Subject Identification

General Template - Drug Clinical Trial
Version Date: October 2014

Protocol Title: An Open-Label Treatment Trial to Assess the Short-Term Tolerability, Safety, and Efficacy of Methylphenidate Hydrochloride Extended-Release Liquid Formulation in High-Functioning Autism Spectrum Disorder Adults with Attention-Deficit/Hyperactivity Disorder

Principal Investigator: Gagan Joshi, M.D.

Site Principal Investigator:

Description of Subject Population: Adults with autism spectrum disorder and ADHD (ages 18-40)

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Some of the people who are eligible to take part in this study may not be able to give consent to take part because of their medical condition. Instead we will ask the person's authorized representative to give consent. Throughout the consent form, "you" always refers to the person who takes part in the study.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why is this research study being done?

We are doing this research study to find out if a liquid formulation of extended release methylphenidate hydrochloride can help people with attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). We also want to find out if extended release methylphenidate hydrochloride is safe to take without causing too many side effects.

The liquid formulation of extended release methylphenidate hydrochloride (Quillivant XR) is approved by the U.S. Food and Drug Administration (FDA) to treat ADHD in children and adults.

This is a pilot study. Pilot studies are done on a small group of subjects to learn if a larger study would be useful.

We are asking you to take part in this research study because you have ASD and ADHD**.**

We expect to enroll about 40 adults in this study at Massachusetts General Hospital (MGH).

Pfizer, Inc. is paying for this research to be done.

How long will I take part in this research study?

It will take you up to 12 weeks to complete this research study. During this time, we will ask you to make 8 visits to MGH.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Screening Visit (Visit 1)

The Screening Visit will take up to 4 hours to complete. The visit can take place over two days, if necessary. At this visit, we will do some tests and procedures to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures. If you do not qualify, the study doctor will tell you why.

At this visit, we will:

- Ask you about your family, education, home environment, occupation, and medical history, including any medications you are taking currently.

- Ask you some questions about your symptoms of ASD and ADHD.
- Ask you to give a urine sample to test for certain types of drugs. This includes prescription drugs and illegal drugs like marijuana, cocaine, PCP, and sedatives (habit- forming drugs that make you sleepy and calm). If the urine drug test shows that you use any of these drugs, you cannot take part in this research. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.
- Test your urine for pregnancy if you can become pregnant. If you have a positive pregnancy test, we will tell you the results. You cannot take part in the study if you are pregnant.
- Do an electrocardiogram (ECG). This is a painless test of the electrical activity of the heart. During an ECG, we will put electrodes (small sticky plastic patches) on your chest, arms, and legs. The electrodes are connected to the ECG machine by wires. The ECG machine will measure and print out a record of the electrical activity of your heart.
- Draw blood for laboratory safety tests. Before blood is drawn, we can use a numbing cream on the place where blood samples will be drawn. If you want to use the numbing cream, we will wait for your skin to become numb before blood samples are drawn.
- Measure your vital signs (blood pressure, heart rate, and weight) and height.
- Do a physical exam.
- Ask you to fill out a questionnaire about some of your symptoms. While we hope you will answer every question, you can skip any question you do not want to answer. This is true for all questionnaires and interviews we use during this study.
- Give you some tests that include puzzles and vocabulary. This testing will take about 30- 45 minutes.
- Ask you to complete an interview about your thoughts and behaviors. This will take about 1 hour.

Audio and Video Recordings
We will make audio and video recordings while you are answering some of our study questions. These recordings help us check the way that study staff members ask questions in this study. To protect your privacy, each recording will be labeled with your initials and an identification number, not your name. We will store these recordings on a password-protected computer or on an encrypted external hard drive, which will be stored in a locked filing cabinet in a secure office.

Stopping Your Current Medications ("The Washout Period")
If you qualify for the study, we will ask you not to take certain medications while you are in this

study. We will discuss with you and your regular doctor which medications you may have to stop taking. This "washout period" allows your regular medications to leave your body before you begin taking the study drug. Without your regular medications, your ASD and ADHD may get worse. If this happens, please call the study doctor at the phone number provided in this consent form.

Baseline Visit (Visit 2)

Visit 2 will take about 3 hours. During this visit, we will:

- Ask you questions about your symptoms of ASD and ADHD and about any other symptoms you may be having.
- Ask about all the medications you took during the week.
- Ask you questions about side effects and health problems since your last visit.
- Measure your vital signs.
- Ask you to fill out questionnaires about some of your symptoms.
- Give you some tests including math problems and computer tasks. This testing will take about 2 hours to complete.
- Give you a supply of the study drug (Quillivant XR).
- If your parent or caregiver is available, we may ask them to complete two questionnaires about your social responsiveness and symptoms associated with ASD.

Taking the Study Drug

At the end of each study visit, we will give you a supply of the study drug that will last until the next visit. We will give you instructions on how much study drug you should take each day and when to take the study drug. It is important for you to follow our instructions about how to take the study drug. Please call your study doctor if you are ever confused about how much study drug you should be taking.

Additionally, the study coordinator will complete scheduled phone check-ins each week during the period when your medication is being adjusted. These phone calls will be made the day before a scheduled dose increase in order to remind you of the scheduled mid-week dose adjustment. If, during the call, you have concerns about dosing or report any changes in your health, the coordinator will transfer your call to a study clinician who will assess whether any dosing adjustments are needed.

Bring any unused study drug to the study center at each visit. We will measure the leftover study drug at each study visit to make sure you are taking the study drug properly.

Weeks 1 through 5 (Visits 3-7)

Visits 3, 4, 6, and 7 will take about 30 minutes each and Visit 5 will take about 1 ½ hours.

During the study visits, we will:

- Ask you about your symptoms of ASD and ADHD.
- Ask you about all of the medications you took during the week.
- Ask you questions about side effects and health problems since your last visit.
- Measure your vital signs.
- Ask you to fill out a questionnaire about your symptoms. During Visit 5 only, we will ask you to fill out additional questionnaires about your symptoms.
- During Visit 5 only, we may ask your parent/caregiver to complete two questionnaires about your social responsiveness and symptoms associated with ASD.
- Ask about any other symptoms you may be having besides your ASD and ADHD symptoms (Visit 5 only).
- Collect any unused study drug.
- Give you a new supply of study drug.

Week 8 (Final Study Visit)
This visit will take about 3 hours. During the last study visit, we will:

- Do a physical examination.
- Measure your vital signs and height.
- Ask you questions about your symptoms of ASD and ADHD, and any other symptoms you may be having.
- Ask you about all of the medications you have taken during the week.
- Ask you questions about side effects and health problems since your last visit.
- Ask you to give a urine sample to test for certain types of drugs.
- Test your urine for pregnancy if you can become pregnant.
- Do an ECG.
- Collect all unused study drug.
- Draw blood samples for safety tests.
- Give you some tests including math problems and computer tasks.
- Ask you to fill out 7 questionnaires about some of your symptoms.
- If your parent or caregiver is available, we may ask them to complete two questionnaires about your social responsiveness and symptoms associated with ASD.

Three Optional Follow-Up Visits
After you complete the study, we will offer you 3 optional follow-up visits with the study doctor at no cost. If you choose to complete these visits, they will take place about once a month. These visits will allow the study doctor to check in with you after the study. These visits will give the study doctor enough time after the study to refer you to a doctor or group in your community.

Total Amount of Blood Drawn
We will draw a total of about 2 tablespoons of blood during this research study.

Stopping the Study Early

You can stop taking part in this study at any time. We may stop this study or remove you from the study at any time if it is necessary or in your best interest. We may stop you from taking part in this study for any of the following reasons:

- If you do not feel well while you are taking the study drug
- If there is new information on the safety of the study drug
- If you become pregnant
- If you are using drugs not allowed in this study
- If you do not follow the study instructions, miss appointments, or do not return unused study drug

If you leave the study early, we will ask you to complete all the procedures that are done during the final study visit (Visit 8). We will tell you how to stop taking the study drug safely. It is important that you return any unused study drug if you leave the study.

If you want, we can refer you to another doctor or group in your area after you stop taking part in the study.

Sending Study Information to Research Collaborators Outside Partners

We may want to use and share your study information with other researchers for future research on autism or other conditions. We will label your health information with a code instead of your name. The key to the code connects your name to your health information. The study doctor will keep the key to the code here at Partners and will not share it with our research collaborators. No one outside of Partners will know which study information or samples are yours.

Do you agree to let us share your study information with other researchers?

☐ Yes ☐ No Initials_____

If later you change your mind, contact the study doctor.

Contacting for Future Research

We would like to contact you about future research studies that you may be interested in taking part.

Do you agree to let us contact you about future research studies?

☐ Yes ☐ No Initials_____

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

What are the risks and possible discomforts from being in this research study?

Taking part in this study may involve risks, some of which are listed below. There may also be other side effects that are not known at this time.

Risks of Taking Quillivant XR

Taking Quillivant XR may cause you to have one or more of the side effects listed below.

Common side effects (experienced by 1 to 4 out of every 45 subjects in earlier research studies):

- Decreased appetite
- Weight loss
- Nausea
- Stomach pain
- Upset stomach
- Dry mouth

- Vomiting
- Insomnia (difficulty falling asleep or staying asleep)
- Anxiety
- Nervousness
- Restlessness
- Mood swings
- Feeling on edge (agitation)
- Irritability
- Dizziness (vertigo)
- Tremor (involuntary shaking or trembling)
- Blurred vision
- Increased blood pressure
- Increased heart rate (tachycardia)
- Increased sweating
- Fever
- Skin irritation or peeling (excoriation)
- Tics
- Motion sickness
- Eye pain
- Rash

Rare but serious side effects of Quillivant XR include changes in behavior or cognition (thinking), including aggression/hostility. These changes could also include manic or psychotic symptoms, such as hearing or seeing things that other people do not see or hear. You should notify the study doctor immediately if you notice any unusual changes in your thoughts or behaviors.

Heart-related problems including sudden death, stroke, and heart attack have been reported with use of stimulant medicines like Quillivant XR. Cases of priapism (prolonged erections) and circulation problems in fingers or toes (including Raynaud's phenomenon) have also been reported with use of stimulant medications.

If you have a history of high blood pressure that is currently under control, you may be allowed to take part in the study if the study doctor believes that it is safe for you to begin taking Quillivant XR. If you have ever had high blood pressure or heart problems, we may ask for your permission to review your medical history with your primary care doctor before you begin taking Quillivant XR. This would be done to make sure that your doctor agrees that it is safe for you to take a stimulant medication. This is because stimulants, including Quillivant XR, may increase your blood pressure.

Quillivant XR is a federally controlled substance that can be abused or lead to dependence (addiction).

There may be other risks of Quillivant XR that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

You should notify the study doctor immediately if you develop an illness or disease that you did not have at the start of the study. If you become pregnant, have an injury or side effect, or develop an unusual health problem during the study, contact the study doctor immediately.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of Quillivant XR on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 7 days after your last dose of study drug.

Acceptable birth control methods for use in this study are:

- Abstinence (no sexual contact)
- Double-barrier method such as which is a diaphragm plus spermicide (a foam, cream, or gel that kills sperm) or a condom plus spermicide AND one of the following:

- Consistent use of an approved birth control pill
- Birth control patch
- Injected contraceptives
- Intraeuterine device (IUD)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study.

Risks of Taking Quillivant XR with Other Medications

It is possible that taking Quillivant XR with your regular medications or supplements may change how Quillivant XR works, or how your regular medications or supplements work. It is very important that you tell the study doctor about all prescription and over-the-counter medications or supplements you are taking during the study.

The study doctor may ask you not to start certain types of medication while you are taking Quillivant XR. Also, if you already take a certain type of medication, the study doctor may ask you not to change the dose while you are taking Quillivant XR.

Do not take the following medications while you are in the study: Monoamine oxidase inhibitors (MAOIs) including: Marplan, Nardil, Eldepryl, and Parnate. Taking these drugs and Quillivant XR together may cause serious side effects.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Risks of Stopping Current Medications

During the washout period when you stop taking your current medication(s), your ASD and/or ADHD symptoms might get worse. If this happens, tell the study doctor.

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Risks of Sharing Sensitive Information

During the study, you will be asked to disclose sensitive, personal information, such as pregnancy or drug use. You may be uncomfortable answering these sensitive, personal questions. Information about illegal activities could have social, economic, or legal risks. Every effort will be made to keep your study information confidential. However, this cannot be guaranteed.

Risks of Completing Study Tests and Questionnaires
You will be asked to complete some study tests, such as computer tests and filling out questionnaires. You may feel uncomfortable or anxious while doing some of the computer tests or questionnaires.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this research study. It is possible that your symptoms of ADHD could temporarily improve while you are taking Quillivant XR.

The results of this study may benefit other adults with ASD and ADHD in the future.

What other treatments or procedures are available for my condition?

You do not have to take part in this study to receive treatment for your ASD or ADHD. There are a number of medications available for the treatment of ADHD symptoms such as:

- Quillivant XR
- Concerta
- Ritalin
- Adderall
- Strattera

While there are no medications approved for the treatment of the core symptoms of ASD, there are standard treatments for other symptoms of ASD, such as risperidone (Risperdal) for irritability and aggression. There are various behavioral treatments that do not use medication available for the management of ASD, such as applied behavioral analysis and occupational therapy.

Talk with the study doctor if you have questions about any of these treatments or procedures.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

We will not pay you to take part in this study. If you drive to study visits, we will give you a voucher to cover the cost of parking in the hospital garage.

What will I have to pay for if I take part in this research study?

Pfizer, Inc. is providing the study drug at no cost.

Study funds will pay for the study visits, study drug, your medical and mental health evaluation, ECGs, lab tests, and all procedures done only for the research.

If you choose to complete the 3 optional follow-up visits after the study is complete, the visits will be provided at no cost to you or your insurance.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Gagan Joshi, MD is the person in charge of this research study. You can call him at (617) 726-7899 (Mondays through Fridays from 9 am to 5 pm). Dr. Joshi is available 24 hours a day by pager by calling the hospital at (617) 726-2066 and asking for page # 38188.

If you have questions about the scheduling of appointments or study visits, please call the study coordinator, Barbora Hoskova, at (617) 724-7301, Mondays through Fridays from 9 am to 5 pm.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject

- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)

- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject _____ Date _____ Time (optional) _____

Signature of Guardian or Authorized Representative for Adult:

I give my consent for the person I am authorized to represent to take part in this research study and agree to allow his/her health information to be used and shared as described above.

Print Name (check applicable box below) _____

- ☐ Court-appointed Guardian
- ☐ Health Care Proxy
- ☐ Durable Power of Attorney
- ☐ Family Member/Next-of-Kin

Signature _____ Date _____ Time (optional) _____

Relationship to Subject:_____

Assent

Statement of Person Giving Assent

- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions, and my questions have been answered.

Signature of Adult:

I agree to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Adult	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: AME 46, 05/30/2017