HRPO# 05-0264

Washington University in St.Louis

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Form 5 1/10
Human Research Protection Office
Box 8089
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Fax (314)367-3041

10/8 DB c

REQUEST FOR AMENDMENT TO AN APPROVED PROTOCOL

FDA requires IRB approval before implementing proposed changes.

Submission instructions

[ ] Behavioral study [x] Biomedical study

DATE: 10/4/2010 HRPO # 05-0264

Principal Investigator	**Newcomer, John W., MD**	**Phone #**	**314/362-2465**
Email address	**newcomerj@psychiatry.wustl.edu**	**Box #**	**8134**
Administrative Person (Receives copies of the paperwork)	**Elizabeth Westerhaus MA**	**Phone #**	**314/747-1134**
	Is this person engaged in the research? [x] Yes [ ] No	**Box #**	**8134**
Email address	**westerhe@psychiatry.wustl.edu**		
Study or Regulatory Coordinator (Can answer protocol questions)	**Elizabeth Westerhaus MA**	**Phone #**	**314/747-1134**
		Box #	**8134**
Email address	**westerhe@psychiatry.wustl.edu**		
Study Title *(include version # if needed)*	**Metabolic Effects of Antipsychotics in Children**		

[ ] **This study is cancer related** (screening, prevention, treatment, follow-up) research. Please send to **PRMC** for review prior to HRPO review. PRMC must continue to receive all revision/amendments until the study is in follow-up only with no participants receiving treatment.

[x] **This study utilizes the GCRC.**

[ ] **This study was reviewed by the RDRC.** Provide the **RDRC#:** _____

I assure the Committee that the proposed changes will not be initiated without HRPO approval, except when necessary to eliminate apparent immediate hazards to the subjects.

Signature of Principal Investigator 10/7/10 *Date*

~ For HRPO Use Only ~

Subcommittee ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 _____ *Date of meeting* Reviewer: Kathy Dodds

☐ Administratively approved by: _____ ☐ Noted ☑ Contingent 10/14/10 ☐ Approved as submitted

☐ Refer to Full Board _____ *date of meeting* ☐ NPC# ___ ☐ CRC# ___

Changes for Access Database: ☐ PI ☐ Title ☐ Accrual numbers ☐ Other _____

Items for stamping:

☑ Consent Form(s) ☑ Protocol 10/14/10 rev ☐ Investigator's Brochure ☐ Questionnaire ☐ Advertisement ☐ Other

Revision or amendment approved on: OCT 18 2010 *Date*

Signature of Committee Chair:

CURRENT STATUS

[x] Enrolling subjects* *Number enrolled to date: 245	[ ] Study Closed to Accrual [subject(s) continue(s) to receive treatment, procedures, care]
	[ ] Follow-up/ Data analysis (all treatment components completed)

A. SUMMARY OF THE PROPOSED CHANGES

complete this table or attach a previously prepared itemized summary.

Proposed Amendment	Justify the Modification** Provide all documentation that supports or explains the change, e.g., letters/notices from federal agencies, notifications from Sponsor	Affected Documents (Consent, protocol, etc.) Highlight all changes
Add additional safety lab timepoints as needed (in the 6-mo study) at the discretion of the treating physician, not limited to 3- and 9-week time points as is currently approved. **Samples will always be collected according to IRB/pediatric guidelines of taking no more than 3 ml of blood per 1 kg of body weight.**	Using the same currently approved criteria, the same currently approved assays/tests (fasting blood glucoce, fasting lipid panel, TPR & B/P, weight/height, waist circumference) will be run should the PI and/or treating physician feel that participants require closer metabolic monitoring to enhance their safety and decrease their risk while continuing to maintain their psychiatric stability.	Protocol, p. 90 and 91 Treatment consent (6-17 y.o.). p. 5 Treatment consent (18 y.o.), p. 5

** "At Sponsor's request" is generally not informative

B. SPECIAL CIRCUMSTANCES

1. **CHANGES TO THE CONSENT FORM:** [ ] new consent added [ ] current consent revised* (Highlight all changes)

   Will subjects be reconsented? [x] **Yes** [] **No**

   If yes, please discuss your plan and submit materials you will use (letter, script, consent addendum)

   Participants currently in the study where additional safety labs beyond 3- and 9-weeks are recommended will be reconsented, however, those not requiring additional testing and those who have already completed the study will not be reconsented.

   If no, please explain.

2. [ ] **INVESTIGATOR'S BROCHURE (IB) VERSION** N/A

   2.1 Please submit the IB with changes highlighted or a listing of the changes (as provided by the sponsor). You may also summarize the changes below:

   N/A

   2.2 The PI has reviewed the changes to the IB and attests to the statement checked below:

   [ ] "I have reviewed the revised Investigator's Brochure and believe the information in the revised brochure does not require a change in the protocol or the consent form."

   OR

   [ ] "I have reviewed the revised Investigator's Brochure and believe the information in the revised brochure does require a change in the protocol or the consent form."

Enclose a revised protocol and/or consent form(s) reflecting updated information, if applicable.

3. **MINORS (AGES 0 THROUGH 17 YEARS):** Does this amendment add minor participants? [ ] **Yes** [x] **No**
   If yes, submit Form E.

4. **GENETIC RESEARCH COMPONENT:** Does this amendment involve collection or use of any type of tissue or data to be used for any form of genetic research? If yes, submit Form H. [ ] **Yes** [x] **No**

5. **FUNDING SOURCE CHANGES** (i.e., adding a funding source or changing funding source status)

Please complete the boxes below.

Name of Grant Source (e.g., NIH)	Grant Number	Alternative Title (if applicable)	Status (Awarded or Pending)
N/A			

- **Attach a copy of the entire grant proposal (excluding appendices) AND the Grants & Contracts Protocol Certification (PC) form submitted to Grants & Contracts/Research Office, if available. Block out salary information.**
- **HRPO is required by the federal Office of Human Research Protection to review the grant proposal and human research application for consistency. You may be asked to explain discrepancies, if any, identified by HRPO during the review process.**

  See http://www.hhs.gov/ohrp/humansubjects/guidance/aplrev.htm for more information about IRB responsibilities regarding grant review.

6. **CHANGES TO THE RESEARCH TEAM** *submission instructions*

Important Note: Individuals being added to the study team must complete the mandatory educational requirement.

Do the individuals being added to the study team have, or anticipate having, any income from or financial interest in: the sponsor of the protocol, the supporting organization, or the company that owns/licenses the technology being studied? [ ] Yes [x] **No**

If yes, submit Form T and apply to the Disclosure Review Committee.

- **Submit one (1) complete copy for review.**
- **Note:** If you plan to submit an identical amendment for multiple studies, then please submit a signed Form 5 and individual supporting documentation for each protocol. Label each Form 5 with one applicable HRPO#.

05-0264

A. Specific Aims

The prevalence of overweight and obesity, insulin resistance and type 2 diabetes mellitus (T2DM) are increasing, particularly in children, with the Centers for Disease Control warning of epidemic rates of these conditions in children in the United States (US). Increased adiposity and related reductions in insulin sensitivity, also referred to as insulin resistance, are major risk factors for the development of dyslipidemia, metabolic syndrome, T2DM, cardiovascular disease (CVD) – e.g., risk of myocardial infarction and stroke, other adverse health outcomes, and reduced psychosocial function. Reductions in lifespan attributable to obesity impact younger, at-risk individuals most measurably, with severely obese 20 year-old African American males expected to lose 20 years of life[1].

Certain medications can increase regional adipose tissue mass and insulin resistance, contributing to both short-term and long-term metabolic risk. Antipsychotic medications are used extensively in children, with some agents producing larger increases in weight and adiposity than any other commonly used drugs in this age group. Recent studies also indicate that some antipsychotics may affect insulin sensitivity independent of adiposity, suggesting a potential additional mechanism for metabolic risk. The use of atypical antipsychotics in children is increasing, and has been stimulated by reported efficacy for aggression and irritability in a variety of childhood psychiatric disorders. However, no study in children has sensitively quantified the adverse metabolic effects of these agents despite reports of alarming levels of weight gain.

The proposed randomized clinical trial aims to assess the metabolic safety of atypical antipsychotic agents in antipsychotic-naive children with aggression in the setting of various childhood psychiatric disorders during 12 weeks of prospective, randomized treatment with olanzapine (Zyprexa), risperidone (Risperdal) or aripiprazole (Abilify).

Primary Aim 1: To evaluate antipsychotic treatment effects on insulin action in skeletal muscle (glucose disposal), liver (glucose production) and adipose tissue (lipolysis). This study hypothesizes that treatments causing greater increases in adiposity (e.g., olanzapine) will be associated with reduced sensitivity to insulin effects on glucose disposal, glucose production, and glycerol/fatty acid release, in comparison to treatments producing less change in adiposity (e.g., aripiprazole). Drug effects on insulin sensitivity that are independent of adiposity will also be detected, with the greatest effect hypothesized for olanzapine. Hypotheses will be evaluated by measuring whole-body glucose and lipid kinetics with the use of stable isotope tracer methodology, using rate of disappearance of glucose (glucose Rd), rate of appearance of glucose (glucose Ra), and rate of appearance of glycerol (glycerol Ra) as the primary endpoints.

Primary Aim 2: To evaluate antipsychotic treatment effects on abdominal fat mass and total body fat. This study hypothesizes that the selected antipsychotic medications have significantly different affects on direct measures of fat mass (olanzapine > risperidone > aripiprazole), with significant increases in fat mass during olanzapine and risperidone treatment in comparison to aripiprazole treatment. These hypotheses will be evaluated by measuring body composition using whole body dual energy x-ray absorptiometry (DEXA) and abdominal magnetic resonance imaging (MRI), quantifying percent total body fat and subcutaneous+visceral abdominal fat as the primary endpoints.

The secondary aims of this study will be to evaluate the effects of selected antipsychotic treatments on 1) insulin secretion, using frequently sampled oral glucose tolerance tests (fsOGTT) to calculate post-load area-under-the-curve insulin, 2) resting metabolic rates, using indirect calorimetry to calculate rates of carbohydrate and fat oxidation, 3) fasting plasma lipids and waist circumference, which are indirect or derivative surrogates for insulin sensitivity and abdominal fat, in order to assess the extent to which changes in the primary endpoints, measured directly with gold-standard tools, are also detectable using measures commonly available to clinicians, and 4) effectiveness for treatment of symptoms of aggression and irritability, using the Clinical Global Impressions Scale (CGI) as the primary endpoint. **Exploratory aims include** the assessment of non-metabolic adverse events (e.g. prolactin elevation), and the assessment of metabolic effects in children with and without concomitant stimulant therapy. Children aged 6-18 will be studied, exploring age-related differences in vulnerability to treatment-induced adverse metabolic changes. Relevant data on the primary aims are critically needed to assess the risks of antipsychotic therapy in children, to identify targets for additional basic research, and to guide clinical decision-making.

REVISIONS APPROVED
Date: OCT 18 2010

APPROVED
Jonathan M. Green, M.D.
Associate Dean and Executive Chair

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Participant's Name _____ HRPO # **05-0264**

Principal Investigator **Newcomer, John W., MD** PI's Phone Number **(314) 362-5939**
Last First Credentials

Title of Project: **Metabolic Effects of Antipsychotics in Children (Treatment study,≥18 y.o.)**

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take the time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decided to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. **Why is this study being done?**
   Use of antipsychotic medication in children and young adults has been shown to be an effective treatment for behaviors such as aggression, but doctors don't know as much about how they may affect weight, glucose (sugar), insulin (a hormone that controls blood sugar levels), and lipids (fats) in younger patients. Although these antipsychotic medications have been FDA-approved by the Food and Drug Administration (FDA) for adults and are now used commonly in children and young adults who have conduct disorder, aggression or other behavioral symptoms, they are not FDA-approved for children. The point of this research is to study side effects of these antipsychotic medications in younger individuals. We will be measuring how these drugs affect body weight and substances in the body such as glucose, insulin, and lipids. Dr. Newcomer and colleagues have performed more than 400 studies of this kind in adults to look at how different types of antipsychotic medications affect weight, glucose, insulin, and lipids. This study will include 325 children and young adults whose doctors want them to start taking antipsychotic medications to treat conduct disorder or other behavior symptoms. Your doctor has determined that one of these medications may be helpful to you.

   For more information regarding minors in research see www.researchchildren.org.

   Being in a research study does not take the place of routine physical exams or visits to your own doctor and should not be relied on to diagnose or treat medical problems.

2. **What am I being asked to do?**
All procedures described below are research-related *except* for the prescribing of an antipsychotic medication to treat a psychiatric diagnosis and a urine drug screen if there is a history of substance abuse.

Study Visit 1: You will be seen by one of our child psychiatrists for a full diagnostic evaluation. Based on the evaluation, if you qualify and you and your parents wish to participate, we will schedule the next two study visits. You and your mom/dad will be asked questions about feelings, emotions, and behavior, and about how you get along at home, school, or work, and with friends. We will first ask your mom/dad these questions and then we will ask you the same questions. These questionnaires will be administered by trained personnel over the telephone or at one of the initial study visits (study visit 2 or 3). The combined length of time for both parent and child for this phase of the study is approximately 4-5 hours.

a) a) Study Visit 2: Within a few days after Study Visit 1, you will be scheduled to go to the Pediatric Clinical Research Unit (PCRU) or Clinical Research Unit (CRU) for blood tests, an EKG, a frequent sample oral glucose tolerance test (fsOGTT), an MRI and a DXA scan. This session will last approximately 3-4 hours. The blood tests, EKG and oral glucose tolerance test are considered standard clinical care for people taking antipsychotics. The DEXA body scan, MRI and insulin/glucose clamp are research related tests. For females of child-bearing age, a urine pregnancy test will be done at baseline and 12 week visits. If you are pregnant or become pregnant during the study, you will be discontinued from the study because hormonal changes could alter test results. You may be asked to submit a urine sample for a drug screening if you and your doctor have been previously concerned about your substance use. Each procedure is described below:

1. **EKG**: You will be given a routine resting electrocardiogram (EKG), where soft electrodes (like small pieces of tape) will be stuck to your chest to measure your heart rhythm.

2. **fsOGTT and Blood tests**: With an oral glucose tolerance test you will be given a sweet drink to see how your body handles extra sugar. On the night before this test, you can't have anything to eat or drink except water after 10:00 p.m. In the morning, you will go to the Pediatric Clinical Research Center (PCRU) or Clinical Research Unit (CRU) where you will lie in a hospital bed or reclining chair. If you are a female of child-bearing age, before the procedure begins you will be given a pregnancy test. A small catheter (a plastic tube, also called an IV) will be inserted into a vein of your hand or wrist or bend in your arm. This feels like getting a shot, but we will numb your skin first with either a cream or an injectable local anesthetic to help it hurt less. This is the only part of the study that hurts a little.

   Once the IV catheter is in your vein, it doesn't hurt and we will use the catheter to get blood samples during the study without hurting you. Your hand or wrist or arm with the IV will be heated in a routinely used temperature-controlled hand-warming box to increase the blood flow to the hand. This box is not FDA approved but is common in many centers.

   You will then drink a very sweet lemon- or orange-flavored drink. Blood samples will be taken from the catheter in your hand or wrist or arm at different times during the study to check sugar levels in your blood along with some other routine blood tests. You can watch cable TV or a video during this study.

After this study, you will be given breakfast.

3. **MRI**: You will also have a magnetic resonance imaging (MRI) scan to measure the fat content in your belly. You wear your clothes or a hospital gown during this scan. During the MRI scan, you will lie on a table inside a tube while your stomach is scanned. The machine will scan your stomach three or four times, for about 30 seconds each time. You will need to hold still during the 30-second scans, but you can wiggle a little in between scans. The whole MRI study takes about 20 minutes. The machine makes some strange noises, but you can't feel it scanning you. You will wear earphones and listen to music while you are being scanned.

4. **DXA**: You will also have a dual-energy x-ray absorptiometry (DXA) scan to measure your body fat and body muscle content. The DXA scan involves lying still on a table in your clothes or a hospital gown (not in a tube this time) and having your body scanned by a machine for about 5 minutes. You can't feel the DXA machine scanning you, either.

b) **Study Visit 3: Insulin/Glucose Clamp:** About a week after Visit 2, you will be come to the PCRU or CRU early in the morning (about 6:30 am) for a test called the Insulin/Glucose Clamp. This is a test that measures blood glucose (sugar), lipids (fats) and other hormones in your body while you are getting IV fluids that contain glucose (sugar) and insulin (a hormone that controls blood sugar levels).

You can't eat or drink anything except tap water after 10:00 p.m. the night before the test. Upon arrival to the PCRU or CRU, your height, weight, and vital signs will be measured. If you are a female of child-bearing age, before the procedure begins you will be given a pregnancy test. You will have two IV catheters inserted, one in each arm, using the injectable anesthetic or numbing cream first.

This large vein site in the one arm will allow us to give you IV fluids that are non-radioactive stable isotopes (rare but natural forms of foods like fat and sugar). These isotopes are already present in your body and there will be no short-term or long-term side effects from the extra isotopes we give you. The second IV will be inserted into a vein of your other hand or wrist or bend in your arm. This IV site will be heated in a temperature-controlled box and blood samples will be taken from this IV at different times during the study. You will be able to watch cable or videos while lying in bed. The study doctor or research nurse and PCRU /CRU nurses will be present throughout the session. Twice during the session, you will wear a special hood (called an indirect calorimeter) that measures your breathing and tells us how many calories you are burning. You will wear this two times during the study, each time for about 30 minutes. If you become uncomfortable wearing the hood, we will remove it. After the study, you will receive a late lunch (around 2:30 p.m.), and the IVs will be removed. You can then go home with your parent or guardian. The session will begin early in the morning following overnight fast and will take approximately 7 1/2 to 8 hours. You will be asked questions about how you are feeling during this session.

The amount of blood drawn during each test will depend on your weight at the time of each OGTT and Insulin/Glucose Clamp. We will follow Washington University School of Medicine Human Research Protection Office's guidelines of drawing no more that 3 ml (3/5 teaspoon)/kg of body weight over a two month period of time. We will do this by decreasing the number of time points for each blood draw for each test.

(Under special circumstances, such as having trouble remembering not to eat after 10:00 pm the night before the test, you might be asked to be stay overnight on the CRU on the night prior to the OGTT or the Insulin/Glucose Clamp.)

We will never sedate you (give you any medication to make you sleepy or calm) for any of these procedures. If you become too uncomfortable, you can stop participating at any time.

Treatment Assignment:

1) In coordination with your physician, after you have completed the baseline OGTT and Insulin/Glucose Clamp, you will be randomly (like the flip of a coin) assigned to receive one of the following newer antipsychotic medications for 12 weeks (3 months): aripiprazole (Abilify), olanzapine (Zyprexa), or risperidone (Risperdal). There is a one out of three chance of receiving one of the three medications. Your physician and the study personnel will closely monitor the addition of this medication. You and your physician will know what medicine you are assigned, and your physician will adjust the dose for you on an individual basis. If you participate in this study, you and your physician will be asked not to use a second antipsychotic or certain other medications along with your antipsychotic, (e.g. antihistamines, tricyclic antidepressants, bupropion, clonidine, pemoline, and mood stabilizing agents). These medications may themselves worsen glucose and lipid control or otherwise make it difficult to assess the effects of your antipsychotic alone.

2) If more than six weeks have passed between your participation in the initial phase of the study and your random assignment to one of the medications, you will be asked to repeat the isotope infusion portion of the study (see c above for description).

3) If more than eight weeks have passed between your participation in the initial phase of the study and your assignment to a different medication, you will be asked to repeat the isotope infusion and repeat the MRI and DXA scans and routine blood tests (see b and c above).

4) You will be asked to refrain from donating blood for two months after the end of the study, since the amount of blood drawn will be close to the maximum guidelines suggested for children.

5) If at any time during the study your weight, blood sugar and/or blood lipid levels show a need to be watched more closely, the study doctor and staff may ask that you come for additional visits at week 3, week 9, or possibly more frequently during the 12 week study.

Weekly Medication Check

You will have weekly medication checks with the study doctor and research assistant. These visits may be over the telephone or as out-patient visits to research offices.

c) **Study Visit 4:** This visit will be approximately six weeks after the Insulin/Glucose Clamp (Study visit #3). This visit will include an fsOGTT and /or, blood tests and DXA as described in Study Visit #2. (There will not be a MRI at this visit). The fsOGTT may not be done if you are younger and a small body size.

d) **Study Visit 5:** This visit will happen approximately 11-12 weeks after you begin the study medication at Study visit #3. Study visit 5 will include an fsOGTT, DXA, MRI and all blood tests as described in Study visit #2.

e) **Study Visit 6:** This visit will happen approximately 1 week after Study Visit #5. This final visit will include a Insulin/Glucose Clamp and all blood tests as described for Study Visit #3.

f) **Extra study visits (safety checks) for some children/teens:** Throughout the study, the study doctor will talk with you and your parents/guardian about your weight and blood tests results. If the study doctor wants to watch your weight and/or blood tests more closely at any time during the study, you will be asked to come to the PCRU/CRU for extra study visits. These will be short visits lasting about 1-hour and may happen as often as every other week or more frequently for as long as you are in the study (including until you complete the 3-month follow up visit if selected to do so).

The safety checks will be approximately **3 weeks after starting study med (visit 3A) and/or 9 weeks after starting study med (visit 4A), but may happen at other times, too, if the study doctor feels they are necessary to keep you healthy.** At the time, if it is decided that extra study visits will be helpful, you will also be given a home monitoring kit that contains strips for testing urine sugar and ketones. You will be given instructions on how to check your urine for sugar and ketones one or more times a week.

h) **3-month follow-up visit (after 12-week study ends)- Visit 7:** At the end of the 12-week study, the study doctors will make recommendations to you, your parents and your treating clinicians regarding the study-related treatment effects on your weight, blood lipids and blood sugar, and behavior. When the ending OGTT and Glucose/Insulin Clamp are completed, you will be returned to the care of your treating physician (child psychiatrist or primary care doctor). If the study doctor recommends that you return for a follow-up visit (after the 12-week study ends) you will be asked to return for this brief follow-up visit in approximately 3 months. During the 3 months following the12-week study visits, you will be under the care of your primary physician and no additional study visits will occur during that time.. Your 3-month lab results will be shared with your treating physician.

For the safety checks and the 3-month follow-up, you will need to be fasting after 10:00 p.m. the night before the study visit. You will have weight, height and waist measured and the PCRU/CRU nurse will blood draw blood from your arm or hand for a fasting blood sugar and a fasting blood lipids (cholesterol and triglycerides). Less than one teaspoon of blood will be drawn at each visit; the amount will depend on your body size. During these study visits, the study staff will ask questions about your medications, how you feel and about any problems you might be having and look at the urine test results.

i) **Optional post-study phone questionnaires:** Someone from the research team may call you during or after your participation to ask about your eating and exercise patterns over the course of the study. The questionnaire will be optional. You can choose to not answer any question, or not to take the survey at all, without incurring any penalty and without jeopardizing your participation in the treatment study. These questions are for research purposes only and the final results of the questionnaires will not be traceable to you or your family.

j) **Optional post-study re-consent to release school records:** At the beginning of the MEAC study, you will be asked to provide permission for study staff to contact your child's school so that we may obtain information about your child's school performance as it relates to his/her symptoms. Your decision whether to allow us to contact your child's school will not affect your child's treatment or you or your child's participation in the study in any way. The release will be good for 1 year, but in some cases, you may be contacted more than one year after your child's participation in MEAC has ended; this is to renew a release that is more than 1 year old.

How long will I be in the study?
You will be in the study approximately 3-4 months unless you have some changes in weight, blood sugar or blood lipid tests that need to be checked approximately 3-months after the 12-week study ends. If that happens, you will be in the study for a total of 6-7 months, but your child psychiatrist or primary care doctor will be in charge of your behavioral/psychiatric treatment after the 12-week study ends. Study staff will assist with referrals to a child psychiatrist or primary care physician at the end of the 12-week study as necessary.

Financial Disclosure of Interest
The study sponsor is paying Washington University to conduct this study. The amount of payment is enough to cover the study doctor's and/or institution's expenses to perform the study.

Participating in Concurrent Studies
You may not be in any other medical studies while you are on this study.

3. What are the costs?
The procedures performed just for this research study are provided at no cost to you. There are no extra charges to you or your insurance company for participating in this study. You or your insurance company will be charged for your antipsychotic medications. If you have no current medical insurance, you will receive the medication for the study at no cost to you during your participation in the study. If you have a history of drug or alcohol dependence, you or your insurance company may be charged for (standard of care) urine drug screening so that you can receive the medical care needed for this condition.

Standard care and research may carry a co-pay or deductible. When insurance pays, you are responsible for the applicable co-pays and deductibles.

Your family will receive a total value of up to $700.00 (up to $775.00 if child has study visit at 3-months following the 12-week study) combined in gift certificates and monetary reimbursement for your participation in the 12-week research study. The child will receive payment in their choice of gift certificates. If you want to stop your participation at any time, you will receive part of the $700 value, based on how far in the study you are. You will receive $75.00 each for baseline and 6-week OGTTs (or 6-week fasting labs) and $100.00 for the 12-week OGTT; $50.00 for the first medication check visit with the study psychiatrist; $175 for the baseline Insulin/Glucose Clamp and $225.00 for the 12-week clamp. If you participate in the 3-month follow-up visit after the 12-week study ends, you will be paid an additional $75.00 in gift certificates and monetary reimbursement for that visit. All compensation will be for time and inconvenience. Gift cards and monetary reimbursement will be available at the next scheduled study visit - they will not be available during the child psychiatrist visits. You will not receive any payment for safety labs.

Because you will be receiving more than $600 in gift certificates, this amount will be considered extra income so you will receive an IRS Tax Form 1099 during tax season from Washington University so you can report it to the IRS.

4. **What are the risks?**

In this study, you will get both routine and research procedures. The overall potential risks of this study are small. All key personnel involved in the design and conduct of the research involving human subjects have received the required education on the protection of human research participants prior to funding of this project. Some of the blood tests could be considered part of the routine diagnostic care of participants at greater risk for developing Type 2 Diabetes, for example, children who are overweight.

Taking part in the study will add the following risks to your care. Research related risks are:

♣ **Blood drawing:**
Likely: The risks of blood drawing and IV insertion include discomfort, bruising, and/or minimal bleeding.
Less Likely: Occasionally during blood drawing procedures, some people experience dizziness or feel faint.
Rare: Very rarely, the site of needle insertion could become irritated or infected. The side effects of the topical anesthesia are very rare. The most common side effects are irritation, redness, itching, or rash. There is also a very small risk of your hand becoming reddened or developing a small blister from warming your hand in the hand-warming box. Side effects associated with topical anesthesia used to numb the area of needle insertion infrequently cause side effects including irritation, redness, itching or rash.

♣ **Interviews or Questionnaires:**
Likely: None
Less Likely: None
Rare: During these questionnaires you may experience minor discomfort when answering some questions. In our experience this discomfort does not happen often, and when it occurs, it does not last long. No major upset has ever happened. All questionnaires are administered by highly trained research staff. Please let the staff know if you feel any discomfort so they may discuss this with you. You may choose not to answer any question that makes you uncomfortable.

♣ **Frequent sample oral glucose tolerance test** (fsOGTT):
Likely: None
Less Likely: None
Rare: there is a small risk of feeling some nausea when drinking the sweet liquid drink. This feeling should pass within a few minutes after drinking the liquid.

♣ **Magnetic resonance imaging (MRI) procedure:**
Likely: None
Less Likely: None
Rare: Having an MRI causes worry or fear for people with claustrophobia (fear of closed-in

spaces), as some persons find the small space in the MRI machine confining and may feel uncomfortable. We find that "rehearsing" prior to the procedure helps to ease this. However, if you should feel afraid or unable to continue, you can request the examiner to stop at any time. Magnetic resonance imaging (MRI) may also be harmful for people with certain kinds of metal in their bodies, especially:

-- someone who had metal fragments in the eye
-- someone with electrical, mechanical, or magnetic activated implants, such as pacemakers and hearing implants.

This procedure will not be performed if you have any of these kinds of metal. Therefore, it is important for you to inform study personnel of any metal in your body. This will not affect payment for your participation. There are no other known risks of magnetic resonance imaging scans at this time.

♣ **ECG:**
Likely: None
Less Likely: There is a small chance that you will experience discomfort from the sticky pads temporarily attached to you in order to perform the EKG.
Rare: None

♣ **Dual-energy x-ray absorptiometry:**
Likely: None
Less Likely: This research involves exposure to radiation from the DXA machine for body fat measurements. You may experience discomfort lying on DEXA scan table. This test has low–dose x-ray exposure (much less than a standard x-ray of your chest, technicians do not wear radiation monitors). The amount of radiation participants will receive from the scan is 1.3% of the amount of natural background radiation exposure people in the United States receive each year. The risk from the radiation exposure in this study is too small to be measured. If you would like more information about radiation exposure, we can provide you with a "Radiation Fact Sheet". If you want to know more about radiation exposure, please see the "Radiation Fact Sheet" located in the Guidelines section of the Human Research Protection Office website, at http://hrpo.wustl.edu, or ask the study staff for a copy.

Rare: None

♣ **Delta Trac:**
Likely: None
Less Likely: None
Rare: There are no physical risks associated with the Delta Trac. Wearing the special hood may cause worry or fear for people with claustrophobia (fear of closed-in spaces). We find that "rehearsing" prior to the procedure helps to ease this. However, if you should feel afraid or unable to continue, you can request the examiner stop at any time.

♣ **Insulin/Glucose Clamp:**
Likely: None
Less Likely: None
Rare: There is a small risk of low blood sugar during the insulin infusion, which might lead to nausea, headache or feeling sweaty or shaky. The risks of infusing stable isotope tracers include the possibility of inflammation or infection. However, all solutions are tested for bacterial, molds, viruses, yeasts, and sterility before infusion and are administered under strict

sterile conditions. There are no known short- or long-term risks associated with the infusion of the isotopes themselves. The special hood to measure breathing may contribute to some feeling of discomfort such as being too warm and/or facial sweating. It will be removed if you are uncomfortable.

Risk of a breach of confidentiality:
With your written permission, we will obtain medical and hospitalization records from your doctors, results from prior blood, diagnostic, and laboratory tests and other information obtained from interviews or questionnaires related to your medical care. We keep this information in a locked area. The information you give us will be given a code number. A master list linking the code number and your identity will be kept separate from the research data. Only the PI and people helping him will be able to see the list, and all staff involved with this project have been thoroughly trained in the protection of research participants. We will protect your information, but there is a chance somebody might see it.

One potential risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure, and we think the risk of accidental disclosure is very small. Please see the *Confidentiality* section of this consent form for more information.

There is the possibility that you will be contacted to see if you are interested in other parts of this study. Being in this part of the study doesn't mean you have to participate in any additional parts. If you are interested in future studies, we would give you a separate consent form to read and sign.

Risks of antipsychotic medications:
There are certain risks and discomforts that may be associated with each medication given in this research study **during the 12 weeks of treatment.** Risks of all medications are listed below, as are ways that we will minimize these risks, but you will only experience risks of the medication treatment group that you are assigned to. These risks include:

Likely Abilify/aripiprazole: Constipation, restlessness, headache, nausea, upset stomach, vomiting, agitation, anxiety, trouble sleeping, sleepiness, lightheadedness, weight gain.

Zyprexa/olanzapine: dizziness, weakness, dry mouth, constipation, upset stomach, sleepiness, accidental injury, trouble sleeping, weight gain, increased appetite, thirst, tremor, depression, shakiness, involuntary movements and, weight gain. Children with borderline abnormal blood lipid levels prior to treatment with olanzapine (cholesterol or triglycerides) may develop abnormal levels while taking this medication.

Risperdal/risperidone: sleepiness, trouble sleeping, agitation, anxiety, stiffness, involuntary movements, headache, upset stomach, runny nose, restlessness, dizziness, extra saliva, constipation, weight gain.

Less Likely Abilify/aripiprazole: Accidental injury, edema, a non- or pre-diabetes increase in fasting blood glucose (below the level of diabetes), high blood pressure, muscle pain, involuntary movement, tremor, increased salivation, inflamed throat and upper digestive tract, cold and flu symptoms, blurred vision, weight gain, tremor, increased mortality and morbidity (cerebral vascular events, including stroke) in elderly patients with dementia-related psychosis, and adverse changes in

blood lipids (cholesterol, triglycerides)., Children with borderline abnormal blood lipid levels (cholesterol, triglycerides) prior to treatment with aripiprazole may develop abnormal levels while taking this medication.

Zyprexa/olanzapine: low blood pressure, a non- or pre-diabetes increase in blood glucose (below the level of diabetes), personality changes (non-aggressive objectionable behavior), restlessness, fever, back pain, chest pain, fast heart beat, high blood pressure, nausea & vomiting, rash, swelling, extremity pain or joint pain, abnormal gait, speech problems, cold and flu symptoms, vision changes, bed wetting, urinary tract infection, increased salivation, memory problems, numbness, confusion, extreme happiness, incoordination, sweating, acne, dry skin, menstrual period changes, vaginal infection, stiffness, dental pain, intestinal gas, joint or bone pain, twitching, abnormal dreams, delusions, emotional changes, eye infection, adverse changes in blood lipids (cholesterol, triglycerides).

Risperdal/risperidone : nausea, vomiting, abdominal pain, a non- or pre-diabetes increase in blood glucose (below the level of diabetes), toothache, coughing, stuffy nose, sore throat, shortness of breath, back pain, chest pain, fever, skin problems, upper respiratory infections, abnormal vision, joint pain, fast heart beat, shakiness, decreased sensation, increased energy, dry mouth, fatigue, injury, coughing, acne, itching, muscle pain, generalized pain, weight increase, high blood pressure, low blood pressure, adverse changes in blood lipids (cholesterol, triglycerides). Children with borderline abnormal blood lipid levels (cholesterol, triglycerides) prior to treatment with risperidone may develop abnormal levels while taking this medication.

Rare Abilify/aripiprazole: pain or tightness (including throat, abdominal, chest, pelvis, extremity, back pain, joint, muscle, jaw, neck or tongue), diarrhea, dry mouth, low appetite, behavioral & emotional changes including psychosis, infection, rash, menstrual periods changes, Neuroleptic Malignant Syndrome (fever, stiffness or involuntary movements, unstable blood pressure), fever, tiredness, migraine, chills, sensitivity to light, bloating, enlarged abdomen, head heaviness, aspiration or food or stomach reflux, heat stroke, enlarged heart, heart attack, heart failure, fast or slow heart beat and/or changes in heart rhythm, pounding heart beat felt by patient, low blood pressure, bleeding, blood clots, pale skin, sudden drop in blood pressure (e.g. when going from sitting or lying down to a standing position), inflamed blood vessels, heart-lung failure, increased appetite, difficulty swallowing, tooth /gums infection or cavities, stomach or intestinal bleeding, rectal bleeding or hemorrhoids, stomach or intestinal gas, esophagus, intestinal or stomach inflammation or bleeding, inflamed gall bladder or gall-stones, ulcers, severe constipation or obstruction, hepatitis, blood in stool, enlarged liver, inflamed pancreas, thyroid changes, bruising of skin, changes in blood tests (various types of anemias or changes in white blood cells), weight loss, changes in metabolic blood tests (sodium, potassium, creatinine, bilirubin, albumin, alkaline phosphatase BUN, SGPT, SGOT, uric acid lactic acid), dehydration, edema, high or low blood sugar, high cholesterol, diabetes mellitus, high triglycerides, thirst, pale or bluish skin, gout, muscle paralysis, muscle tone abnormality, weakness or spasm, bursitis, inflamed tendons, abnormal dream, emotional ups and downs, twitch, rigidity, impaired concentration, dilated blood vessels and arteries, numbness, extremity tremor, hypersensitive skin, dizziness, slowed movement or response, lack of interest, panic attack, unsteady gait, visual hallucination, stroke, impaired memory, hyperactivity, slowed reflexes, restless leg, pain or numbness in nerves, increased reflexes, loss of voluntary movement, slowed thinking, blunted affect, extreme happiness, inability to rotate eyes, obsessive thought, decreased muscle tone or reflexes, bleeding in brain, sinus infection, difficult breathing or shortness of breath, pneumonia, asthma, bloody nose, hiccup, temporary voice loss from inflammation, aspiration pneumonia, decreased oxygen to lungs, respiratory failure, dry nasal passages, bloody sputum, skin ulcer, sweating dry

skin, acne, skin discoloration, hair loss, dandruff, dermatitis, eye infection, ear pain, dry eye, eye pain, ringing in ears, cataract, ear infection, altered taste, inflammation of eyelid, eye bleeding, deafness, double vision, frequent blinking, lazy eye, poor vision in one eye, fear of light, bed wetting, difficulty or abnormal conditions of urination, vaginal bleeding, kidney failure, enlarged breasts, kidney stones, breast pain, female lactation, pain or tenderness in penis, severe allergic reaction (difficulty breathing, swelling and/or rash), diabetes mellitus, somnolence prolonged drowsiness or sleepiness, extrapyramidal movements (such as muscle rigidity, difficulty walking), orthostatic hypotension, tremor, fatigue, akathisia (muscle restlessness, blurred vision), producing more than the usual amount of salivary hypersecretion, increased risk of suicidal thoughts, potential for cognitive and motor impairment, difficulty with body temperature regulation, and dysphagia (difficulty swallowing), dizziness, and leucopenia, neutropenia, and/or agranulocytosis (abnormalities in your white blood cell count), especially in people with a history of a significant low white blood cell count. Seizure activity is a very rare risk with uncertain relationship to this medication.

Zyprexa/olanzapine: abdomen enlarged, chills, face edema, intentional injury, tiredness, infection, neck pain, pelvic pain, sensitivity to light, fever, hangover effect, cardiac (heart beat) changes, stroke, congestive heart failure, heart attack, hemorrhage, migraine, pallor changes in blood vessels and arteries, inflammation, blood clots, difficulty swallowing, inflammation of the esophagus, severe constipation, fecal incontinence, stomach pain or discomfort, inflamed gums, hepatitis, blood in stool, mouth ulceration, tooth abscess or caries, stomach gas, esophageal or stomach ulcer, intestinal obstruction, liver changes, high blood sugar, diabetes mellitus, diabetic acidosis, ketosis or coma, goiter, changes blood count, pale or bluish skin cast, acidosis, alkaline phosphatase blood test increased, bilirubinemia, dehydration, high cholesterol, high triglycerides, gout, high sodium, potassium, bilirubin, uric acid and/or protein in the blood, water intoxication, leg cramps, abnormal changes in muscle tissue, brittle bones, voluntary and involuntary movement disorders, antisocial behavior, ataxia, central nervous system stimulation, rigidity, delirium, dementia, speech and language disturbance, less sensitive or reactive to stimulation, slowed movement, loss of muscle tone or coordination, obsessive compulsive symptoms, extreme unfounded fears, physical symptoms of anxiety, alcohol, drug or tobacco misuse, stuttering, withdrawal syndrome, coma, any disorder of the brain, nerve pain or numbness, eyelid twitching, paralysis, bleeding in the brain, periods of difficult, decreased or absent breathing, asthma, nose bleed, blood in sputum, sweating, hair loss, dry skin, dandruff, skin discoloration, skin ulcer, increased hair growth, difficulty adjusting to a situation or experience, cataract, deafness, double vision, dry eyes, ear pain, eye hemorrhage, various eye disorders breast pain, difficult or painful urination, female lactation, changes in urine or the process of urination, uterine fibroids enlarged, extreme vaginal bleeding, breast enlargement or inflammation, allergic reaction (can be severe with difficulty breathing, swelling, and/or rash), inflamed pancreas, pain & tenderness of penis, severe skeletal muscle disease potentially causing death, and blood clotting events. Seizure activity is a very rare risk with uncertain relationship to this medication.

Risperdal/risperidone : increased dream activity, nervousness, trouble concentrating, depression, lack of interest, catatonic reaction, extreme happiness, increased libido, trouble remembering, sudden mood changes, nightmares, confusion, yawning, longer sleeping time, speech problems, spinning sensation, excess sedation, numbness or tingling, allergic reaction, leg cramps, stiff neck, coma, migraine, reflex changes, loss of appetite, reduced salivation, intestinal gas, diarrhea, increased appetite, swelling, flu-like symptoms, enlarged abdomen, skin irritations, fast breathing, pneumonia, asthma, trouble breathing, skin reaction to sunlight, increased sweating, acne, decreased sweating, hair loss, blocked veins or arteries in the heart, heart attack, eye pain, itchy eyes, low blood sodium or potassium or protein levels, blood

chemical changes, increased thirst, weight decrease, diabetes mellitus (high blood sugar), anemia (low iron), dehydration, hyperphosphatemia (high phosphate levels in the body), hypertriglyceridemia (high triglycerides in the blood), hyperuricemia (high uric acid in the body), hypoglycemia (low blood sugar), increased urination/increased thirst, bed-wetting, hematuria (blood in urine), problems urinating, problems with the kidneys, joint pain, arthritis, missed menstrual periods, breast pain, bleeding, liver failure, hepatitis (liver inflammation), decreased blood clotting , blood clots, ringing in the ears, decreased hearing, ear problems, hormones problems, high prolactin levels in the blood, problems regulating body temperature, bitter taste, a change in the time it takes for the heart to conduct normal electrical signals (QTc prolongation) has also been associated with olanzapine use. Neuroleptic Malignant Syndrome (fever, stiffness or involuntary movements, unstable blood pressure). Seizure activity is a very rare risk with uncertain relationship to this medication.

It is important to note that these side effects do not occur in everyone. We expect that you, your parents/guardians, and your doctor will be going over the side effects that you might watch for while taking any of these medications. The possibility of a suicide attempt is inherent in some psychiatric disorders, and close supervision of high-risk persons should accompany drug therapy.

Participants will be followed closely and monitored for side effects of medications and tests. Withdrawal of the study medication and/or treatment of medication side effects will be provided as indicated. Participants will participate in medication check-ups or telephone calls at least once per week and will be asked to report any concerns or adverse events during these times. To be sure that you/your child can always communicate with the research team, families will be provided with a 24-hour telephone number of a research clinician who will answer any questions and speak with any community physicians or dentists who the participants visit during the study. All families will also be instructed to tell any doctors or dentists they encounter that their children/adolescents are on the study medications.

The risk of your side effects will be minimized, or reduced should they occur, through the following steps:

1. Sometimes Abilify (aripiprazole), Zyprexa,(olanzapine) or Risperdal (risperidone) can cause nausea or vomiting. To prevent the nausea, it is best for you to have something to eat in the morning before the a.m. dose.

2. Participants will be monitored for neuromuscular side effects at each weekly visit. Neuromuscular side effects include developing a walking style that seems to be shuffling along rather than lifting one's legs, stiffness in the movements of wrist and elbow joints, shaking of the hands when the hands are not busy and a loss of facial expression. Also, children/adolescents may also develop a problem that looks as if they are restless (called akathisia). These side effects can sometimes be reduced by lowering the dose of medication or adding an appropriate medication to treat the side effect. Participants will also be monitored for tardive dyskinesia (unusual movements of the mouth area, cheek, tongue or other parts of the body such as the shoulders and extremities). Study medications will be discontinued if tardive dyskinesia occurs.

3. Participants will be regularly monitored for changes in blood triglycerides or blood glucose. Problems with the way the body handles glucose (sugar) and lipids (triglycerides) can occur with Abilify, (aripiprazole), Zyprexa (olanzapine), or Risperdal (risperidone) potentially resulting in diabetes or a condition called the metabolic syndrome. These blood glucose and lipid problems can occur without any symptoms. That is why blood glucose and lipids are monitored in this study.

If your fasting blood glucose becomes elevated at any point in the study to the level that is called diabetes, you will be withdrawn from the study. If you blood triglycerides become elevated to a serious degree that can increase the risk of an inflamed pancreas, then you will be withdrawn from the study. If your blood glucose or lipids become elevated during the study below the levels noted above, we will increase the frequency with which you blood is monitored for any further changes.

4. If your body weight increases 10% or more from when you first began taking the study medication, you will be monitored on a weekly or biweekly basis for other events that may occur in the setting of weight gain, especially hyperglycemia and hyperlipidemia.

During this study, you must avoid over-the-counter drugs and herbal supplements as these may interfere with treatment results.

As with any research procedure, unforeseen problems or side effects can occur. **Participation in this study may cause all, some or none of the side effects listed above which, if severe, may cause death**. You will be told of any changes in the way the study will be done and of any newly identified risks to which you may be exposed.

Data and Safety Monitoring Committee
An independent group of medical and research professionals, called a Data and Safety Monitoring Committee (DSMC), has been established to monitor the data collected from this study and look for ways to continually improve the safety of all the procedures and medications administered as part of this project. The PI and study staff are responsible for sending regular reports to the DSMC detailing our findings, particularly highlighting any adverse or serious adverse events that occur. Having a DSMC makes sure that someone outside of the project knows about any problems and can provide an objective opinion about what needs to be done to fix or minimize them. It is the job of the DSMC to maintain the highest level of safety for our participants.

Study Discontinuation
When you discontinue the study early due to an adverse event, or on schedule due to study completion, we will carefully work with you and your treating psychiatrist to evaluate the risks versus the benefits of ongoing treatment with the medication you were assigned to. At that time we can discuss the advantages and disadvantages of staying on that medication, switching to a different antipsychotic medication, or discontinuing antipsychotic medication. In all cases we will provide individualized consultation with parents and treating psychiatrist and/or pediatricians to provide the safest plan to continue the ongoing individualized therapy.

Breast Feeding

You must tell the study doctor if you are breast-feeding.

Certificate of Confidentiality

One potential risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure, and we think the risk of accidental disclosure is very small. Please see the *Confidentiality* (Item 7) section of this consent form for more information.

Coded Data

The information you give us will be given a code number. A master list linking the code number and your identity will be kept separate from the research data. Only the PI and people helping him/her will be able to see the list. We will protect your information, but there is a chance somebody might see it.

Pregnancy/Childbearing Potential

If you are a woman of childbearing potential, please read and sign below.

Some parts of this study might cause physical or mental problems in an unborn baby. You must tell the doctor immediately if there is any chance you are pregnant. You must also tell the doctor if your birth control method fails while you are on the study.

To take part in this study, you must have a pregnancy test before starting the study. You must use an acceptable method of birth control and must not become pregnant.

Please discuss with your research physician how long you need to wait before becoming pregnant. By signing below, you agree to follow these rules.

Signature Date

What happens if you are injured because you took part in this study?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator (John Newcomer MD at 314/362-5939) and/or the Human Research Protection Office at (314) 633-7400 or 1-(800)-438-0445.

Decisions about payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

5. **Are there benefits to taking part in the study?**

These medicines may improve your symptoms with aggressive behavior or conduct disorder. In addition, you/your child will be checked for serious medical conditions that may not show any symptoms, such as high blood pressure or diabetes. Finding these conditions may improve your medical care. This study will help doctors to understand how antipsychotic medications may affect diabetes risk and ways to address the risk of diabetes in children with conduct disorder, aggression or other behavior problems.

6. **What other options are there?**

Taking part in this research study is voluntary. You may choose not to take part in this research study or you may withdraw your consent at any time. You may withdraw by telling the study team you are no longer interesting in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at http://hrpo.wustl.edu under Information for Research Participants. Your choice will not at any time affect the commitment of your health care providers to administer care. There will be no penalty or loss of benefits to which you are otherwise entitled.

Other than not taking part in the research, you may choose to have your doctor write a prescription for you if he/she feels it is in your best interest to receive this drug outside of the study. The study

drugs, olanzapine, risperidone and aripiprazole are available to you even if you do not participate in this study. Please discuss all alternatives with your doctor including psychotherapy and behavior management.

7. What about privacy and confidentiality?

We will do everything we can to protect your privacy.

Providing your social security number is optional and you can fully participate in the study whether you disclose it or not. If you choose to provide your social security number, we will use your social security number to locate you in the future if we are unable to locate you at your home address, and to search vital records. We will not share your social security number or leave it accessible to theft.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study explained in this consent form.

In addition to health information that may be created by the study, the research team may access the following sources of your health information to conduct the study: hospital/physician medical records; lab, pathology and/or radiology results; information derived from biological samples (including blood); interviews/questionnaires; mental health records; physiologic imaging.

A Certificate of Confidentiality has been obtained from the Department of Health and Human Services. This will help further protect information that may identify you. The Certificate prevents the investigator from being forced to disclose identifying information for use in court. The investigator may not even be forced by court subpoena. Courts that may be prevented from getting your information include any federal, state, local civil, criminal, administrative, legislative, or other court proceeding.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. The investigator may not withhold information if you give your insurer or employer permission to receive information about your participation in this research. This means that you and your family must also actively protect your own privacy.

The Certificate does not prevent the researchers from taking steps, including reporting to authorities, to prevent serious harm to yourself or others. Such disclosures will be made as described below.

The research team may share your information with:

- The Department of Health and Human Services (DHHS) to complete federal responsibilities for audit or evaluation of this study.
- Public health agencies to complete public health reporting requirements
- Hospital or University representatives, to complete Hospital or University responsibilities for oversight of this study.
- Your primary care physician if a medical condition that needs urgent attention is discovered

- Appropriate authorities to the extent necessary to prevent serious harm to yourself or others.
- Because the research takes place at the Pediatric Clinical Research Unit (PCRU) and the Clinical Research Unit (CRU), the Medical officer or the research Subject Advocate on the PCRU and CRU may review your medical record.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form.
If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer, at 866-747-4975.

This study is sponsored by National Institute of Mental Health (NIMH). Representatives of the sponsor will have access to your research and/or medical records for monitoring the study. The research team will also send study results to the sponsor. Information sent to the sponsor will be summarized and coded so that it cannot be associated with your PHI. The sponsor is not required to abide by the HIPAA regulations, but agrees to protect the confidentiality of your information. The sponsor reviews the study summary to verify that the research is progressing toward stated goals.

You will always have access to your medical record. Some of the individual results from tests to be performed during this research study might be of interest to you or your primary care physician. At your request, the researchers will share the medical information gained from this study with you and your referring and/or primary care doctors. If we become aware of any important health information during the course of your participation in this study, we may be obligated/required to share this information with your treatment team. You will not have access to your research record.

If you decide not to sign this form, it will not affect
-your treatment or the care given by your health provider.
-your insurance payment or enrollment in any health plans.
-any benefits to which you are entitled.
However, it will not be possible for you to take part in the study.

If you sign this form:
- You authorize the use of your PHI for this research
  - Your signature and this form will not expire as long as you wish to participate.
  - You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at http://hrpo.wustl.edu (or use the direct link: http://hrpohome.wustl.edu/participants/WithdrawalTemplate.rtf) or you may request that the Investigator send you a copy of the letter.
      - **If you revoke your authorization:**

- ♣ The research team may only use and share information already collected for the study.
  - ♣ Your information may still be used and shared if necessary for safety reasons.
  - ♣ You will not be allowed to continue to participate in the study.

Please specify any contact restrictions you want to request for this study only.
(Example – no calls at home, no messages left for you, no e-mails, etc.)

_____

_____

Notice of Privacy Practices

The Notice of Privacy Practices is a separate document. It describes the procedures used by WU to protect
your information. If you have not already received the Notice of Privacy Practices, the research team will make one available to you.

_____ I have been offered a copy of the Notice of Privacy Practices.
Initial

8. Whom do I call if I have questions or problems?

Please contact the researcher listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: John Newcomer MD at 314/362-5939
Research Coordinators: Martha Hessler at 314/362-2423 or Julie Schweiger at 314/362-3153
Mailing Address: 660 S. Euclid Ave., Campus Box 8134; St. Louis, MO 63110

If you wish to talk to someone else, or have questions or concerns about your rights as a research participant, call Washington University's Human Research Protection Office (WU HRPO) at (314) 633-7400, or 1-(800)-438-0445. For questions about the Clinical Research Unit (CRU) or Pediatric Clinical Research Unit (PCRU) please call Michelle Jenkerson, Research Participant Advocate at 314-362-5626.

Request Permission for Future Contact

May we contact you for future undetermined studies conducted by Dr. Newcomer, Haupt, and Nicol? If yes, we will need to look at your Protected Health Information (PHI) to check for study eligibility.	___ Yes	___ No
May other WU physicians conducting research contact you? If yes, your PHI will be shared with other WU physicians.	___ Yes	___ No

Taking part in future studies is optional. You can ask us at any time to take you off our contact list.

9. The Principal Investigator (PI) may withdraw you from the study without your consent if considered appropriate (i.e. certain medical conditions, use of illegal drugs). It may be in your best interest to allow follow-up outside the study. The PI will share any new information that could change how you feel about continuing in the study.

10. You will be given a signed copy of this consent form for your records.

Please mark all that apply. This section is optional.
[] Not Hispanic or Latino [] Hispanic or Latino [] Unknown
[] Asian [] Black or African-American [] Caucasian [Native American or Alaskan Native [] Native Hawaiian or Pacific Islander [] Other [] Unknown
The Office of Management and Budget has declared that Hispanic/Latino is an ethnicity. National Institutes of Health, in an effort to ensure diversity in research, requests that you report your ethnicity. (http://grants.nih.gov/grants/funding/women_min/women_min.htm)

SIGNATURES FOR ADULT PARTICIPANTS

Research Participant:
I have read this consent form and have been given the chance to ask questions. I agree to participate in this research described above, titled: **Metabolic Effects of Antipsychotics in Children (Treatment Study, ≥18 y.o.).**

HRPO does not require participants to re-sign the consent form unless a change is made; the investigator, however, may choose to re-consent participants at any time.

Signature: _____

Printed Name: _____ Date of Signature: _____

Principal Investigator (or Designee):
I have given this research participant (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The participant has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Signature: _____ Title: _____

Printed Name: _____ Date of Signature: _____

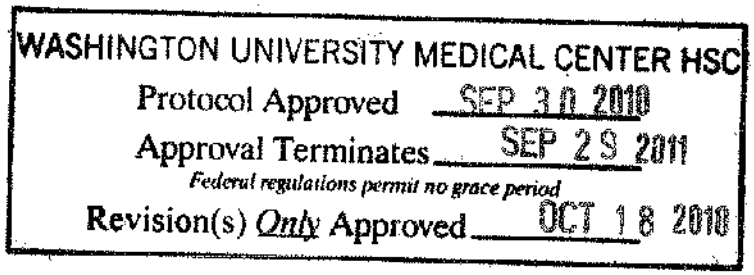
Witness (optional):

I observed the above participant (or his/her legally authorized representative, if applicable) sign this consent document.

Signature: _____

Printed Name: _____ Date of Signature: _____

This form is valid only with the Human Research Protection Office's current stamp of approval.



INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Participant's Name _____ HRPO # **05-0264**

Principal Investigator **Newcomer, John W., MD** PI's Phone Number **(314) 362-5939**
Last First Credentials

Title of Project: **Metabolic Effects of Antipsychotics in Children (Treatment study,<18 y.o.)**

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take the time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decided to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. Why is this study being done?

Being in a research study does not take the place of routine physical exams or visits to your own doctor and should not be relied on to diagnose or treat medical problems.

Use of antipsychotic medication in children and young adults has been shown to be an effective treatment for behaviors such as aggression, but doctors don't know as much about how they may affect weight, glucose (sugar), insulin (a hormone that controls blood sugar levels), and lipids (fats) in younger patients. Although these antipsychotic medications have been FDA-approved by the Food and Drug Administration (FDA) for adults and are now used commonly in children and young adults who have conduct disorder, aggression or other behavioral symptoms, they are not FDA-approved for children. The point of this research is to study side effects of these antipsychotic medications in younger individuals. We will be measuring how these drugs affect body weight and substances in the body such as glucose, insulin, and lipids. Dr. Newcomer and colleagues have performed more than 400 studies of this kind in adults to look at how different types of antipsychotic medications affect weight, glucose, insulin, and lipids. This study will include 325 children and young adults whose doctors want them to start taking antipsychotic medications to treat conduct disorder or other behavior symptoms. Your doctor has determined that one of these medications may be helpful to you.

For more information regarding minors in research see www.researchchildren.org.

2. **What am I being asked to do?**
All procedures described below are research-related *except* for the prescribing of an antipsychotic medication to treat a psychiatric diagnosis and a urine drug screen if there is a history of substance abuse.

Study Visit 1: Your child will be seen by one of our child psychiatrists for a full diagnostic evaluation. Based on the evaluation, if your child qualifies and you wish to participate, we will schedule the next two study visits. You and your child will be asked questions about feelings, emotions, and behavior, and about how your child gets along at home, school, or work, and with friends. We will first ask you these questions and then we will ask your child the same questions. These questionnaires will be administered by trained personnel over the telephone or at one of the initial study visits (study visit 2 or 3). The combined length of time for both parent and child for this phase of the study is approximately 4-5 hours.

a) Study Visit 2: Within a few days after Study Visit 1, your child will be scheduled to go to the Pediatric Clinical Research Unit (PCRU) or Clinical Research Unit (CRU) for blood tests, an EKG, a frequent sample oral glucose tolerance test (fsOGTT), an MRI and a DXA scan. This session will last approximately 3-4 hours. The blood tests, EKG and oral glucose tolerance test are considered standard clinical care for people taking antipsychotics. The DEXA body scan, MRI and insulin/glucose clamp are research related tests. For females of child-bearing age, a urine pregnancy test will be done at baseline and 12 week visits. If your child is pregnant or becomes pregnant during the study, she will be discontinued from the study because hormonal changes could alter test results. Your child may be asked to submit a urine sample for a drug screening if s/he and her/his doctor have been previously concerned about substance use. Each procedure is described below:

1. **EKG**: Your child will be given a routine resting electrocardiogram (EKG), where soft electrodes (like small pieces of tape) will be stuck to his/her chest to measure their heart rhythm.

2. **fsOGTT and Blood tests**: With an oral glucose tolerance test, your child will be given a sweet drink to see how his/her body handles extra sugar. On the night before this test, your child can't have anything to eat or drink except water after 10:00 p.m. In the morning, your child will go to the Pediatric Clinical Research UNIT (PCRU) or Clinical Research Unit (CRU) where he/she will lie in a hospital bed or reclining chair. If your child is a female of child-bearing age, before the procedure begins she will be given a pregnancy test. A small catheter (a plastic tube, also called an IV) will be inserted into a vein of your child's hand or wrist or bend in his/her arm. This feels like getting a shot, but we will numb your child's skin first with either a cream or an injectable local anesthetic to help it hurt less.

   Once the IV catheter is in your child's vein, it doesn't hurt and we will use the catheter to get blood samples during the study without hurting him/her. Your child's hand or wrist or arm with the IV will be heated in a routinely used temperature-controlled hand-warming box to increase the blood flow to the hand. This box is not FDA approved but is common in many centers.

   Your child will then drink a very sweet lemon- or orange-flavored drink. Blood samples will be taken from the catheter in your child's hand or wrist or arm at different times during the

study to check sugar levels in your blood along with some other routine blood tests. He/she can watch cable TV or a video during this study.

After this study, your child will be given breakfast.

3. **MRI**: Your child will also have a magnetic resonance imaging (MRI) scan to measure the fat content in your belly. He/she will wear their clothes or a hospital gown during this scan. During the MRI scan, your child will lie on a table inside a tube while his/her stomach is scanned. The machine will scan your child's stomach three or four times, for about 30 seconds each time. Your child will need to hold still during the 30-second scans, but he/she can wiggle a little in between scans. The whole MRI study takes about 20 minutes. The machine makes some strange noises, but your child can't feel it scanning. Your child will wear earphones and listen to music while he/she is being scanned.

4. **DXA**: Your child will also have a dual-energy x-ray absorptiometry (DXA) scan to measure his/her body fat and body muscle content. The DXA scan involves lying still on a table in street clothes or a hospital gown (not in a tube this time) and having your child's body scanned by a machine for about 5 minutes. Your child won't be able to feel the DXA machine scanning, either.

b) **Study Visit 3**: **Insulin/Glucose Clamp:** About a week after Visit 2, your child will be come to the PCRU or CRU early in the morning (about 6:30 am) for a test called the Insulin/Glucose Clamp. This is a test that measures blood glucose (sugar), lipids (fats) and other hormones in your child's body while he/she is getting IV fluids that contain glucose (sugar) and insulin (a hormone that controls blood sugar levels).

Your child can't eat or drink anything except water after 10:00 p.m. the night before the test. Upon arrival to the PCRU or CRU, your child's height, weight, and vital signs will be measured. If your child is a female of child-bearing age, before the procedure begins she will be given a pregnancy test. Your child will then have two IV catheters inserted, one in each arm, using the injectable anesthetic or numbing cream first.

This large vein site in the one arm will allow us to give your child IV fluids that are non-radioactive stable isotopes (rare but natural forms of foods like fat and sugar). These isotopes are already present in your child's body and there will be no short-term or long-term side effects from the extra isotopes we give him/her. The second IV will be inserted into a vein of your child's other hand or wrist or bend in your arm. This IV site will be heated in a temperature-controlled box and blood samples will be taken from this IV at different times during the study. Your child will be able to watch cable or videos while lying in bed. The study doctor or research nurse and PCRU /CRU nurses will be present throughout the session. Twice during the session, your child will wear a special hood (called an indirect calorimeter) that measures your breathing and tells us how many calories you are burning. Your child will wear this two times during the study, each time for about 30 minutes. If he/she become uncomfortable wearing the hood, we will remove it. After the study, your child will receive a late lunch (around 2:30 p.m.), the IVs will be removed, and then you can take them home. The session will begin early in the morning following overnight fast and will take approximately 7 1/2 to 8 hours. Your child will be asked questions about how he/she is feeling during this session.

The amount of blood drawn during each test will depend on your child's weight at the time of each OGTT and Insulin/Glucose Clamp. We will follow Washington University School of Medicine Human Study Committee Research Protection Office's guidelines of drawing no more that 3 ml (3/5 teaspoon)/kg of body weight over a two month period of time. We will do this by decreasing the number of time points for each blood draw for each test.

(Under special circumstances, such as having trouble remembering not to eat after 10:00 pm the night before the test, your child might be asked to be stay overnight on the CRU on the night prior to the OGTT or the Insulin/Glucose Clamp.)

We will never sedate your child (give him/her any medication to make them sleepy or calm) for any of these procedures. If your child becomes too uncomfortable, he/she can stop participating at any time.

Treatment Assignment:

1) In coordination with your child's physician, after he/she has completed the baseline OGTT and Insulin/Glucose Clamp, he/she will be randomly (like the flip of a coin) assigned to receive one of the following newer antipsychotic medications for 12 weeks (3 months): aripiprazole (Abilify), olanzapine (Zyprexa), or risperidone (Risperdal). There is a one out of three chance of receiving one of the three medications. Your child's physician and the study personnel will closely monitor the addition of this medication. You and your child's physician will know what medicine your child has been assigned, and your physician will adjust the dose on an individual basis. If your child participates in this study, your child's physician will be asked not to use a second antipsychotic or certain other medications along with the antipsychotic, (e.g. antihistamines, tricyclic antidepressants, bupropion, clonidine, pemoline, and mood stabilizing agents). These medications may themselves worsen glucose and lipid control or otherwise make it difficult to assess the effects of the antipsychotic alone.

2) If more than six weeks have passed between your child's participation in the initial phase of the study and his/her random assignment to one of the medications, he/she will be asked to repeat the isotope infusion portion of the study (see c above for description).

3) If more than eight weeks have passed between your child's participation in the initial phase of the study and his/her assignment to a different medication, he/she will be asked to repeat the isotope infusion and repeat the MRI and DXA scans and routine blood tests (see b and c above).

4) Your child will be asked to refrain from donating blood for two months after the end of the study, since the amount of blood drawn will be close to the maximum guidelines suggested for children.

5) If at any time during the study your weight, blood sugar and/or blood lipid levels show a need to be watched more closely, the study doctor and staff may ask that your child come for additional visits at week 3, week 9, or possibly more frequently during the 12 week study.

Weekly Medication Check

Your child will have weekly medication checks with the study doctor and research assistant.

These visits may be over the telephone or as out-patient visits to research offices.

c) **Study Visit 4:** This visit will be approximately six weeks after the Insulin/Glucose Clamp (Study visit #3). This visit will include an fsOGTT and /or, blood tests and DXA as described in Study Visit #2. (There will not be a MRI at this visit). The fsOGTT may not be done if your child is younger and a small body size.

d) **Study Visit 5:** This visit will happen approximately 11-12 weeks after your child begins the study medication at Study visit #3. Study visit 5 will include an fsOGTT, DXA, MRI and all blood tests as described in Study visit #2.

e) **Study Visit 6:** This visit will happen approximately 1 week after Study Visit #5. This final visit will include a Insulin/Glucose Clamp and all blood tests as described for Study Visit #3.

f) **Extra study visits (safety checks) for some children/teens:** Throughout the study, the study doctor will talk with you and your child about your child's weight and blood tests results. If the study doctor wants to watch your child's weight and/or blood tests more closely at any time during the study, you will be asked to come to the PCRU/CRU for extra study visits. These will be short visits lasting about 1-hour and may happen as often as every other week or more frequently for as long as your child is in the study (including until your child completes the 3-month follow up visit if selected to do so).

The safety checks will be approximately **3 weeks after starting study med (visit 3A) and/or 9 weeks after starting study med (visit 4A), but may happen at other times, too, if the study doctor feels they are necessary to keep your child healthy.** At the time, if it is decided that extra study visits will be helpful, your child will also be given a home monitoring kit that contains strips for testing urine sugar and ketones. You and your child will be given instructions on how to check your urine for sugar and ketones one or more times a week.

h) **3-month follow-up visit (after 12-week study ends)- Visit 7:** At the end of the 12-week study, the study doctors will make recommendations to you, your child, and your treating clinicians regarding the study-related treatment effects on your weight, blood lipids and blood sugar, and behavior. When the ending OGTT and Glucose/Insulin Clamp are completed, your child will be returned to the care of your treating physician (child psychiatrist or primary care doctor). If the study doctor recommends that he/she return for a follow-up visit (after the 12-week study ends) you will be asked to return for this brief follow-up visit in approximately 3 months. During the 3 months following the12-week study visits, your child will be under the care of your primary physician and no additional study visits will occur during that time. Your child's 3-month lab results will be shared with your treating physician.

For the safety checks and the 3-month follow-up, your child will need to be fasting after 10:00 p.m. the night before the study visit. He/she will have weight, height and waist measured and the PRU/CRU nurse will blood draw blood from his/her arm or hand for a fasting blood sugar and a fasting blood lipids (cholesterol and triglycerides). Less than one teaspoon of blood will be drawn at each visit; the amount will depend on his/her body size. During these study visits, the study staff will ask questions about your child's medications, how he/she feels and about any problems he/she might be having and look at the urine test results.

i) **Optional post-study phone questionnaires:** Someone from the research team may call you during or after your participation to ask about your child's eating and exercise patterns over the course of the study, as well as your own experiences and attitudes toward psychotherapy. Both questionnaires will be optional. You can choose to not answer any question, or not to take the questionnaires at all, without incurring any penalty and without jeopardizing your participation in the treatment study. These questions are for research purposes only and the final results of the questionnaires will not be traceable to you or your family.

j) **Optional post-study re-consent to release school records:** At the beginning of the MEAC study, you will be asked to provide permission for study staff to contact your child's school so that we may obtain information about your child's school performance as it relates to his/her symptoms. Your decision whether to allow us to contact your child's school will not affect your child's treatment or you or your child's participation in the study in any way. The release will be good for 1 year, but in some cases, you may be contacted more than one year after your child's participation in MEAC has ended; this is to renew a release that is more than 1 year old.

How long will I be in the study?

Your child will be in the study approximately 3-4 months unless he/she has some changes in weight, blood sugar or blood lipid tests that need to be checked approximately 3-months after the 12-week study ends. If that happens, your child will be in the study for a total of 6-7 months, but your child psychiatrist or primary care doctor will be in charge of your child's behavioral/psychiatric treatment after the 12-week study ends. Study staff will assist with referrals to a child psychiatrist or primary care physician at the end of the 12-week study as necessary.

Financial Disclosure of Interest

The study sponsor is paying Washington University to conduct this study. The amount of payment is enough to cover the study doctor's and/or institution's expenses to perform the study.

Participating in Concurrent Studies

Your child may not be in any other medical studies while in this study.

3. **What are the costs?**

The procedures performed just for this research study are provided at no cost to you and your child. There are no extra charges to you or your insurance company for participating in this study. You or your insurance company will be charged for your antipsychotic medications. If your child has no current medical insurance, he/she will receive the medication for the study at no cost to you during your participation in the study. If your child has a history of drug or alcohol dependence, you or your insurance company may be charged for (standard of care) urine drug screening so that your child can receive the medical care needed for this condition.

Standard care and research may carry a co-pay or deductible. When insurance pays, you are responsible for the applicable co-pays and deductibles.

Your family will receive a total value of up to $700.00 (up to $775.00 if child has study visit at 3-months following the 12-week study) combined in gift certificates and monetary reimbursement for your participation in the 12-week research study. The child will receive payment in their choice of gift certificates. If you want to stop your participation at any time, you will receive part of the $700 value, based on how far in the study you are. You will receive $75.00 each for baseline and 6-

week OGTTs (or 6-week fasting labs) and $100.00 for the 12-week OGTT; $50.00 for the first medication check visit with the study psychiatrist; $175 for the baseline Insulin/Glucose Clamp and $225.00 for the 12-week clamp. If you participate in the 3-month follow-up visit after the 12-week study ends, you will be paid an additional $75.00 in gift certificates and monetary reimbursement for that visit. All compensation will be for time and inconvenience. Gift cards and monetary reimbursement will be available at the next scheduled study visit - they will not be available during the child psychiatrist visits. You will not receive any payment for safety labs.

Because you will be receiving more than $600 in gift certificates, this amount will be considered extra income so you will receive an IRS Tax Form 1099 during tax season from Washington University so you can report it to the IRS.

4. What are the risks?

In this study, your child will get both routine and research procedures. The overall potential risks of this study are small. All key personnel involved in the design and conduct of the research involving human subjects have received the required education on the protection of human research participants prior to funding of this project. Some of the blood tests could be considered part of the routine diagnostic care of participants at greater risk for developing Type 2 Diabetes, for example, children who are overweight.

Taking part in the study will add the following risks to your care. Research related risks are:

♣ **Blood drawing:**
Likely: The risks of blood drawing and IV insertion include discomfort, bruising, and/or minimal bleeding.
Less Likely: Occasionally during blood drawing procedures, some people experience dizziness or feel faint.
Rare: Very rarely, the site of needle insertion could become irritated or infected. The side effects of the topical anesthesia are very rare. The most common side effects are irritation, redness, itching, or rash. There is also a very small risk of your child's hand becoming reddened or developing a small blister from warming his/her hand in the hand-warming box. Side effects associated with topical anesthesia used to numb the area of needle insertion infrequently cause side effects including irritation, redness, itching or rash.

♣ **Interviews or Questionnaires:**
Likely: None
Less Likely: None
Rare: During these questionnaires you/your child may experience minor discomfort when answering some questions. In our experience this discomfort does not happen often, and when it occurs, it does not last long. No major upset has ever happened. All questionnaires are administered by highly trained research staff. Please let the staff know if you feel any discomfort so they may discuss this with you and your child. You/your child may choose not to answer any question that makes you uncomfortable.

♣ **Frequent sample oral glucose tolerance test** (fsOGTT):
Likely: None
Less Likely: None

Rare: There is a small risk of feeling some nausea when drinking the sweet liquid drink. This feeling should pass within a few minutes after drinking the liquid.

♣ **Magnetic resonance imaging (MRI) procedure:**
Likely: None
Less Likely: None
Rare: Having an MRI causes worry or fear for people with claustrophobia (fear of closed-in spaces), as some persons find the small space in the MRI machine confining and may feel uncomfortable. We find that "rehearsing" prior to the procedure helps to ease this. However, if your child should feel afraid or unable to continue, he/she can request the examiner to stop at any time. Magnetic resonance imaging (MRI) may also be harmful for people with certain kinds of metal in their bodies, especially: someone who had metal fragments in the eye, someone with electrical, mechanical, or magnetic activated implants, such as pacemakers and hearing implants.

This procedure will not be performed if your child have any of these kinds of metal. Therefore, it is important for your child to inform study personnel of any metal in his/her body. This will not affect payment for his/her participation. There are no other known risks of magnetic resonance imaging scans at this time.

♣ **ECG:**
Likely: None
Less Likely: There is a small chance that you will experience discomfort from the sticky pads temporarily attached to your child in order to perform the EKG.
Rare: None

♣ **Dual-energy x-ray absorptiometry:**
Likely: None
Less Likely: This research involves exposure to radiation from the DXA machine for body fat measurements. Your child may experience discomfort lying on DEXA scan table. This test has low–dose x-ray exposure (much less than a standard x-ray of your chest, technicians do not wear radiation monitors). The amount of radiation participants will receive from the scan is 1% of the amount of natural background radiation exposure people in the United States receive each year. The risk from the radiation exposure in this study is too small to be measured. If you would like more information about radiation exposure, we can provide you with a "Radiation Fact Sheet". If you want to know more about radiation exposure, please see the "Radiation Fact Sheet" located in the Guidelines section of the Human Research Protection Office website, at http://hrpo.wustl.edu, or ask the study staff for a copy.

Rare: None

♣ **Delta Trac:**
Likely: None
Less Likely: None
Rare: There are no physical risks associated with the Delta Trac. Wearing the special hood may cause worry or fear for people with claustrophobia (fear of closed-in spaces). We find that "rehearsing" prior to the procedure helps to ease this. However, if your child should feel afraid or unable to continue, he/she can request the examiner stop at any time.

♣ **Insulin/Glucose Clamp:**
***Likely*:** None
***Less Likely*:** None
Rare: There is a small risk of low blood sugar during the insulin infusion, which might lead to nausea, headache or feeling sweaty or shaky. The risks of infusing stable isotope tracers include the possibility of inflammation or infection. However, all solutions are tested for bacterial, molds, viruses, yeasts, and sterility before infusion and are administered under strict sterile conditions. There are no known short- or long-term risks associated with the infusion of the isotopes themselves. The special hood to measure breathing may contribute to some feeling of discomfort such as being too warm and/or facial sweating. It will be removed if your child is uncomfortable.

Risk of a breach of confidentiality:
With your written permission, we will obtain medical and hospitalization records from your child's doctors, results from prior blood, diagnostic, and laboratory tests and other information obtained from interviews or questionnaires related to your medical care. We keep this information in a locked area. The information you and your child give us will be given a code number. A master list linking the code number and your child's identity will be kept separate from the research data. Only the PI and people helping him will be able to see the list, and all staff involved with this project have been thoroughly trained in the protection of research participants. We will protect your child's information, but there is a chance somebody might see it.

One potential risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure, and we think the risk of accidental disclosure is very small. Please see the *Confidentiality* section of this consent form for more information.

As with any research procedure, unforeseen problems or side effects can occur. You will be told of any changes in the way the study will be done and of any newly identified risks to which you may be exposed.

Participation in this study may cause all, some or none of the side effects listed above. In addition, there is always the risk of developing previously unknown side effects. The investigators are willing to discuss any questions you might have about the severity, frequency, and duration of these risks and discomforts.

There is the possibility that your child will be contacted to see if you are interested in other parts of this study. Being in this part of the study doesn't mean your child has to participate in any additional parts. If your child is interested in future studies, we would give him/her a separate consent form to read and sign.

Risks of antipsychotic medications:
There are certain risks and discomforts that may be associated with each medication given in this research study **during the 12 weeks of treatment.** Risks of all medications are listed below, as are ways that we will minimize these risks, but your child will only experience risks of the medication treatment group that he/she is assigned to. These risks include:

Likely Abilify/aripiprazole: Constipation, restlessness, headache, nausea, upset stomach, vomiting,

agitation, anxiety, trouble sleeping, sleepiness, lightheadedness, weight gain.

Zyprexa/olanzapine: dizziness, weakness, dry mouth, constipation, upset stomach, sleepiness, accidental injury, trouble sleeping, weight gain, increased appetite, thirst, tremor, depression, shakiness, involuntary movements and, weight gain., Children with borderline abnormal blood lipid levels prior to treatment with olanzapine (cholesterol or triglycerides) may develop abnormal levels while taking this medication.

Risperdal/risperidone: sleepiness, trouble sleeping, agitation, anxiety, stiffness, involuntary movements, headache, upset stomach, runny nose, restlessness, dizziness, extra saliva, constipation, weight gain.

Less Likely

Abilify/aripiprazole: Accidental injury, edema, a non- or pre-diabetes increase in fasting blood glucose (below the level of diabetes), high blood pressure, muscle pain, involuntary movement, tremor, increased salivation, inflamed throat and upper digestive tract, cold and flu symptoms, blurred vision, weight gain, tremor, increased mortality and morbidity (cerebral vascular events, including stroke) in elderly patients with dementia-related psychosis, and adverse changes in blood lipids (cholesterol, triglycerides)., Children with borderline abnormal blood lipid levels (cholesterol, triglycerides) prior to treatment with aripiprazole may develop abnormal levels while taking this medication.

Zyprexa/olanzapine: low blood pressure, a non- or pre-diabetes increase in blood glucose (below the level of diabetes), personality changes (non-aggressive objectionable behavior), restlessness, fever, back pain, chest pain, fast heart beat, high blood pressure, nausea & vomiting, rash, swelling, extremity pain or joint pain, abnormal gait, speech problems, cold and flu symptoms, vision changes, bed wetting, urinary tract infection, increased salivation, memory problems, numbness, confusion, extreme happiness, incoordination, sweating, acne, dry skin, menstrual period changes, vaginal infection, stiffness, dental pain, intestinal gas, joint or bone pain, twitching, abnormal dreams, delusions, emotional changes, eye infection, adverse changes in blood lipids (cholesterol, triglycerides).

Risperdal/risperidone : nausea, vomiting, abdominal pain, a non- or pre-diabetes increase in blood glucose (below the level of diabetes), toothache, coughing, stuffy nose, sore throat, shortness of breath, back pain, chest pain, fever, skin problems, upper respiratory infections, abnormal vision, joint pain, fast heart beat, shakiness, decreased sensation, increased energy, dry mouth, fatigue, injury, coughing, acne, itching, muscle pain, generalized pain, weight increase, high blood pressure, low blood pressure, adverse changes in blood lipids (cholesterol, triglycerides). Children with borderline abnormal blood lipid levels (cholesterol, triglycerides) prior to treatment with risperidone may develop abnormal levels while taking this medication .

Rare

Abilify/aripiprazole: pain or tightness (including throat, abdominal, chest, pelvis, extremity, back pain, joint, muscle, jaw, neck or tongue), diarrhea, dry mouth, low appetite, behavioral & emotional changes including psychosis, infection, rash, menstrual periods changes, Neuroleptic Malignant Syndrome (fever, stiffness or involuntary movements, unstable blood pressure), fever, tiredness, migraine, chills, sensitivity to light, bloating, enlarged abdomen, head heaviness, aspiration or food or stomach reflux, heat stroke, enlarged heart, heart attack, heart failure, fast or slow heart beat and/or changes in heart rhythm, pounding heart beat felt by patient, low blood pressure, bleeding, blood clots, pale skin, sudden drop in blood pressure (e.g. when going from sitting or lying down to a standing position), inflamed blood vessels, heart-lung failure, increased appetite, difficulty swallowing, tooth /gums infection or cavities, stomach or intestinal bleeding,

rectal bleeding or hemorrhoids, stomach or intestinal gas, esophagus, intestinal or stomach inflammation or bleeding, inflamed gall bladder or gall-stones, ulcers, severe constipation or obstruction, hepatitis, blood in stool, enlarged liver, inflamed pancreas, thyroid changes, bruising of skin, changes in blood tests (various types of anemias or changes in white blood cells), weight loss, changes in metabolic blood tests (sodium, potassium, creatinine, bilirubin, albumin, alkaline phosphatase BUN, SGPT, SGOT, uric acid lactic acid), dehydration, edema, high or low blood sugar, high cholesterol, diabetes mellitus, high triglycerides, thirst, pale or bluish skin, gout, muscle paralysis, muscle tone abnormality, weakness or spasm, bursitis, inflamed tendons, abnormal dream, emotional ups and downs, twitch, rigidity, impaired concentration, dilated blood vessels and arteries, numbness, extremity tremor, hypersensitive skin, dizziness, slowed movement or response, lack of interest, panic attack, unsteady gait, visual hallucination, stroke, impaired memory, hyperactivity, slowed reflexes, restless leg, pain or numbness in nerves, increased reflexes, loss of voluntary movement, slowed thinking, blunted affect, extreme happiness, inability to rotate eyes, obsessive thought, decreased muscle tone or reflexes, bleeding in brain, sinus infection, difficult breathing or shortness of breath, pneumonia, asthma, bloody nose, hiccup, temporary voice loss from inflammation, aspiration pneumonia, decreased oxygen to lungs, respiratory failure, dry nasal passages, bloody sputum, skin ulcer, sweating dry skin, acne, skin discoloration, hair loss, dandruff, dermatitis, eye infection, ear pain, dry eye, eye pain, ringing in ears, cataract, ear infection, altered taste, inflammation of eyelid, eye bleeding, deafness, double vision, frequent blinking, lazy eye, poor vision in one eye, fear of light, bed wetting, difficulty or abnormal conditions of urination, vaginal bleeding, kidney failure, enlarged breasts, kidney stones, breast pain, female lactation, pain or tenderness in penis, severe allergic reaction (difficulty breathing, swelling and/or rash), diabetes mellitus, somnolence prolonged drowsiness or sleepiness, extrapyramidal movements (such as muscle rigidity, difficulty walking), orthostatic hypotension, tremor, fatigue, akathisia (muscle restlessness, blurred vision), producing more than the usual amount of salivary hypersecretion, increased risk of suicidal thoughts, potential for cognitive and motor impairment, difficulty with body temperature regulation, and dysphagia (difficulty swallowing), dizziness, and leucopenia, neutropenia, and/or agranulocytosis (abnormalities in your white blood cell count), especially in people with a history of a significant low white blood cell count. Seizure activity is a very rare risk with uncertain relationship to this medication.

Zyprexa/olanzapine: abdomen enlarged, chills, face edema, intentional injury, tiredness, infection, neck pain, pelvic pain, sensitivity to light, fever, hangover effect, cardiac (heart beat) changes, stroke, congestive heart failure, heart attack, hemorrhage, migraine, pallor changes in blood vessels and arteries, inflammation, blood clots, difficulty swallowing, inflammation of the esophagus, severe constipation, fecal incontinence, stomach pain or discomfort, inflamed gums, hepatitis, blood in stool, mouth ulceration, tooth abscess or caries, stomach gas, esophageal or stomach ulcer, intestinal obstruction, liver changes, high blood sugar, diabetes mellitus, diabetic acidosis, ketosis or coma, goiter, changes blood count, pale or bluish skin cast, acidosis, alkaline phosphatase blood test increased, bilirubinemia, dehydration, high cholesterol, high triglycerides, gout, high sodium, potassium, bilirubin, uric acid and/or protein in the blood, water intoxication, leg cramps, abnormal changes in muscle tissue, brittle bones, voluntary and involuntary movement disorders, antisocial behavior, ataxia, central nervous system stimulation, rigidity, delirium, dementia, speech and language disturbance, less sensitive or reactive to stimulation, slowed movement, loss of muscle tone or coordination, obsessive compulsive symptoms, extreme unfounded fears, physical symptoms of anxiety, alcohol, drug or tobacco misuse, stuttering, withdrawal syndrome, coma, any disorder of the brain, nerve pain or numbness, eyelid twitching, paralysis, bleeding in the brain, periods of difficult, decreased or absent breathing, asthma, nose bleed, blood in sputum, sweating, hair loss, dry skin, dandruff, skin discoloration,

skin ulcer, increased hair growth, difficulty adjusting to a situation or experience, cataract, deafness, double vision, dry eyes, ear pain, eye hemorrhage, various eye disorders breast pain, difficult or painful urination, female lactation, changes in urine or the process of urination, uterine fibroids enlarged, extreme vaginal bleeding, breast enlargement or inflammation, allergic reaction (can be severe with difficulty breathing, swelling, and/or rash), inflamed pancreas, pain & tenderness of penis, severe skeletal muscle disease potentially causing death, and blood clotting events. Seizure activity is a very rare risk with uncertain relationship to this medication.

□Risperdal/risperidone : increased dream activity, nervousness, trouble concentrating, depression, lack of interest, catatonic reaction, extreme happiness, increased libido, trouble remembering, sudden mood changes, nightmares, confusion, yawning, longer sleeping time, speech problems, spinning sensation, excess sedation, numbness or tingling, allergic reaction, leg cramps, stiff neck, coma, migraine, reflex changes, loss of appetite, reduced salivation, intestinal gas, diarrhea, increased appetite, swelling, flu-like symptoms, enlarged abdomen, skin irritations, fast breathing, pneumonia, asthma, trouble breathing, skin reaction to sunlight, increased sweating, acne, decreased sweating, hair loss, blocked veins or arteries in the heart, heart attack, eye pain, itchy eyes, low blood sodium or potassium or protein levels, blood chemical changes, increased thirst, weight decrease, diabetes mellitus (high blood sugar), anemia (low iron), dehydration, hyperphosphatemia (high phosphate levels in the body), hypertriglyceridemia (high triglycerides in the blood), hyperuricemia (high uric acid in the body), hypoglycemia (low blood sugar), increased urination/increased thirst, bed-wetting, hematuria (blood in urine), problems urinating, problems with the kidneys, joint pain, arthritis, missed menstrual periods, breast pain, bleeding, liver failure, hepatitis (liver inflammation), decreased blood clotting , blood clots, ringing in the ears, decreased hearing, ear problems, hormones problems, high prolactin levels in the blood, problems regulating body temperature, bitter taste, a change in the time it takes for the heart to conduct normal electrical signals (QTc prolongation) has also been associated with olanzapine use. Neuroleptic Malignant Syndrome (fever, stiffness or involuntary movements, unstable blood pressure). Seizure activity is a very rare risk with uncertain relationship to this medication.

It is important to note that these side effects do not occur in everyone. We expect that you, your child, and your child's doctor will be going over the side effects that you might watch for while taking any of these medications. The possibility of a suicide attempt is inherent in some psychiatric disorders, and close supervision of high-risk persons should accompany drug therapy.

Participants will be followed closely and monitored for side effects of medications and tests. Withdrawal of the study medication and/or treatment of medication side effects will be provided as indicated. Participants will participate in medication check-ups or telephone calls at least once per week and will be asked to report any concerns or adverse events during these times. To be sure that you/your child can always communicate with the research team, families will be provided with a 24-hour telephone number of a research clinician who will answer any questions and speak with any community physicians or dentists who the participants visit during the study. All families will also be instructed to tell any doctors or dentists they encounter that their children/adolescents are on the study medications.

The risk of your child's side effects will be minimized, or reduced should they occur, through the following steps:

1. Sometimes Abilify (aripiprazole), Zyprexa,(olanzapine) or Risperdal (risperidone) can cause

nausea or vomiting. To prevent the nausea, it is best for your child to have something to eat in the morning before the a.m. dose.

2. Participants will be monitored for neuromuscular side effects at each weekly visit. Neuromuscular side effects include developing a walking style that seems to be shuffling along rather than lifting one's legs, stiffness in the movements of wrist and elbow joints, shaking of the hands when the hands are not busy and a loss of facial expression. Also, children/adolescents may also develop a problem that looks as if they are restless (called akathisia). These side effects can sometimes be reduced by lowering the dose of medication or adding an appropriate medication to treat the side effect. Participants will also be monitored for tardive dyskinesia (unusual movements of the mouth area, cheek, tongue or other parts of the body such as the shoulders and extremities). Study medications will be discontinued if tardive dyskinesia occurs.

3. Participants will be regularly monitored for changes in blood triglycerides or blood glucose. Problems with the way the body handles glucose (sugar) and lipids (triglycerides) can occur with Abilify, (aripiprazole), Zyprexa (olanzapine), or Risperdal (risperidone) potentially resulting in diabetes or a condition called the metabolic syndrome. These blood glucose and lipid problems can occur without any symptoms. That is why blood glucose and lipids are monitored in this study. If your child's fasting blood glucose becomes elevated at any point in the study to the level that is called diabetes, he/she will be withdrawn from the study. If his/her blood triglycerides become elevated to a serious degree that can increase the risk of an inflamed pancreas, then he/she will be withdrawn from the study. If your child's blood glucose or lipids become elevated during the study below the levels noted above, we will increase the frequency with which his/her blood is monitored for any further changes.

4. If your child's body weight increases 10% or more from when he/she first began taking the study medication, he/she will be monitored on a weekly or biweekly basis for other events that may occur in the setting of weight gain, especially hyperglycemia and hyperlipidemia.

During this study, your child/adolescent must avoid over-the-counter drugs and herbal supplements as these may interfere with treatment results.

As with any research procedure, unforeseen problems or side effects can occur.

Participation in this study may cause all, some or none of the side effects listed above which, if severe, may cause death.

You will be told of any changes in the way the study will be done and of any newly identified risks to which you may be exposed.

Data and Safety Monitoring Committee

An independent group of medical and research professionals, called a Data and Safety Monitoring Committee (DSMC), has been established to monitor the data collected from this study and look for ways to continually improve the safety of all the procedures and medications administered as part of this project. The PI and study staff are responsible for sending regular reports to the DSMC detailing our findings, particularly highlighting any adverse or serious adverse events that occur. Having a DSMC makes sure that someone outside of the project knows about any problems and can provide an objective opinion about what needs to be done to fix or minimize them. It is the job of the DSMC to maintain the highest level of safety for our participants.

Study Discontinuation
When your child discontinues the study early due to an adverse event, or on schedule due to study completion, we will carefully work with him/her and their treating psychiatrist/physician to evaluate the risks versus the benefits of ongoing treatment with the medication your child was assigned to. At that time we can discuss the advantages and disadvantages of staying on that medication, switching to a different antipsychotic medication, or discontinuing antipsychotic medication. In all cases we will provide individualized consultation with parents and treating psychiatrist and/or pediatricians to provide the safest plan to continue the ongoing individualized therapy.

Breast Feeding
Your child must tell the study doctor if you are breast-feeding.

Certificate of Confidentiality
One potential risk of participating in this study is that confidential information about your child may be accidentally disclosed. We will use our best efforts to keep the information about him/her secure, and we think the risk of accidental disclosure is very small. Please see the *Confidentiality* (Item 7) section of this consent form for more information.

Coded Data
The information you and your child give us will be given a code number that includes your child's initials. A master list linking the code number and your identity will be kept separate from the research data. Only the PI and people helping him/her will be able to see the list. We will protect your child's information, but there is a chance somebody might see it.

You may experience all or some of the risks listed above. There may also be unknown risks. The PI will answer any questions you have about these risks.

Pregnancy/Childbearing Potential

If you are a woman of childbearing potential, please read and sign below.

Some parts of this study might cause physical or mental problems in an unborn baby. Your child must tell the doctor immediately if there is any chance she is pregnant. She must also tell the doctor if her birth control method fails while she is in the study.

To take part in this study, your child must have a pregnancy test before starting the study. She must use an acceptable method of birth control and must not become pregnant.

Please discuss with your child's research physician how long your child needs to wait before becoming pregnant.

By signing below, you agree to have your child follow these rules.

_____
Signature Date

What happens if you are injured because you took part in this study?
Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator

(John Newcomer MD at 314/262-5939) and/or the Human Research Protection Office at (314) 633-7400 or 1-(800)-438-0445.

Decisions about payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

5. Are there benefits to taking part in the study? These medicines may improve your child's symptoms of aggressive behavior or conduct disorder. In addition, your child will be checked for serious medical conditions that may not show any symptoms, such as high blood pressure or diabetes. Finding these conditions may improve your child's medical care. This study will help doctors to understand how antipsychotic medications may affect diabetes risk and ways to address the risk of diabetes in children with conduct disorder, aggression or other behavior problems.

6. What other options are there? Taking part in this research study is voluntary. Your child may choose not to take part in this research study or he/she may withdraw consent at any time. Your child may withdraw by telling the study team he/she is no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at http://hrpo.wustl.edu under Information for Research Participants. Your child's choice will not at any time affect the commitment of your health care providers to administer care. There will be no penalty or loss of benefits to which you are otherwise entitled.

Other than not taking part in the research, your child may choose to have your doctor write a prescription for him/her if he/she feels it is in your best interest to receive this drug outside of the study. The study drugs, olanzapine, risperidone and aripiprazole are available to your child even if he/she does not participate in this study. Please discuss all alternatives with your child's doctor, including psychotherapy and behavior management.

7. What about privacy and confidentiality?
We will do everything we can to protect your privacy.

Providing your and/or your child's social security numbers is optional and you can fully participate in the study whether you disclose them or not. If you choose to provide your and/or your child's social security numbers, we will use them to locate you in the future if we are unable to locate you at your home address, and to search vital records. We will not share your and/or your child's social security numbers or leave them accessible to identity theft.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you and your child must give the research team permission to use and disclose (share) your child's PHI for the study explained in this consent form.

In addition to health information that may be created by the study, the research team may access the following sources of your child's health information to conduct the study: hospital/physician medical records; lab, pathology and/or radiology results; information derived from biological samples (including blood); interviews/questionnaires; mental health and substance abuse records;

physiologic imaging.

A Certificate of Confidentiality has been obtained from the Department of Health and Human Services. This will help further protect information that may identify your child. The Certificate prevents the investigator from being forced to disclose identifying information for use in court. The investigator may not even be forced by court subpoena. Courts that may be prevented from getting your child's information include any federal, state, local civil, criminal, administrative, legislative, or other court proceeding.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. The investigator may not withhold information if you or your child give your insurer or employer permission to receive information about your participation in this research. This means that you and your family must also actively protect your own privacy.

The Certificate does not prevent the researchers from taking steps, including reporting to authorities, to prevent serious harm to yourself or others. Such disclosures will be made as described below.

The research team may share your information with:

- The Department of Health and Human Services (DHHS) to complete federal responsibilities for audit or evaluation of this study.
- Public health agencies to complete public health reporting requirements
- Hospital or University representatives, to complete Hospital or University responsibilities for oversight of this study.
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Appropriate authorities to the extent necessary to prevent serious harm to yourself or others.
- Because the research takes place at the Pediatric Clinical Research Unit (PCRU) and the Clinical Research Unit (CRU), the Medical officer or the research Subject Advocate on the PCRU and CRU may review your medical record.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

This study is sponsored by National Institute of Mental Health (NIMH). Representatives of the sponsor will have access to your child's research and/or medical records for monitoring the study. The research team will also send study results to the sponsor. Information sent to the sponsor will be summarized and coded so that it cannot be associated with your child's PHI. The sponsor is not required to abide by the HIPAA regulations, but agrees to protect the confidentiality of your child's information. The sponsor reviews the study

summary to verify that the research is progressing toward stated goals.

You/your child will always have access to his/her medical record. Some of the individual results from tests to be performed during this research study might be of interest to your child or your primary care physician. At your request, the researchers will share the medical information gained from this study with you and your referring and/or primary care doctors. If we become aware of any important health information during the course of your participation in this study, we may be obligated/required to share this information with your treatment team. You will not have access to your child's research record.

If you decide not to sign this form, it will not affect
your child's treatment or the care given by your health provider.
your child's insurance payment or enrollment in any health plans.
any benefits to which your child is entitled.
However, it will not be possible for your child to take part in the study.

If you sign this form:

- You authorize the use of your child's PHI for this research
  - Your signature and this form will not expire as long as your child wishes to participate.
  - Your child may later change your mind and not let the research team use or share your child's information (your child may revoke your authorization).

  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at http://hrpo.wustl.edu (or use the direct link: http://hrpohome.wustl.edu/participants/WithdrawalTemplate.rtf) or you may request that the Investigator send you a copy of the letter.

  - **If your child revokes your authorization:**
    - The research team may only use and share information already collected for the study.
    - Your child's information may still be used and shared if necessary for safety reasons.
    - Your child will not be allowed to continue to participate in the study.

Please specify any contact restrictions you want to request for this study only.
(Example – no calls at home, no messages left for you, no e-mails, etc.)

_____

_____

Notice of Privacy Practices –
The Notice of Privacy Practices is a separate document. It describes the procedures used by WU to protect your child's information. If you/your child have not already received the Notice of Privacy Practices, the research team will make one available to you and your child.

_____ I have been offered a copy of the Notice of Privacy Practices.
Initial

8. Whom do I call if I have questions or problems?
Please contact the researcher listed below to:

- Obtain more information about the study
  - Ask a question about the study procedures or treatments
  - Report an illness, injury, or other problem (you may also need to tell your regular doctors)
  - Leave the study before it is finished
  - Express a concern about the study

Principal Investigator: John Newcomer MD at 314/362-5939
Research Coordinators: Martha Hessler at 314/362-2423 or Julie Schweiger at 314/362-3153
Mailing Address: 660 S. Euclid Ave., Campus Box 8134; St. Louis, MO 63110

If you wish to talk to someone else, or have questions or concerns about your child's rights as a research participant, call Washington University's Human Research Protection Office (WU HRPO) at (314) 633-7400, or 1-(800)-438-0445. For questions about the Clinical Research Unit (CRU) or Pediatric Clinical Research Unit (PCRU) please call Michelle Jenkerson, Research Participant Advocate at (314) 362-5626.

Request Permission for Future Contact

May we contact you for future undetermined studies conducted by Dr. Newcomer, Haupt, and Nicol?□If yes, we will need to look at your Protected Health Information (PHI) to check for study eligibility.	___ Yes	___ No
May other WU physicians conducting research contact you? If yes, your PHI will be shared with other WU physicians.	___ Yes	___ No

Taking part in future studies is optional. Your child can ask us at any time to take him/her off our contact list.

9. The Principal Investigator (PI) may withdraw your child from the study without your/his/her consent if considered appropriate (i.e. certain medical conditions, use of illegal drugs). It may be in your child's best interest to allow follow-up outside the study. The PI will share any new information that could change how you and your child feel about continuing in the study.

10. You will be given a signed copy of this consent form for your records. If your ability to consent for yourself changes, you or your legal representative may be asked to re-consent prior to your continued participation in this study.

Please mark all that apply. This section is optional.
[] Not Hispanic or Latino [] Hispanic or Latino [] Unknown
[] Asian [] Black or African-American [] Caucasian [] Native American or Alaskan Native
[] Native Hawaiian or Pacific Islander
[] Other [] Unknown
The Office of Management and Budget has declared that Hispanic/Latino is an ethnicity. National Institutes of Health, in an effort to ensure diversity in research, requests that you report your ethnicity. (http://grants.nih.gov/grants/funding/women_min/women_min.htm)

CONSENT FOR MINOR PARTICIPANTS

Parent or Legal Guardian: (If participant is less than 18 years of age.)
I have read this consent form and have been given the chance to ask questions. I give permission for my child to participate in this research described above, titled: **Metabolic Effects of Antipsychotics in Children (Treatment Study, 6-17 y.o.)**

HRPO does not require participants to re-sign the consent form unless a change is made; the investigator, however, may choose to re-consent participants at any time.

Signature: _____

Printed Name: _____ Date of Signature: _____

Relationship to Child:
☐ Father ☐ Mother ☐ Grandmother ☐ Grandfather ☐ Legal Guardian ☐ Other*: _____

***If the minor participant is in foster care or a ward of the State, please contact HRPO at 633-7400 for assistance.**

Signature of Second Parent or Legal Guardian: [OPTIONAL]

Signature: _____

Printed Name: _____ Date of Signature: _____

Relationship to Child:

☐Father ☐Mother ☐Grandmother ☐Grandfather ☐Legal Guardian ☐Other: _____

If Parent/Legal Guardian is also a Research Participant:
I have read this consent form and have been given the chance to ask questions. I agree to participate in this research described above, titled: **Metabolic Effects of Antipsychotics in Children (Treatment Study, 6-17 y.o.)**

HRPO does not require participants to re-sign the consent form unless a change is made; the investigator, however, may choose to re-consent participants at any time.

Signature: _____

Printed Name: _____ Date of Signature: _____

Principal Investigator (or Designee):

I have given this research participant (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The participant has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Signature: _____ Title: _____

Printed Name: _____ Date of Signature: _____

DOCUMENTATION OF ASSENT (FOR PARTICIPANTS WHO ARE MINORS)

Participant's Assent:

The doctor or nurse has told me what will happen if I choose to be in this study. I understand what they have said, and I understand that my parents and I may later change our minds and stop being in the study.

Signature: _____

Printed Name: _____ Date of Signature: _____

ASSENT CONSIDERED INAPPROPRIATE (for minors)

We believe that requiring the signature of the minor is not appropriate for the following reason(s):

_____

_____

_____ _____

Physician Date Parent/Guardian Date

This form is valid only with the Human Research Protection Office's current stamp of approval.

WASHINGTON UNIVERSITY MEDICAL CENTER HSC
Protocol Approved SEP 30 2010
Approval Terminates SEP 29 2011
Federal regulations permit no grace period
Revision(s) *Only* Approved OCT 18 2010