses occur with almost every response (80-100% of responses)
  9. Not ratable (use only when all efforts to rate this item have failed)
2. **Restricted speech quantity.** This item assesses the amount of speech the subject provides in the course of the interview. Ratings on this item suggest that the subject gives brief answers to questions and/or provides elaborating details only after the interviewer prods him.
  1. Normal speech quantity
  2. Minimal reduction in quantity, may be extreme of normal
  3. Speech seems reduced, but more can be obtained with minimal prodding
  4. Speech is maintained only by regularly prodding the subject
  5. Responses are usually limited to a few words and/or details are only obtained by prodding or bribing
  6. Responses are usually non-verbal or limited to 1 or 2 word answers (despite one's best efforts to get the subject to elaborate)
  9. Not ratable (use only when all efforts to rate this item have failed)
3. **Impoverished speech content.** The subject may talk a lot or a little but the information conveyed is very limited. If this symptom is pronounced, you will feel you have little more information at the end of the conversation than at the beginning. For subjects who give minimal responses, rate item based on what the interviewer knows after asking probing questions.
  1. Normal speech content
  2. Minimal reduction in content, may be extreme of normal
  3. Ideas are sometimes vague
  4. Ideas are vague and/or some ideas remain vague even after the interviewer asks for clarification
  5. Ideas remain vague even after the interviewer asks for clarification
  6. No ideas can be clarified beyond vague
  9. Not ratable (use only when all efforts to rate this item have failed)

4. **Inarticulate speech.** The subject's speech cannot be understood because enunciation is poor. Do not rate psychotic sub-vocalizations if the rest of the subject's speech is normal and these utterances are not addressed to the interviewer. For subjects with a strong dialect, rate on the basis of the subject's ability to articulate and not on their competence with the language.
  1. Clear speech, not mumbled
  2. Minimal garbled speech, may be extreme of normal
  3. A few words slurred, but can be understood in context
  4. The subject must occasionally be asked to repeat mumbled words
  5. Many words are difficult to understand; the subject must frequently be asked to repeat, but on repeating can usually be understood
  6. Little language can be understood even after repeating
  9. Not ratable (use only when all efforts to rate this item have failed)
5. **Emotion: Reduced range.** Emotion is the feeling content of a person's inner life. This item assesses the range of emotion experienced by the subject during the last week (or other specified time period). Base ratings on the subject's answers to queries of whether he/she has felt happy, sad, etc. during the last week, as well as any reports of having these emotions later in the interview. A full range of emotions would include, but not be limited to happiness, sadness, pride, fear, surprise, and anger. This item should be distinguished from the capacity to display affect, which is rated elsewhere. (If you sense that a subject's emotional life is autistic and not contextually validated, rate his/her emotional range according to your interpretations of his/her experience.)
  1. Normal range of emotion
  2. Minimal reduction in range, may be extreme of normal
  3. Range seems restricted relative to a normal person, but during the specified time frame subject convincingly reports at least 4 emotions.
  4. Subject convincingly identifies 2 or 3 emotional experiences
  5. Subject convincingly identifies only 1 emotional experience
  6. Subject reports little or no emotional range
  9. Not ratable (use only when all efforts to rate this item have failed)
6. **Affect: Reduced modulation of intensity.** This item assesses the subject's modulations of intensity of affect shown during the interview while discussing matters that would be expected to elicit significantly different affective intensities in a normal person
  1. Normal modulations of affect
  2. Minimal reduction of modulation, may be extreme of normal
  3. Affective intensity is muted relative to normal, but some spontaneous change in affective intensity appropriate to the content of conversation is observed
  4. Affective responses are clearly blunted; but by asking more pointed questions, appropriate changes in affective intensity can be elicited
  5. Intensity of affect is modulated only slightly, even after prodding
  6. Affective responses are never modulated, even after prodding
  9. Not ratable (use only when all efforts to rate this item have failed)

7. **Affect: Reduced display on demand.** Affect is the outward expression of a person's feelings. This item assesses the subject's ability to display a range of affect as expressed by changes in his/her facial expression and gestures when asked by the interviewer to show how his/her face appears when he/she feels happy, sad, proud, scared, surprised, and angry. (Although capable, some subjects are reticent about making facial expressions on demand. The interviewer may encourage the subject until convinced that he/she is unable, or unwilling to assume the expression. Do not accept correct affective expressions that are half-hearted and unconvincing, and do not accept descriptions of affective expressions.)
1. Subject convincingly displays all requested affective expressions
  2. Subject convincingly displays 5 of 6 requested affective expressions
  3. Subject displays any 4 of 6 requested affective expressions
  4. Subject displays any 2 or 3 of 6 requested affective expressions
  5. Subject displays any 1 of 6 requested affective expressions
  6. Subject is unable to display any of the affective expressions
  9. Not ratable (use only when all efforts to rate this item have failed)
8. **Reduced social drive.** This item assesses how much the subject desires to initiate social interactions. Desire may be measured in part by the number of actual or attempted social contacts with others. To rate severity probes the type of social interactions, **and** their frequency. Remember the reference range is a normal 20 year old. Many subjects may be rated 2 to 3.
1. Normal social drive
  2. Minimal reduction in social drive, may be extreme of normal
  3. Desire for social interactions seems somewhat reduced
  4. Obvious reduction in desire to initiate social contacts, but a number of contacts are initiated each week
  5. Marked reduction in the subject's desire to initiate social contacts, but a few contacts are maintained at subject's initiation (as with family)
  6. No desire to initiate any social interactions
  9. Not ratable (use only when all efforts to rate this item have failed)
9. **Poor rapport with interviewer.** This item assesses the interviewer's subjective sense that he/she and the subject are actively engaged in communication with one another. Evaluate both verbal and nonverbal aspects of communication. Do not rate hostility as lack of rapport.
1. Normal rapport
  2. Minimal reduction in rapport, may be extreme of normal
  3. Interviewer sometimes has to carry the conversation because the subject's interest seems reduced
  4. Interchanges are generally dull and uninspiring; interviewer must often lead the conversation because subject is detached
  5. Interviewer must prod to engage the subject in the interview
  6. Prodding does not result in engagement with the interviewer
  9. Not ratable (use only when all efforts to rate this item have failed)



10. **Interest in emotional and physical intimacy.** This item assesses how much the subject retains interest in emotional and/or physical intimate activities. Do not exclusively rate actual performance even though in many instances performance might indicate desire and non-performance the absence of it. Take the subject's marital and environmental situations into account when rating this item. (Because of his/her illness, he/she may be unable to find a suitable partner; if hospitalized, he/she may be discouraged from being intimate with others.) Emotional and physical intimacy interest can be expressed by a wide variety of activities. If the subject claims to be interested in emotional and physical intimacy interest but his/her performance is not consistent with his/her claim, the rater should ask him/her to account for this discrepancy.
1. Desires to engage in some form of emotional and/or physical intimate activity once a day or more
  2. Desires to engage in some form of emotional and/or physical intimate activity 3-6 times a week
  3. Desires to engage in some form emotional and/or physical intimate activity once or twice a week
  4. Desires to engage in some form of emotional and/or physical intimate activity 1-3 time a month
  5. Desires to engage in some form of emotional and/or physical intimate activity several times a year
  6. No emotional and/or physical intimate interest is reported
  9. Not ratable (use only when all efforts to rate this item have failed)
11. **Poor grooming and hygiene.** The subject presents with poorly groomed hair, disheveled clothing, etc. Do not rate grooming as poor if it is simply done in what a middle-class observer might consider poor taste (e.g.; wild hairdo or excessive facial makeup).
1. Normal grooming and hygiene
  2. Minimal reduction of grooming and hygiene, may be extreme of normal
  3. Clean but untidy, or clothes are mismatched
  4. Clothes are unkempt and unbuttoned (looks as if subject just got out of bed)
  5. Clothes are dirty or stained, or has an odor
  6. Clothes are badly soiled and/or subject has a foul odor
  9. Not ratable (use only when all efforts to rate this item have failed)
12. **Reduced sense of purpose.** This item assesses whether the subject posits integrated goals for his/her life. If the subject already has what seems to be a satisfactory and well-integrated life, it is not necessary that he/she be planning a change to be judged as having a good sense of purpose.
1. Normal sense of purpose
  2. Minimal reduction in purpose, may be extreme of normal
  3. Life goals somewhat vague, but current activities suggest purpose
  4. Subject has difficulty coming up with life goals, but activities are directed toward limited goal or goals
  5. Goals are very limited or have to be suggested, and activities are not focused toward achieving any of them
  6. No identifiable life goals
  9. Not ratable (use only when all efforts to rate this item have failed)
13. **Reduced hobbies and interest.** This item assesses the range and intensity of the subject's interests.

1. Normal interests
  2. Minimal reduction in interests, may be extreme of normal
  3. Range of interests and/or commitment to them seems diminished
  4. Range of interests is clearly diminished and is not particularly committed to interests held
  5. Only 1 or 2 interests reported, and these pursued superficially
  6. No identifiable goals
  9. Not ratable (use only when all efforts to rate this item have failed)
14. **Reduced daily activity.** This item assesses the level of the subject's daily activity and his/her failure to take advantage of the opportunities his/her environment offers. Get a complete account of what the subject does from the time he/she gets up until he goes to bed. Compare his/her activities with those of a young person who is not mentally ill. If the subject participates as an outpatient in a mental health program, determine the level of his/her participation, i.e. whether he/she is actively involved, or just passes time there. If the subject is hospitalized rate his/her daily activity as you would for a young person who is not hospitalized and without regard for the limitations that the hospital routine may place on him/her.
1. Normal daily activity
  2. Minimal reduction in activity, may be extreme of normal
  3. Employed, attends school or volunteers, but is underachieving; few hobbies
  4. Not involved in the activities expected of a normal young person (may be unemployed, or minimally employed for education, but may be involved in a mental health program one or more days a week)
  5. Most of day spent doing activities, things that require minimal mental or physical exertion (watches TV, smokes, drinks coffee, walks to store, but may be involved in a mental health program one or more days a week)
  6. Most of day is spent sitting in a chair or lying in bed; has little or no regard for what goes on in immediate environment
  9. Not ratable (use only when all efforts to rate this item have failed)
15. **Reduced expressive gestures.** Gestures and body movements that normally facilitate communication during speech are less than normal, or are not observed at all. Do not rate involuntary movement disorders.
1. Normal expressive gestures
  2. Minimal reduction in gestures, may be extreme of normal
  3. Hand and head gestures normally seen during conversation are reduced
  4. Hand or head gestures are infrequent; gestures may be limited to periods when the subject is discussing topics of special interest
  5. Gestures infrequent even during discussion of highly emotional topics
  6. Gestures are never observed
  9. Not ratable (use only when all efforts to rate this item have failed)
16. **Slowed movements.** This item assesses how much the subject's voluntary movements are slowed. At a minimum one should rate movements as gait and those of rising from a chair. Rate these movements in comparison to a normal young person
1. Normal speed of movements
  2. Minimal reduction in speed of movements, may be extreme of normal
  3. Voluntary movements are slightly retarded or slowed
  4. Movements are generally sluggish
  5. Most movements are retarded and made with effort
  6. All movements are made with extreme effort; subject must be assisted from chair
  9. Not ratable (use only when all efforts to rate this item have failed)



**GLOBAL NEGATIVE SYMPTOMS RATING.** Rate this item on the basis of overall impression of negative symptoms in the subject, not on the basis of a single item or total score.

1. No evidence of negative symptoms
2. Minimal evidence of negative symptoms
3. Mild evidence of negative symptoms
4. Moderate evidence of negative symptoms apparent to the casual observer
5. Marked evidence of negative symptoms readily apparent to the casual observer
6. Severe evidence of negative symptoms marked and obvious impact on functioning
7. Extremely severe negative symptoms (incapacitating)

**APPENDIX J. PATIENT SATISFACTION WITH MEDICATION  
QUESTIONNAIRE (PSMQ)-MODIFIED (SAMPLE)**

## MODIFIED MEDICATION SATISFACTION QUESTIONNAIRE (MSQ)

Overall, how satisfied are you with your current medication?

Very  
Dissatisfied

☐

1

Somewhat  
Dissatisfied

☐

2

Neither  
Dissatisfied  
nor Satisfied

☐

3

Somewhat  
Satisfied

☐

4

Very  
Satisfied

☐

5

Overall, do you prefer your current LAI medication or your previous LAI medication for the treatment of Schizophrenia (prior to your participation in this study)?

Much  
Prefer  
Previous LAI

☐

1

Prefer  
Previous LAI

☐

2

Neither  
Prefer  
Previous nor  
Current LAI

☐

3

Prefer  
Current LAI

☐

4

Much Prefer  
Current LAI

☐

5

How would you rate the side effects of your current LAI medication, compared with previous LAI medication for the treatment of Schizophrenia (prior to your participation in this current study)?

Much Less  
Side Effects

☐

1

Less Side  
Effects

☐

2

The Same  
as Previous

☐

3

More Side  
Effects

☐

4

Much More  
Side Effects

☐

5

**APPENDIX K. SIXTH EDITION OF THE TREATMENT SERVICES  
REVIEW (TSR-6) (SAMPLE)**

## TREATMENT SERVICES REVIEW (Version 6) – Modified for Mental Health

*This interview asks about different services you may have received over the past \_\_\_ days, since DATE. It includes medical services, emotional or psychological services, family, marital or parenting services, financial or housing services, and legal services. Do you have any questions before we get started?*

**TIME STARTED:**

DEMOGRAPHIC INFORMATION			
Patient initials:		Interviewer Name:	
Patient Number:		Date of Interview:	
Patient Marital Status (circle one):	<div style="display: flex; justify-content: space-between;"> <div> 1. Married 2. Living as married 3. Widowed 4. Divorced </div> <div> 5. Separated 6. Never married 7. No reply </div> </div>		
<b>Coverage Period</b>			
	From:		To:
<b>NUMBER OF DAYS IN RECALL PERIOD:</b>			

G1 Where did you stay for the past ___ days?		# of Days
1. Alone (in private house, apartment, hotel, etc.)		___
2. With others (in private house, apartment, hotel, group home, assisted living residence, etc.)		___
3. Institution, e.g. hospital, jail, prison (controlled environment)		
(a) Hospital/Residential treatment		___
(b) Jail or prison		___
(c) Day treatment or partial hospital program		___
4. Homeless shelter		___
5. Homeless, i.e. on the street, in an abandoned building, in a car		___



<b>MEDICAL SERVICES</b>		
Questions about any medical treatment you have received over the past ____ days		
<b>M1</b>	How many nights were you an inpatient in a medical hospital, nursing home, or medical rehabilitation facility?	_____
	1a) Specify:	
	Medical hospital	_____
	Nursing home or medical rehab	_____
	<b>If 0, Skip to M2</b>	
	1b) Diagnosis/major problem _____	
	1c) Major procedures or evaluations _____	
<b>?</b>	ON PAST ____ DAYS WHEN <b>NOT</b> IN A MEDICAL HOSPITAL:	
<b>M2</b>	How many times did you visit an <b>emergency room</b> ?	_____
	<b>IF 0, SKIP TO M3</b>	
	2a) What was your reason(s) for visiting the ER? Check all that apply:	
	Medical	1 – Yes 2 – No
	Psychological	1 – Yes 2 – No
	Substance Use	1 – Yes 2 – No
	2b) Diagnosis/major problem _____	
	2c) Major procedures or evaluations _____	
<b>M3</b>	How many times did you visit a medical doctor (physician, psychiatrist) for testing, examination, treatment, or care of <b>medical</b> concerns/problems? Note: we will ask you about visits for psychological or emotional concerns later.	_____
	<b>If 0, SKIP TO M4</b>	
	3a) Diagnosis/major problem _____	
	3b) Major procedures or evaluations _____	
<b>M4</b>	How many times did you visit any <b>other medical professional</b> (e.g. dentist, optometrist, nurse, physical therapist, X-ray or lab technician) for testing, examination, or treatment of medical concerns/problems?	_____
	<b>If 0, SKIP TO M5</b>	
	4a) Diagnosis/major problem _____	
	4b) Major procedures or evaluations _____	

<b>M5</b>	How many (individual or group) <b>counseling sessions</b> did you attend with <b>non-medical personnel</b> during which medical concerns/problems were the main focus (exclude all previously recorded visits)?		_____
<b>If 0, SKIP TO M6</b>			
5a) Number of sessions with:			_____
Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)			_____
Physician assistant, Nurse prescriber (Practitioner, APNP)			_____
Nurse			_____
Other clinician (e.g. counselor, social worker, case manager, clergy)			_____
Group member(s) (i.e. a support group not professionally led)			_____
Don't know			_____
5b) On average, how long did a session last? (record # of minutes)			_____ mins
5c) How many of these were group sessions?			_____
<b>PSYCHOLOGICAL SERVICES</b>			
Questions about any emotional or psychological services received over the past _____ days			
<b>P1</b>	How many <b>nights</b> were you an <b>inpatient</b> in a psychiatric hospital or psych treatment unit (i.e., stayed overnight)? Where? _____		_____
1a) Diagnosis/major problem _____			
1b) Major procedures or evaluations _____			
<b>?</b>	On past _____ days <b>NOT</b> in psychiatric inpatient treatment:		
<b>P2</b>	On how many days did you attend any <b>treatment</b> for mental health, emotional or psychological problems?		_____
Where? _____			
2a) How many of these were day hospital or intensive outpatient programs?			_____
<b>P3</b>	How many <b>individual (one-on-one)</b> sessions did you attend during which your mental health, emotional or psychological problems were the main purpose of the discussion (not including inpatient or day hospital/intensive outpatient programs)?		_____
<b>If 0, SKIP TO P4</b>			
3a) Number of individual sessions with:			_____
Medical doctor (e.g. psychiatrist or physician)			_____
Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)			_____
Physician assistant, Nurse prescriber (Practitioner, APNP)			_____
Nurse			_____
Other clinician (e.g. counselor, social worker, case manager, clergy)			_____
Group member(s) (i.e. a support group not professionally led)			_____
Don't know			_____
3b) On average, how long did each individual session last? (# of minutes)			_____ mins

<b>P4</b>	How many <b>group sessions</b> did you attend for mental health, emotional or psychological problems?		_____
<b>If 0, SKIP TO FAMILY SERVICES</b>			
4a) Number of group sessions with:			
	Medical doctor (e.g. psychiatrist or physician)		_____
	Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)		_____
	Physician assistant, Nurse prescriber (Practitioner, APNP)		_____
	Nurse		_____
	Other clinician (e.g. counselor, social worker, case manager, clergy)		_____
	Group member(s) (i.e. a support group not professionally led)		_____
	Don't know		_____
4b) On average, how long did a group session last? (# of minutes)			_____ mins
4c) On average, how many other patients were in a group?			_____
4d) On average, how many group leaders were present in each session?			_____
<b>FAMILY SERVICES</b>			
Questions about family or parenting services received over past ____ days.			
<b>F1</b>	How many classes or sessions did you attend to help with <b>parenting or problems with children</b> ?		_____
<b>If 0, SKIP TO F3</b>			
1a) Number of sessions with:			
	Medical doctor (e.g. psychiatrist or physician)		_____
	Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)		_____
	Physician assistant, Nurse prescriber (Practitioner, APNP)		_____
	Nurse		_____
	Other clinician (e.g. counselor, social worker, case manager, clergy)		_____
	Group member(s) (i.e. a support group not professionally led)		_____
	Don't know		_____
1b) On average, how long did a session last?			_____ mins
1c) In how many of these sessions were members of <b>other</b> families present?			_____
<b>F2</b>	How many treatment sessions did you attend with <b>some member(s) of your family or significant other</b> ? (exclude those recorded in previous sections)		_____
2a) Number of those with:			
	Medical doctor (e.g. psychiatrist or physician)		_____
	Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)		_____
	Physician assistant, Nurse prescriber (Practitioner, APNP)		_____
	Nurse		_____
	Other clinician (e.g. counselor, social worker, case manager, clergy)		_____
	Group member(s) (i.e. a support group not professionally led)		_____
	Don't know		_____

	2b) On average, how long did a session last? (# of minutes)		__ __ mins
	2c) In how many of these sessions were members of <b>other</b> families present?		__ __ __
<b>F3</b>	How many sessions did you attend to deal with <b>relationship issues</b> (e.g. domestic violence, communication issues) where <b>no other family member</b> was present? (exclude any previously recorded)		__ __ __
	3a) Number of those with:		
	Medical doctor (e.g. psychiatrist or physician)		__ __ __
	Non-medical doctor (e.g. psychologist – Ph.D./Psy. D.)		__ __ __
	Physician assistant, Nurse prescriber (Practitioner, APNP)		__ __ __
	Nurse		__ __ __
	Other clinician (e.g. counselor, social worker, case manager, clergy)		__ __ __
	Group member(s) (i.e. a support group not professionally led)		__ __ __
	Don't know		__ __ __
	3b) On average, how long did a session last? (# of minutes)		__ __ mins
	3c) How many of these were group sessions?		__ __ __
<b>FINANCIAL/EMPLOYMENT/HOUSING SERVICES</b>			
Questions about any specialized educational, financial, employment, or housing services received over the past __ days.			
<b>E1</b>	How many days did you attend <b>school</b> or <b>formal training</b> (e.g. apprenticeship, internship)?		__ __ __
<b>E2</b>	How many days did you work in a <b>therapeutic work setting/sheltered workshop</b> ?		__ __ __
<b>E3</b>	How many sessions did you attend where <b>job/education counseling or placement</b> was the main focus?		__ __ __
	3a) Number of those with:		
	Job or education counselor		__ __ __
	Anyone else (i.e. non-specialist)		__ __ __
<b>E4</b>	How many sessions did you attend where specific <b>housing services</b> were the main focus?		__ __ __
	4a) Number of those with:		
	Any housing specialist		__ __ __
	Anyone else (i.e., non-specialist)		__ __ __

<b>E5</b>	How many sessions or classes did you attend where <b>financial/benefits issues</b> were main focus?		_____
	5a) Number of those with:		
	Benefits or financial counselor, or any other financial specialist?		_____
	Anyone else (i.e. non-specialist)		_____
<b>LEGAL SERVICES</b>			
Following questions concern any legal or correctional involvement over past ____ days.			
<b>L1</b>	<b>Have you been arrested, picked up, or transported by police in the last ____ days? YES OR NO</b>		1 – Yes 2 – No
	1a) If yes, why? (Check all that apply)		
	Vagrancy (street person/begging/homelessness/transient)		1 – Yes 2 – No
	Related to Drug/Alcohol use or possession		1 – Yes 2 – No
	Disorderly conduct/disturbing the peace		1 – Yes 2 – No
	Public endangerment		1 – Yes 2 – No
	Other: _____		1 – Yes 2 – No
	1b) If yes, for how many days were you incarcerated?		_____
<b>OTHER SERVICES</b>			
<b>O1</b>	Did you receive any other services during past ____ days (e.g. food bank, soup kitchen)?		1 – Yes 2 – No
	1a) Specify: _____		
	1b) Specify: _____		
	1c) Specify: _____		
	1d) Specify: _____		
<b>O2</b>	In the past ____ days, did someone help you manage your overall condition – including your physical health, mental health, social, housing, financial and legal situation – by giving you information about the kind of help that is available or by putting you in touch with others who could help you? (e.g. case management) [not including services already recorded]		1 – Yes 2 – No
	2a) On how many days did you meet/speak with him/her?		_____

**O3** Throughout this interview, you've told me about different services you've received over the past \_\_\_\_ days *[give examples of services patient has described]*. I realize things aren't that cut and dried – I know, for example, that you don't just talk about medical issues; you can talk about social or emotional or family or medical problems. The same is true when you go to the doctor – you don't just talk about medical problems; you can talk about emotional issues or a lot of other things. What I'd like to do now is to get a sense of that. Given all the services and treatments and contacts you've had in the past \_\_\_\_ days, how much of all of that dealt with:

3a) Your physical health or medical problems?

0	1	2	3	4
None	A little bit	Some	Quite a bit	A lot

3b) Your mental health or psychological problems and issues?

0	1	2	3	4
None	A little bit	Some	Quite a bit	A lot

3c) Your family problems and issues?

0	1	2	3	4
None	A little bit	Some	Quite a bit	A lot

3d) Your employment, education, finances, or house?

0	1	2	3	4
None	A little bit	Some	Quite a bit	A lot

3e) Your legal or criminal problems and issues?

0	1	2	3	4
None	A little bit	Some	Quite a bit	A lot

**TIME ENDED:**

**APPENDIX L. CAREGIVER QUALITY OF LIFE (CARERQOL) –  
BURDEN DIMENSIONS (7D) [BROUWER WBF, 2006]  
AND VISUAL ANALOG SCALE (VAS) (SAMPLE)**

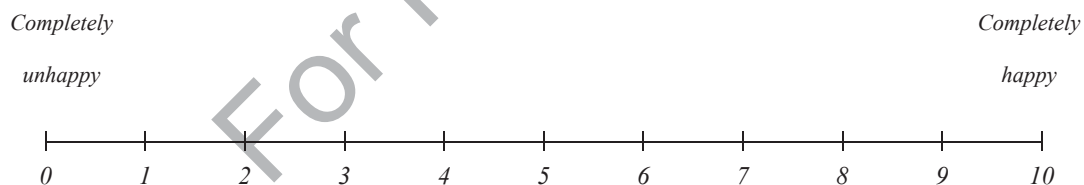
## CarerQol-7D

Please draw an "X" to indicate which description best fits your current care giving situation

- |           | no                       | some                     | a lot of                 |  |
|-----------|--------------------------|--------------------------|--------------------------|--|
| a. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | fulfillment with carrying out my care tasks.   |
| b. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | relational problems with the care receiver (e.g., he/she is very demanding, he/she behaves differently, we have communication problems). |
| c. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problems with my own mental health (e.g., stress, fear, gloominess, depression, concern about the future).                               |
| d. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problems combining my care tasks with my daily activities (e.g., household activities, work, study, family and leisure activities).      |
| e. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | financial problems because of my care tasks.   |
| f. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | support with carrying out my care tasks, when I need it (e.g., from family, friends, neighbors, acquaintances).                          |
| g. I have | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problems with my own physical health (e.g., more often sick, tiredness, physical stress).  |

## CarerQol-VAS

Please draw an "X" on the scale below to indicate how happy you feel at this moment



Derived from Brouwer WB, van Exel NJ, van Gorp B, Redekop WK. The CarerQol instrument: a new instrument to measure care-related quality of life of informal caregivers for use in economic evaluations. Qual Life Res. 2006 Aug;15(6):1005-21.



## **APPENDIX M. BURDEN ASSESSMENT SCALE (SAMPLE)**

### Burden Assessment Scale (BAS)

I am going to read a list of things which other people have found to happen to them because of their relative's illness. Would you tell me to what extent you have had any of the following experiences in the past six months.

Not at all 1	A little 2	Some 3	A lot 4	N/A 9
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Because of (name's) illness, to what extent have you:

1. Had financial problems
2. Missed days at work (or school)
3. Found it difficult to concentrate on your own activities
4. Had to change your personal plans like taking a new job, or going on vacation
5. Cut down on leisure time
6. Found the household routine was upset
7. Had less time to spend with friends
8. Neglected other family members' needs
9. Experienced family frictions and arguments
10. Experienced frictions with neighbors, friends, or relatives outside the home
11. Became embarrassed because of (name's) behavior
12. Felt guilty because you were not doing enough to help
13. Felt guilty because you felt responsible for causing (name's) problem
14. Resented (name) because s/he made too many demands on you
15. Felt trapped by your caregiving role
16. Were upset about how much (name) had changed from his or her former self
17. Worried about how your behavior with (name) might make the illness worse
18. Worried about what the future holds for (name)
19. Found the stigma of the illness upsetting

Burden Assessment Scale, Reinhard SC, Gubman GD, Horwitz AV, Minsky S. Burden Assessment Scale for families of the seriously mentally ill. Evaluation and Program Planning. 1994;17(3):261-269.

## **APPENDIX N. BIRCHWOOD INSIGHT SCALE (BIS) (SAMPLE)**

### **IS – (present)**

Please read the following statements carefully and then tick the box which best applies to you.

	<b>Agree</b>	<b>Disagree</b>	<b>Unsure</b>
1. Some of the symptoms were made by my mind			
2. I am mentally well			
3. I do not need medication			
4. My stay in hospital was necessary			
5. The doctor is right in prescribing medication for me			
6. I do not need to be seen by a doctor or psychiatrist			
7. If someone said I had a nervous or mental illness then they would be right			
8. None of the unusual things I experienced are due to an illness			

## Insight Scale (IS)

### (Coding Schedule)

	Agree	Disagree	Unsure
1. Some of the symptoms were made by my mind	2	0	1
2. I am mentally well	0	2	1
3. I do not need medication	0	2	1
4. My stay in hospital was necessary	2	0	1
5. The doctor is right in prescribing medication for me	2	0	1
6. I do not need to be seen by a doctor or psychiatrist	0	2	1
7. If someone said I had a nervous or mental illness then they would be right	2	0	1
8. None of the unusual things I experienced are due to an illness	0	2	1

Maximum Score = 12 - Full insight  
 Minimum Score = 0 - No insight  
 (9 and above = good insight)

### Subscales

Items		Possible Total
1, 8	Awareness of symptoms	<b>4</b> (3 or 4 = good insight, 1 or 2 = poor insight)
2, 7	Awareness of illness	<b>4</b> (3 or 4 = good insight, 1 or 2 = poor insight)
3, 4, 5, 6	Need for treatment (items need to be added and divided by 2)	<b>4</b> (3 or 4 = good insight, 1 or 2 = poor insight)

**APPENDIX O. NEW YORK ASSESSMENT OF ADVERSE COGNITIVE  
EFFECTS OF NEUROPSYCHIATRIC TREATMENT  
(NY-AACENT) SUBSCALES (SAMPLE)**

## New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment

**Description:** The NY-AACENT is intended to be used to detect changes in cognitive function subsequent to pharmacological or similar treatments for neurological or psychiatric problems. It is originally designed to be used in pediatric populations, but can be utilized with other age groups as appropriate. Each of the seven items is derived from the seven domains identified by MATRICS<sup>1</sup>. When coupled with similar adverse event assessments (such as the PAERS<sup>2</sup>) that are intended to be used in drug treatment studies, data on select items on the NY-AACENT (e.g. item #2, Attention/Vigilance) may be imputed from other, identical items (e.g. item #9 on the PAERS.)

**Instructions:** It is recommended that the patient and caregiver forms be completed first as a brief interview, conducted separately with subjects and parents. After this has been completed, the forms should be reviewed and the clinician form completed, summarizing best judgment. If specific symptoms are reported to be present, please determine:

- Whether the symptoms are likely due to a study medication or concomitant medication (if used in the context of a research study);
- The time-frame of the symptoms, i.e. whether or not they have only emerged or changed subsequent to beginning treatment;
- The extent to which the symptom does or does not have an impact on functioning.

After all information has been collected, the clinician or researcher is instructed to complete the Clinician Form, scoring each section accordingly.

*Conducting the Interviews.* Brief, separate interviews with both patients and caregivers are recommended. For certain subjects, it is advisable to interview the patient prior to interviewing the caregiver. In cases where the patient is a poor historian or presents with other impairments that reduce the validity of side effect reporting, both the patient and caregiver may be interviewed together. The interview should cover each domain of cognition and focus on eliciting specific examples, determining the extent to which social, academic or role functioning are impaired, and the emergence of symptoms in relation to the administration of a specific medication. If etiology is unclear, it is advisable to ask follow-up questions.

**Domains:** Seven domains of cognition are covered in the NY-AACENT. These include –

1. Working memory
2. Attention/Vigilance
3. Verbal Learning/Memory
4. Visual Learning/Memory
5. Reasoning & Problem Solving
6. Speed of Processing
7. Social Cognition

It is strongly advised that prior to conducting the interviews, investigators review the domains of cognition carefully and ensure that when querying patients or caregivers, that the proper aspects of cognition and functioning are being considered.

<sup>1</sup> Green MF, Nuechterlein KH, Gold JM, Barch DM, Cohen J, Essock S, Fenton WS, Frese F, Goldberg TE, Heaton RK, Keefe RS, Kern RS, Kraemer H, Stover E, Weinberger DR, Zalcman S, Marder SR. Approaching a consensus cognitive battery for clinical trials in schizophrenia: the NIMH-MATRICES conference to select cognitive domains and test criteria. *Biol Psychiatry*. 2004; 56(5):301-7.

<sup>2</sup> March J, Karaya O, Chrisman A. CAPTN: The Pediatric Adverse Event Rating Scale. Paper presented at: Scientific Proceedings of the 2007 Annual Meeting of the American Academy of Child and Adolescent Psychiatry; October 23-28, 2007, 2007; Boston, MA.

NY-AACENT-R, ©2012, M. Opler, D. Antonius, C. Correll. All Rights Reserved.

**Patient Form:** Please focus on the past week. (If you have experienced one of these problems, but not in the past week, check "Not Present.") If present in the past week, indicate the extent to which the described symptom bothered you or was a problem for you.

1. Do you have trouble remembering things that people (co-workers, clinicians, caregivers, friends, relatives) have said to you, immediately after you hear them?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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2. Do you have trouble paying attention in different settings (home, work, clinic, day programs etc), watching TV, browsing the internet or using computers?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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3. Is it difficult for you to learn or remember words to things (books, songs, TV shows)? Are you able to come up with words in conversation?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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4. Do you have difficulty recalling how things look, including shapes, colors?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 5. Do you have trouble managing money, solving problems, doing puzzles, dealing with new challenges?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 6. Do you feel "slowed down", does it take you longer than usual to do things?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 7. Do you have trouble understanding what other people intend or want from you, participating in social situations, or interacting with others?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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**Caregiver Form:** Please focus on the past week. If the patient has experienced one of these problems, but not in the past week check "Not Present." If present in the past week, indicate the extent to which the item bothered him/her by checking one of the boxes marked 1 through 4.

1. Patient has trouble remembering things that people (co-workers, clinicians, caregivers, friends, relatives) have just said immediately after hearing them?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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2. Patient has trouble paying attention in in different settings (home, work, clinic, day programs etc) or while playing games, watching TV, browsing the internet or using computers?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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3. Is it difficult to for the patient to learn or remember words to things (book, songs, TV shows)? Is the patient able to come up with words in conversation?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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4. Does the patient have difficulty recalling how things look, such as shapes and colors?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 5. Does the patient have trouble managing money, solving problems, doing puzzles, dealing with new challenges?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 6. Does the patient feel "slowed down", does it take him/her longer than usual to do things?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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## 7. Does the patient have trouble understanding what other people intend, participating in social situations, or interacting with others?

<input type="checkbox"/> Not Present	<input type="checkbox"/> A little bit bothersome/ a <b>mild</b> problem	<input type="checkbox"/> Somewhat bothersome/ a <b>moderate</b> problem	<input type="checkbox"/> Quite bothersome/ a <b>severe</b> problem	<input type="checkbox"/> Very bothersome / an <b>extreme</b> problem	<input type="checkbox"/> Not applicable <input type="checkbox"/> Not medication related <input type="checkbox"/> Possibly due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Quite likely due to a specific medication/medications (please list:) <hr/> <input type="checkbox"/> Almost definitely due to a specific medication/medications (please list:) <hr/>
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**Clinician Form:** Please complete each section below:

1. Working memory: Trouble remembering things that people (co-workers, clinicians, caregivers, friends, relatives) have just said?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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2. Attention/Vigilance: Trouble paying attention in in different settings (home, work, clinic, day programs etc) or while playing games, watching TV, browsing the internet or using computers?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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3. Verbal Learning/Memory: Difficulty remembering or learning words to things (book, songs, TV shows)? Trouble coming up with words in conversation?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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4. Visual Learning/Memory: Patient has difficulty recalling how things look, such as shapes and colors?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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5. Reasoning & Problem Solving: Trouble managing money, solving problems, doing puzzles, dealing with new challenges?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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6. Speed of Processing: Feeling "slowed down", does it take you longer than usual to do things?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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7. Social Cognition: Trouble understanding what other people intend, participating in social situations, or interacting with others?

<input type="checkbox"/> Present during past week <input type="checkbox"/> Not present in past week	<input type="checkbox"/> Evident During Visit <input type="checkbox"/> Not Evident During Visit	<input type="checkbox"/> Not drug related <input type="checkbox"/> Due to study drug <input type="checkbox"/> Other drug <input type="checkbox"/> Drug/drug interaction <input type="checkbox"/> Not applicable	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe <input type="checkbox"/> Extreme <input type="checkbox"/> Not applicable	<input type="checkbox"/> Functional/ Role Impairment <input type="checkbox"/> No Functional/ Role Impairment <input type="checkbox"/> Not applicable
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Notes:

**APPENDIX P. MINI INTERNATIONAL NEUROPSYCHIATRIC  
INTERVIEW (M.I.N.I.) – MODULES I AND J (SAMPLE)**

**APPENDIX Q. LIST OF POTENT CYTOCHROME P450 3A4 (CYP3A4)  
INDUCERS AND MODERATE-TO-STRONG  
INHIBITORS OF 3A4 OR 2D6**

<b>3A4</b>		<b>2D6</b>
<b>Inducers</b>	<b>Inhibitors</b>	<b>Inhibitors</b>
<ul style="list-style-type: none"> <li>• Carbamazepine</li> <li>• Barbiturates (eg, Phenobarbital)</li> <li>• Phenytoin</li> <li>• Rifampin</li> <li>• Modafinil</li> <li>• Cyproterone (eg, antiandrogen, progestin, Diane-35)</li> <li>• Non-nucleotide reverse transcriptase inhibitors (eg, efavirenz, nevirapine, etravirine)</li> <li>• Hyperforin; St. John's Wort</li> </ul>	<ul style="list-style-type: none"> <li>• Ketoconazole</li> <li>• Itraconazole</li> <li>• Fluconazole</li> <li>• Clarithromycin</li> <li>• Erythromycin</li> <li>• Telithromycin</li> <li>• Nefazodone</li> <li>• Fluvoxamine</li> <li>• Protease inhibitors (ritonavir, indinavir, nelfinavir)</li> <li>• Verapamil</li> <li>• Grapefruit juice</li> <li>• Bergamottin</li> <li>• Quercetin</li> </ul>	<ul style="list-style-type: none"> <li>• Quinidine</li> <li>• Selective serotonin reuptake inhibitors (eg, fluoxetine, paroxetine)</li> <li>• Duloxetine</li> <li>• Bupropion</li> <li>• MDMA (3,4-Methylenedioxymethamphetamine; Ecstasy)</li> <li>• Terbinafine</li> <li>• Goldenseal (Hydrastis canadensis)</li> </ul>