Study Consent

Official title: A Pilot/Feasibility Study of the Use of High Dose Propranolol to Treat Severe and Chronic Challenging Behaviors in Adolescents and Adults with Autism Spectrum Disorders

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RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

PARENTAL/LEGAL GUARDIAN PERMISSION TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: A Pilot/Feasibility Study of the Use of High Dose Propranolol to Treat Severe and Chronic Challenging Behaviors in Adolescents and Adults with Autism Spectrum Disorders

Principal Investigator (PI): Barbie Zimmerman-Bier, M.D.

STUDY SUMMARY: This consent form is part of an informed consent process for a research study and it will provide information that will help you decide whether you want your child/dependent to take part in this study. It is your choice for him/her to take part or not. The purpose of the research is to examine whether a medication that helps with high blood pressure (propranolol) can also help adolescents/ young adults with autism who engage in very severe and challenging behaviors. In order to be certain that propranolol is responsible for improving behavior, we will need to compare your child's/dependents behavior on placebo (sugar pill or liquid) to your child's behavior on Propranolol. Both you and the study doctor will not know whether your child/dependent was taking Propranolol first or Placebo first. This is called the Double Blind Placebo Controlled portion of the study. In the last phase of the study (OPEN LABEL) you and the study doctor will learn whether your child/dependent was taking Propranolol or Placebo first, and determine if propranolol should be continued.

If your child/dependent takes part in the research, the study doctors will do tests to see if your child/dependent is suitable for this study. The screening tests include: medical history including current home medications, vital signs (pulse, temperature, and blood pressure), physical examination (including weight and height), psychiatric and behavioral evaluation, and a complete cardiac/heart evaluation (including 24-hour electrocardiogram which records electrical activity of the heart). A pregnancy test will be completed by female participants. If your child/dependent is suitable for the study and you sign consent, he/she will be enrolled in the study. YOUR CHILD WILL REMAIN ON ALL MEDICATIONS HE/SHE IS ON AT THE TIME OF ENROLLMENT.

If at any time your child's/dependent's cannot complete the double blind phases of the study, the STUDY BLIND will be broken and you will be informed whether your child/dependent was taking Propranolol or Placebo. You and the study doctor can then decide to have your child/dependent enter the Open Label portion of the study or leave the study and follow up with your treating physician. However, if you decide to leave the Open Label portion of the study, your treating physician may not follow the specific drug dosing schedule in the study.

Your child's/dependents time in the study will vary depending on how they respond to the study drug/placebo, but in general all four phases should take about 5-7 months. Your child/dependent will be required to have 4-5 office visits. In addition, there will be weekly telemedicine visits with the study doctor/psychiatrist to monitor your child's/dependents response to the study drug/placebo. You will complete 4 weekly questionnaires online via the optional loaned tablet or your personal cell phone/computer. In addition, you will be required to take your child's/dependents blood pressure.

Possible harms or burdens of taking part in the study may be side effects from the propranolol (may cause drowsiness, slower heart rate, diarrhea, dry eyes, hair loss, nausea, weakness or tiredness). Propranolol can interact with other medications your child may be taking. The possible benefits of taking part may be an improvement in your child's/dependent's behavior. For example, it is possible that your child/dependent may show less aggressive outbursts. It is also possible that you may notice some improvements in your child's/dependent's speech.

Your child/dependent does not have to take part in this research study. Instead of taking part in this research study, you may choose to have your child's/dependents standard behavior therapy (such as Applied Behavior Analysis) or other medications for challenging behaviors with your treating physician.

The information in this consent form will provide more details about the research study and what will be asked of your child/dependent if you permit him/her to take part in it. If you have any questions now or during the study, you should feel free to ask them and should expect to be given answers you completely understand. After all of your questions have been answered and you wish your child/dependent to take part in the research study, you will be asked to sign this permission form. You are not giving up any of your child/dependent's legal rights by permitting him/her to take part in this research or by signing this parental permission form.

Who is conducting this research study?
Dr. Barbie Zimmerman-Bier is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the research. However, there are often other individuals who are part of the research team, such as Dr. Eric London. Dr. London is a psychiatrist and will be the doctor for this study who will be doing weekly calls with each participant.

Dr. Zimmerman-Bier may be reached at

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The Principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

SPONSOR OF THE STUDY:
The New Jersey Governor's Council on Medical Research and Treatment of Autism is the sponsor of this research study. The study doctor is being paid to conduct this study according to a budget that will cover the costs of the study. The costs that are usually covered include things such as: physical examinations, study drugs, cardiology tests required by the study, and the costs of collecting all of the information required by the study.

Why is this study being done?
We are examining whether a medication that helps with high blood pressure (propranolol) can also help people with autism who engage in severe challenging behaviors.

Why has your child /dependent been asked to take part in this study?
Your child/dependent is being asked to take part in this study because he/she is diagnosed with autism and also engages in challenging behaviors. He/she also receives behavior intervention and has tried at least two different medications to treat his/her behavior including one antipsychotic medication that have not helped with these challenging behaviors.

Who may take part in this study?
1. Males and females
2. Between the ages of 12-30 years
3. Reside in the state of New Jersey
4. Diagnosis of autism
5. Engages in at least one of the following challenging behaviors:
    a. Self-injurious behavior (e.g., hitting oneself, head banging, or banging of other body parts causing some degree of tissue damage);
    b. Physical aggression towards others (e.g., hitting, kicking, pushing, or throwing objects at others);
    c. Disruptive behaviors including property destruction, excessive screaming which interferes with functioning; and
    d. The challenging behaviors are generally (but not necessarily exclusively) associated with a congruent affect (i.e., anger or rage when aggressing) as determined by the study psychiatrist.
6. At least two previous medications were tried without much success, including one antipsychotic medication. If your child has shown some (partial) improvement on one or more medications, he/she will be eligible for the study.
7. English speaking parent/legal guardian able to complete questionnaires
8. Medical and cardiac (heart) clearance.

Who may not take part?
1. People with asthma or any history of asthma or any disorder involving constriction of the airways in the lungs
2. Heart disease where propranolol is unsafe such as Wolff-Parkinson-White syndrome
3. Uncontrolled seizure disorder (has had a seizure in the last year or has had a change in seizure medication in the previous 6 months)
4. Diabetes or ketoacidosis (severe diabetes complication)
5. People with hyperactive thyroid (someone with an excess level of thyroid hormones)
6. People who have a significant coexisting psychiatric disorder, including: schizophrenia, mood disorder, psychotic disorders
7. Current alcohol or drug abuse
8. History of allergy to propranolol or problems with propranolol in the past.

9. Any other medical disorder or medication which would render the use of propranolol unsafe
10. Pregnant females

How long will the study take and how many subjects will participate?
The duration of your child's/dependent's participation will vary depending on his/her response to the study drug but it will generally be between 5-7 months. We will recruit 24 participants in this study from the state of New Jersey. A total of 17 participants are needed to complete the entire study. The study will take about two years to be complete.

What will your child/dependent be asked to do if he/she takes part in this research study?
If you agree to volunteer your child/dependent for this study, after signing this informed consent, the study doctors will do tests to see if your child/dependent is suitable for this study. The screening tests include:

- Medical history including current home medications
- Vital signs (pulse, temperature, and blood pressure)
- Physical examination (including weight and height)
- Psychiatric and behavioral evaluation
- Cardiac/heart evaluation (including 24-hour electrocardiogram which records electrical activity of the heart).
- A pregnancy test will be completed by female participants.
- You will also be asked to fill out several questionnaires at each visit.

Sometimes we do not know which way of treating people is best. To find out, we randomly put people into different treatment groups. The results are then compared to see if one treatment is better. There are two treatment groups in this study.

Your child/dependent has a 1 out of 2 chance (or 50% chance) of receiving Propranolol first, and a 1 out of 2 chance (or 50% chance) of receiving placebo first.

What is a Placebo?

- Placebo is like a "sugar" pill / liquid. It does not contain any active drug.
- Even though placebo dosage will be increased, it will <u>not</u> contain any active drug.
- Propranolol and placebo will look identical.
- Only the research pharmacy will know whether your child/dependent is receiving propranolol or placebo.

How is Propranolol taken?

- Propranolol and placebo will be available in liquid format as well as capsule.

- The standard study drug dosing will be:
  DOSE 1: 10 mg (three times per day) (PHASE A) or matching placebo (PHASE B)
  DOSE 2: 40 mg (three times per day) (PHASE A) or matching placebo (PHASE B)
  DOSE 3: 80 mg (three times per day) (PHASE A) or matching placebo (PHASE B)
  DOSE 4: 120 mg (three times per day) (PHASE A) or matching placebo (PHASE B)
  DOSE 5: 160 mg (three times per day) (PHASE A) or matching placebo (PHASE B)
  DOSE 6: 200 mg (three times per day) (PHASE A) or matching placebo (PHASE B)

<u>STUDY SCHEDULE</u>

1. **PLEASE NOTE THAT THE PARTICIPANT WILL REMAIN ON THEIR SAME REGIMEN OF HOME MEDICATIONS THROUGHOUT THIS STUDY. THESE**

MEDICATIONS WILL CONTINUE TO BE PRESCRIBED BY CHILD'S/DEPENDENT'S PHYSICAN.

2. **You will use a secure** interactive two-way audio-video communication via internet **for visits with the psychiatrist. These are called telemedicine visits. Please allow for at least 30 minutes for telemedicine visits.**

3. **What happens if your child/dependent is experiencing difficulty with study?** - if at any time you feel that your child/dependent is having difficulty completing study you can ask to have the blind broken with consultation of the study physician. You will be informed if your child/dependent was taking placebo or propranolol. If choose to enter the open label portion of the study you will continue to follow weekly with the study doctor. If you choose to leave the study, your child/dependent will need to be titrated off of the propranolol over a one to two-week period. However, if your child/dependent was taking placebo no titration will be needed.

Study Drug Titration and Maintenance (Phase A and Phase B) see below[1] * continue on same home medication regimen

- The titration schedule is <u>not set</u>. The reasons for the flexibility of the dosing schedule are for the safety of your child/dependent.
- The decision to increase the dose of the study drug will be made each week with you (participant's family/guardian) and the study doctor (psychiatrist). The decision to raise the study drug dosage will depend on the improvement in behavior and tolerability of the study drug.
- The dose will be titrated upwards (increased) until adequate outcome is obtained (as decided by you and the study doctor or up to 600 mg per day (note: propranolol is FDA-approved up to a dose of 640 mg).
- You will be given a portable heart rate and blood pressure device, and you will receive training and instructions on how to use this device.
- You will collect blood pressure and heart rate for the first 3 days of a dose change (take at same time each night) or for significant side effects.
- If the dose is held steady for 6 weeks (or dose 6 is reached), that will be considered the maintenance or optimal dose.
- **The titration and maintenance phase can last up to 12weeks for each phase of the study**
- **Dosing Delays or Reduction**
    - Scheduled study drug dose increases could be delayed because mild side effects (i.e., some nausea, tiredness, or difficulty adjusting to medication or parent preference) or because of marked improvement at a lower dose.
    - Dose reductions to manage side effects are allowed at any time.
    - Study drug will be held steady for blood pressure < (less than) 90/50 mm HG or heart rate < (less than)50 beats per minute taken at same time each night or for significant side effects.

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CROSSOVER* continue on same home medication regimen

1. **Washout**

- During drug washout, study drug dosage/placebo will be tapered over a 2-week period until your child is off of the study drug/placebo.
- The downward titration schedule (decreasing dosage of study drug) can be slower, depending on your child's clinical presentation

2. **Titration and Maintenance see above[1]* continue on same home medication regimen**

- Your child will switch from [Phase A to Phase B] or [Phase B to Phase A] (switching to either placebo or propranolol depending on the initial group assignment. The procedures will be repeated.

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End of Both Phases* **continue on same home medication regimen**

- The blind will be broken. You and the study doctor will find out which group your child was assigned.
- You and the study doctor will evaluate whether there was benefit for your child on propranolol, and if so, which dose was optimal.

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Open-Label Study* **continue on same home medication regimen**

- After completing the double-blind, crossover study, you and your child will be invited to participate in an open-label study. This means you and the study doctor will know exactly how much propranolol your child is taking.
- You will be offered the opportunity to again have your child/dependent titrated to the optimal dose for two months. The propranolol dose will be increased weekly until the optimal dose (up to 600 mg/day) is reached. This may allow for a possible repeat of the results seen in the clinical study; giving a longer period of time on the propranolol to examine if the benefits persist; and the benefit of having your child stay on propranolol after the study has ended.
- Since propranolol is available on the market, during the open-label trial, you can choose to have your child/dependent transition back to their treating physicians on a dose of propranolol which has been deemed optimal.
- Your child will be eligible for the open-label study whether or not he/she completes the crossover portion of the study.

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How often are the Study Visits?

Below are the visits that will occur every week during the study. The exact date and time of the visit will be decided upon with you and the study doctor. The length of time for each study visit will vary as follows

Visit 1: Pre enrollment-one hour
Visit 2: Screening- 1 ½ hours.
Visit 3 and Visit 4: Baseline- 30 minutes
Visits 5-15: Titration and Maintenance – 30 minutes via telemedicine
VISITS 12-27: Crossover- 30 minutes via telemedicine and 2 office visits for 30 minutes (as study drug is decreased).

Visit 1: Pre-Enrollment - WEEK 1

You will attend the pre-enrollment visit in person. During the pre-enrollment visit, the following procedures will be conducted:

- Consent to participate
- Medical and behavioral history and review of previous testing (clinical information)
- Review legal guardianship papers
- List of previous medication trials and current medications your child/dependent is taking.
- You will receive information on how to measure vital signs and to transmit the information to the study doctors

You will complete a questionnaire that will describe your child's /guardians behavior challenges:

- ❖ Aberrant Behavior Checklist—Community (ABC-C)

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Visit 2: Screening - WEEK 2

You will attend the screening visit in person with your child/dependent. During the screening visit the following procedures will be conducted:

- Physical examination
- Vital signs (blood pressure and pulse)
- Cardiac evaluation
- Holter monitoring (this device is used to measure and record your heart's activity (ECG) continuously for up to 24 hours, you will take one home with you)
- Pregnancy test for female participants
- You will again receive training on how to measure vital signs and transmit the information to the study doctors.

In addition, your child /dependent may need to complete the following tests:

- A standardized cognitive and behavioral test known as the Autism Diagnostic Observation Schedule (ADOS-2) if not previously available or SCQ (social communication questionnaire)
- A standardized Cognitive Evaluation assessment to measure the participant's mental ability (if unavailable from the past 3 years)

You will complete the following questionnaire that will describe your child's/guardians self-care skills:

- ❖ Vineland Adaptive Behavior Scale—III (VABS-3)

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Visit 3 and 4: Baseline WEEK 3 and WEEK 4 - Your child /dependent will remain in baseline for 2 weeks. Your child/dependent will be randomly assigned into one of the two groups (PHASE A or PHASE B).

You will visit the study doctor in person with your child during week 3. During this visit, the following tests and evaluations will be conducted. Starting with this visit, you will begin taking vital signs and transmit the information to the study doctors daily.

- Review study entry requirements to ensure that your child is eligible to continue
- Vital signs (blood pressure and pulse)
- Cardiac evaluation /24-hour Holter monitor results
- Training on how to administer the study drug
- The study doctor and the research assistant will train you to use the HIPAA-compliant telemedicine platform. Telemedicine uses live, interactive two-way audio-video communication via internet. You will also have the option of using either the tablet on loan from the study or your personal smart phone. At the scheduled time, you will "log-on" to the telemedicine platform and the study psychiatrist will "call" you. At the end of the telemedicine visit, you will log-out from the telemedicine platform.

During week 4 you will visit the study doctor via telemedicine.
During week 4 your child/dependent randomly assigned into one of the two groups (PHASE A or PHASE B).

You will complete the following questionnaires for WEEK 3 and WEEK 4 to record any your child's/guardians behavior and health at the start of the study:

- ❖ Aberrant Behavior Checklist—Community (ABC-C)

- ❖ IBR Modified Overt Aggression Scale (MOAS)
- ❖ Side Effects Survey

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Visits 5-15: TITRATION AND MAINTENANCE: will last from 6-12 weeks
WEEK 5 – WEEKS 11 to 15. * **continue on same home medication regimen**

- Your child/dependent will be assigned to Phase A (study drug) or Phase B (placebo).
- You will visit the study doctor via telemedicine weekly.
- Your child/dependent will be given the study medication at the same or increased dosage to take as directed by the study doctor.
- You will continue to take vital signs and transmit the information to the study doctors daily for days 1-3 of a new dose. A Holter monitor (up to 24 hours) will be completed at dose level 3.

You will complete the following questionnaires each week to record any changes in your child's/guardians behavior and health :

- ❖ Aberrant Behavior Checklist—Community (ABC-C)
- ❖ IBR Modified Overt Aggression Scale (MOAS)
- ❖ Side Effects Survey

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VISITS 12-27: CROSSOVER – will last between 6-15 weeks -(WEEK 12 - WEEK 18-27). * **continue on same home medication regimen**

Washout-

1. You will decrease the study drug every 3 days until your child/dependent is off all study drug You will contact the RA or study doctor if your child /dependent experiences headaches / increase in behavior problems / difficulty with decreasing dose (see STUDY CONTACT INFO SHEET)
2. You will continue to take vital signs and transmit the information to the study doctors daily.
3. You and your child/dependent will visit the study doctor in-person each week because your child's heart needs to be checked. The following assessments will be performed
   - Vital signs (blood pressure and pulse) and auscultation (the study doctor will listen to the child/adults heart).
4. You will complete questionnaire each week to monitor your child's/guardians health
   - ❖ :Side Effects Survey

Titration and Maintenance

1. Your child/dependent will switch from Phase A to Phase B or from Phase B to Phase A.
2. You will visit the study doctor via telemedicine weekly.
3. Your child/dependent will be given the study medication at the same or increased dosage to take as directed by the study doctor.
4. You will continue to take vital signs and transmit the information to the study doctors daily for days 1-3 of a new dose.
5. A 24-hour Holter monitor will be completed if your child/dependent
   a. reaches dose level 3 dose
   b. reaches dose level 6 or maintenance dose (six weeks at same dose).

You will complete the following questionnaires each week to record any changes in your child's/guardians behavior and health:

- ❖ Aberrant Behavior Checklist—Community (ABC-C)
- ❖ IBR Modified Overt Aggression Scale (MOAS)
- ❖ Side Effects Survey

BREAK BLIND * continue on same home medication regimen

- You will find out if your child just completed the placebo or medication phase.

Visits 19-35: OPEN LABEL WEEK 19 - WEEKS 27-35 (8-week open label) * continue on same home medication regimen

1. You will visit the study doctor via telemedicine weekly.
2. Your child will be given the study medication to take as directed by the study doctor.
3. You will continue to take vital signs (blood pressure and pulse) for days 1-3 of each dose change and transmit the information to the study doctor. The open-label phase will last 8 weeks.
4. For those participants who enter Open Label without completing Phase A and B
   a. A 24-hour Holter monitor will be completed if your child/dependent
   b. reaches dose level 3 dose
   c. reaches dose level 6 or maintenance dose (six weeks at same dose).

You will also complete the following questionnaires **to record any changes in your child's/guardians behavior and health:**

- ❖ Aberrant Behavior Checklist—Community (ABC-C)
- ❖ IBR Modified Overt Aggression Scale (MOAS)
- ❖ Side Effects Survey

What are the risks and/or discomforts your child might experience if he/she takes part in this study?

Propranolol may cause some side effects that are usually mild and go away in a few days or couple of weeks.

While on the study, your child is at risk for the side effects described below. You should discuss these with the investigator and/or their doctor. There may also be other side effects that we cannot predict. Many side effects go away shortly after the drugs are stopped, but in some cases side effects can be serious or long-lasting or permanent.

Propranolol [pro-pran'-o-lol] is commonly used to decrease high blood pressure. This drug can cause problems for persons with depression, diabetes, thyroid disease, very slow heart rates, very low blood pressure, fluid in the lungs from heart failure, and asthma. The side effects related to this drug are given below. These symptoms are most present within 5 hours of the drug administration. None of these symptoms will be present once the single dose is washed out of the system, which can take up to 24 hours.

Based on Frequency of Occurrence:

Side Effect	Frequency	Severity
Bradycardia (abnormally slow heart action)	Common	Mild
Fatigue (extreme tiredness)	Common	Mild
Dizziness	Common	Mild
Hypotension (abnormally low blood pressure)	Common	Moderate

Light headedness	Occasional	Mild
Constipation	Uncommon	Mild
Paresthesia (abnormal sensation, typically tingling or pricking) of hands	Rare	Mild
Vivid dreams	Rare	Mild
Dry eyes	Rare	Mild
Urticaria (hives)	Rare	Mild
Diarrhea	Rare	Mild
Abdominal cramping	Rare	Mild
Nausea	Rare	Mild
Epigastric distress (Upper abdominal pain)	Rare	Mild
Impotence (inability to achieve or maintain an erection)	Rare	Mild
Nightmares	Rare	Mild
Depression	Rare	Moderate
Lassitude (lack of energy)	Rare	Moderate
Weakness	Rare	Moderate
Visual disturbances	Rare	Moderate
Hallucinations (experience of something that is not actually present)	Rare	Moderate
Disorientation (mental confusion about time, place or identity)	Rare	Moderate
Emotional lability (excessive emotional reactivity and frequent mood changes)	Rare	Moderate
Slightly clouded sensorium (inability to think clearly or concentrate)	Rare	Moderate
Decreased performance on neuropsychometrics (tests to assess psychological functioning)	Rare	Moderate
Peyronie's disease (scar tissue inside the penis causing curved, painful erections)	Rare	Moderate
Allergy	Rare	Serious
Catatonia (inability to move normally)	Rare	Serious
Intensification of AV block (Worsening of a type of heart block)	Rare	Serious
Arterial insufficiency (slowing or stopping of blood flow through arteries (blood vessels))	Rare	Serious
Alopecia (sudden hair loss with one or more circular patches)	Very rare	Mild
Exfoliative dermatitis (reddening and scaling of skin)	Very rare	Moderate
Psoriasisform rashes (plaque-like rashes)	Very rare	Moderate
Vomiting	Very rare	Moderate
Amnesia (partial or total loss of memory)	Very rare	Serious
Erythema multiforme (bulls-eye-shaped lesions on skin)	Very rare	Serious
SLE-like reaction (a disorder where the body mistakenly attacks healthy tissues in the body)	Very rare	Serious
Congestive heart failure (inefficient pumping of the heart)	Very Rare	Severe
Stevens Johnson Syndrome (disorder of skin and mucous membranes)	Extremely Rare	Serious
Agranulocytosis (deficiency of granulocytes in blood; increased vulnerability to infection)	Extremely rare	Serious

Nonthrombocytopenic purpura (spontaneous bruising without decrease in levels of blood cells that prevent bleeding)	Extremely rare	Serious
Thrombocytopenic purpura (low levels of blood cells that prevent bleeding)	Extremely rare	Serious
Toxic Epidermal Necrolysis (skin condition)	Extremely Rare	Life threatening
Mesenteric arterial thrombosis (injury of the small intestine due to lack of blood supply)	Extremely rare	Life threatening
Ischemic colitis (injury of the large intestine due to lack of blood supply)	Extremely rare	Life threatening

DO NOT STOP YOUR CHILD'S/DEPENDENT'S DRUG WITHOUT CONSULTING THE STUDY TEAM. Propranolol also needs to be lowered gradually before discontinuing, to avoid side effects such as high blood pressure and dizziness. You should not stop the study drug abruptly without informing the study coordinator and study doctor. The team will guide you on how to safely lower the drug dose.

Propranolol can interact with other medications your child/dependent may be taking. An interaction is when a substance changes the way a drug works. This can be harmful or prevent the drug from working well. To help avoid interactions, your study doctor will manage your child's medications carefully. You should also tell the study doctor about all medicines that other doctors may have prescribed for your child /dependent to take. Your child should not take any over-the-counter medicines, herbal products, vitamins, alcoholic beverages, or food supplements while taking part in this study, unless you, the parent/guardian tell the study doctor and get permission from the study doctor for your child/dependent to continue taking them. Your child should follow the instructions of the study doctor about the use of any of these products. YOU MUST NOTIFIY THE STUDY COORDINATOR IMMEDIATELY IF THERE ARE ANY CHANGES TO YOUR CHILD'S/ DEPENDENTS HOME MEDICATION REGIMEN.

Reproductive Risks of Harm

Propranolol is a "category C" pregnancy drug. That means research in animals has shown adverse effects to the fetus when the mother takes the drug. There haven't been enough studies done in humans to be certain how the drug might affect the fetus. The drug under study may cause birth defects in people. For this reason, no one can be in this study who is pregnant or who could get pregnant while taking the study drug. If your child/dependent is a woman of childbearing age and she is sexually active, she will be asked to use one of the following methods of contraception while taking the study drug

- hormonal contraceptives or intrauterine device
- and barrier (i.e. condoms, diaphragm or cervical cap).

If your daughter/dependent is unwilling to use adequate birth control measures, you should not volunteer your daughter/dependent for this study and you should not to sign this consent form. If your daughter becomes pregnant during the course of this study, you should notify the study doctor of this fact immediately since the risks to a fetus or your child are unknown.

Are there any benefits for your child if you choose to allow them to take part in this research study?

During your child's /dependent's participation in this study, the study doctor will follow him/her closely. It is expected that new information about propranolol, which may benefit your child/dependent or other people with similar conditions, will be obtained by this study.

It is possible that taking part in this study may improve your child's/dependent's behavior, and that this study may be helpful in developing a new therapy for others with similar challenging behaviors, although this cannot be guaranteed. For example, it is possible that your child/dependent may show less aggressive outbursts. It is also possible that you may notice some improvements in your child's/dependent's speech.

It is also possible that *no benefit* may result during or after this study. Your child's /dependents challenging behaviors may even *worsen* during this study.

What are your alternatives if you don't want your child to take part in this study?
Instead of taking part in this study, you may choose to receive standard behavior or medical intervention for challenging behaviors. The following alternative treatments are available if you choose not to allow your child/dependent to take part in this study:

- *Applied Behavior Analysis* (ABA): A method of identifying the reason for the challenging behavior is called *functional behavior assessment* (FBA). Based on the results of the FBA, a function-based intervention can be developed to decrease challenging behaviors.
- *Medical*: Abilify and Risperdal are the two FDA-approved medications for irritability (e.g., challenging behaviors) associated with autism. Other medications such as mood stabilizers and antianxiety medication may be used as well.

How will you know if new information is learned that may affect whether you are willing to allow your child to stay in this research study?
During the course of the study, you will be updated about any new information that may affect whether you want to continue allowing your child/dependent to take part in the study. If new information is learned that may affect your child/dependent completes the study, you will be contacted.

Will I receive the results of the research?
The results of the cardiac evaluation will be given to given to you. This includes:

- Physical Exam
- EKG (a recording of the heart's electrical activity)
- and Holter Monitoring (a portable device used to measure your hearts rhythm for up to 24 hours)

If we find something of urgent medical importance to your child/dependent, we will inform you, and then discuss the results with you and your child's/dependent's doctor. If we find something that makes your child/dependent not able to enroll in the study, we will discuss with you and/or your child's/dependents doctor.

Will there be any cost for my child/dependent to take part in this study?
The study drug and all procedures in the study will be provided at no charge to you. At the end of the 8-week day open-label phase of the study, the study drug (propranolol) will not be available to your child/dependent free-of-charge. However, you can discuss with the study doctor about a prescription of propranolol and may continue this treatment with your child's/dependent's physician. You can also continue the treatment your child/dependent was on before participating in this study or discuss with the primary care doctor about other alternatives.

Will my child/dependent be paid to take part in this study?
At the end of your child's /dependent's participation in the study, you will receive a total of [$50.00] to help you cover some of your expenses (e.g., travel, parking) for attending study visits.

How will information about your child/dependent be kept private or confidential?
There is minimal risk of loss of privacy. All efforts will be made to keep your and your child's/dependent's personal information in their research record confidential, but total confidentiality cannot be guaranteed. We will take the following precautions.

- Your child will be assigned a unique study number. A patient identification key that links your child's /dependent's study ID to his/her name, date of birth, address and other contact information

will be recorded in a password protected database on the study investigator's computer. Only the Investigators and study coordinator will have access to the patient identification key.

- All electronic storage of study-related documents and data will be stored in a separate secured, password protected database at Robert Wood Johnson Medical School. Your child/dependent will only be identified by the unique study number (e.g., A 111). Only the research team will have access to the study data. Photocopies of all applicable medical records will also be placed in securely stored study binders. All identifying information that can be linked to participants (e.g. name, date of birth etc) will be removed from the records and they will be stored in folders labeled with the research ID. This is done to protect your privacy.

A description of this clinical trial will be available on **https://clinicaltrials.gov**, as required by U.S. Law. This website will not include information that can identify your child/dependent. The website will include a summary of the results. You can search this website at any time.

What will happen to my child's information or biospecimens collected for this research after the study is over?

- After information that could identify your child has been removed, the information collected for this research may be used by or distributed to investigators for other research without obtaining additional informed consent from you.

What will happen if your child/dependent is injured during this study?

Participants in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, which are described throughout this consent form. In addition, it is possible that during the course of this study, new adverse effects of Propranolol that result in personal injury may be discovered. The University will make appropriate referrals for medical treatment for participants who sustain personal injuries or illnesses as a direct consequence of participation in the research. The participant's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

What will happen if you do not wish for your child/dependent to take part in the study or if you later decide not to keep your child/dependent in the study?

Participation in this study is voluntary. You may choose not to allow your child /dependent to participate or you may change your mind about their participation at any time.

If you do not want your child/dependent to enter the study or decide to stop your child's/dependents participation, he/she may need to gradually decrease the study drug. Do not suddenly stop the study drug without first consulting with the study doctor. If you decide to stop your child's participation in this research, his/her relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which your child is otherwise entitled.

You may also withdraw your consent for the use of data already collected about your child/dependent, but you must do this in writing to:

Dr. Barbie Zimmerman-Bier
Department of Pediatrics
Children's Health Institute
89 French Street RM 1218
New Brunswick, NJ 08901

Any data that has already been sent to the New Jersey Governor's Council on Autism (sponsor of this study) cannot be withdrawn because there may not be any identifiers connected with the data.

At any time, the study doctor can take your child/dependent out of this study because it would not be in his/her best interest to stay in it. The study doctor can stop treatment even if you are willing to allow your child /dependent to stay in the study.

Even if you decide to withdraw your child/dependent from the study for any reason, your child/dependent may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?

If you have questions about your child's/dependent's behaviors or side effects while in the study, please call the study doctor:

Eric B. London, M.D.
Department of Psychology
New York State Institute for Basic Research
1050 Forest Hill Road
Staten Island, NY 10314
Cell 347 578 0671
Or
Barbie Zimmerman-Bier, M.D.
Department of Pediatrics
Division of Pediatric Neurology
Robert Wood Johnson Medical School (RWJMS)
Children's Health Institute
89 French Street, RM 1218
New Brunswick, NJ 08901
Telephone: (732) 235-7083/cell 201-621-2246

If you have any questions about your child taking part in this study or if you feel your child may have suffered a research related injury, you can call the study doctor:

Barbie Zimmerman-Bier, M.D.
Department of Pediatrics
Division of Pediatric Neurology
Robert Wood Johnson Medical School (RWJMS)
Children's Health Institute
89 French Street, RM 1218
New Brunswick, NJ 08901
Telephone: (732) 235-7083/cell 201-621-2246

If you have any questions about your child's rights as a research subject, you can call:

IRB Director New Brunswick/Piscataway Health Sci: (732) 235-9806
Or the Rutgers Human Subjects Protection Program at (973) 972-1149.

What are your rights if you decide to allow your child to take part in this research study?

You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOUR CHILD FOR A RESEARCH STUDY

Information about your child/dependent is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your child's health information in this research study. Your child's/dependent's information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your child's/dependent's health information. If you sign this parental consent form, you agree to let the researchers' use your child's/dependent's information in the research and share it with others as described below.

What is the purpose of this research study and how will my child's health information be used?

You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your child's/dependent's health information for this study is to help researchers answer the questions that are being asked in the research.

- Information regarding your child's /dependent's medical history (including pregnancy and birth history) and development
- Medical history or treatment
- Medications- current and previous trials
- Consultations regarding ASD diagnosis
- Diagnostic tests- such as ADOS or cognitive testing
- EKG and/or EEG reports
- Psychological testing, surveys or questionnaires
- Other (specify): School study team evaluations or behavioral intervention reports

Who may use, share or receive my information?

The research team may use or share your information collected or created for this study with the following people and institutions:

- Rutgers University researchers involved in the study: Dr. Zimmerman-Bier
- Non-Rutgers researchers on the study team:
    - Eric London, M.D. (Co-Investigator) is a board-certified psychiatrist and Director Autism Treatment Research Laboratory at the Institute for Basic Research (IBR). He has 34 years of clinical experience treating comorbid psychiatric disorders in ASD with specific expertise in the use of propranolol in highly aggressive individuals.
    - J. Helen Yoo, Ph.D., BCBA-D (Co-Investigator) is a licensed psychologist and a licensed behavior analyst with 20 years of experience in the field of developmental disabilities and has worked in inpatient and outpatient hospital settings treating challenging behaviors.
- The New Jersey Governor's Council on Autism (sponsor of this study)
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services

- Federal Drug Administration (FDA)

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my child's research record while the research is ongoing?

No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact Dr. Barbie Zimmerman-Bier, the person in charge of this research study.

Do I have to give my permission?

No. You do not have to permit use of your child's /dependent's information. But, if you do not give permission, your child /dependent cannot take part in this research study. (Saying 'no' does not stop your child from getting medical care or other benefits he/she are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my child's /dependent**'s permission later?**

Yes. You may change your mind and not allow the continued use of your child's/dependents information (and to stop taking part in the study) at any time. If you take away this permission, your child's/dependents information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say 'yes' now but change your mind later, you must write to the study doctor of your decision:

Barbie Zimmerman-Bier, M.D.
Department of Pediatrics
Division of Pediatric Neurology
Robert Wood Johnson Medical School (RWJMS)
Children's Health Institute
89 French Street, RM 1218
New Brunswick, NJ 08901
Telephone Number: (732) 235-7083

How long will my child's permission last?

There is no set date when your permission will end. Your child's/dependents de-identified health information may be studied for up to six years after study completion or after publication of study results.

PARENTAL PERMISSION FOR CHILD/DEPENDENT

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

I am the [ ] parent or [ ] legal guardian of _____ (name of child/dependent) and I agree for my child/dependent to take part in this research study.

Subject/Child/dependent's Name:_____
Parent's Signature:_____ Date:_____
Parent's Signature:_____ Date:_____
Or
Guardian Signature _____ Date: _____

Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____

Subject Assent

Assent Obtained [ ] Witnessed By _____

Re-Contacting your family in the future

The research team may be interested in re-contacting (get in touch with) families who participate in this study, for future research studies, including but not limited to, follow-up questionnaire information, or a wish to re-test your child/dependent at a later date so as to chart their development over time. Even if you agree to be contacted in the future, you can always change your mind and decide not to participate. Please check one of the following sentences:

_____ I agree to be contacted by the investigators for future research studies.
_____ I do not agree to be contacted by the investigators for future research studies.