BROWN

Adolescent Clinical Research Program
Center for Alcohol & Addiction Studies
Box G-S121-5
Providence, Rhode Island 02912

STUDY CONSENT/ASSENT FORM

Adolescents are invited to be in a research study titled "Effects of Topiramate on Adolescent Alcohol Use: Efficacy and Mechanisms." The reason for this study is to test whether a certain medication reduces alcohol craving and use in adolescents who drink alcohol. This form will describe the nature and possible risks of this study. It will be explained to you and you should also read it yourself. Please ask us to explain any words or information that you do not clearly understand. Then, if you decide to take part in this project please sign this form in front of the researcher and a witness.

A. Purpose of the Project

- The **goal of this study** is to learn about the effects of Topamax® (up to 200 mg/day) on alcohol craving and use in adolescents. Topamax® is a medication approved by the Food and Drug Administration (FDA) to treat certain types of seizures in people of all ages, ranging from young children to adults. Although more than 2 million people have been treated with Topamax ® worldwide, only recently did researchers start to study its usefulness for treating alcohol, marijuana, and other drug misuse. Based on its chemical effects on the brain, Topamax® might lessen an adolescent's desire to drink alcohol and lessen the good feelings that adolescents often have when they drink.

B. Explanation of What Will be Done

- BEFORE YOU START THE STUDY

  Medical Screening Appointment (*about 4 hours long*): If you want to be in this study and your parent/legal guardian agrees that you can (if you're less than 18 years old), you will come to our office for a screening appointment, in order to make sure that you qualify to be in this study. During this appointment, you and your parent/legal guardian (if you're less than 18 years old) will be asked about your medical background, including your mental health and any medications you're taking. The interview about your mental health will be audio taped to ensure the accuracy of the assessment. Audio tapes will be destroyed after being reviewed. You'll also be asked about your alcohol and any drug use, and we'll take your blood pressure, pulse, weight, height, and temperature. You will complete measures regarding your alcohol use and you will complete a series of short tests.

  If it seems you qualify for this study, you will have your blood taken (approximately 2 teaspoons) and provide a urine sample at our offices or a nearby laboratory. Your blood will be used to test your health. Your urine will be tested for drug use and, if you're female, for pregnancy. You cannot be in this study if you're pregnant or breastfeeding.

Physical Exam and Picture Rating Appointment (*about 40 minutes long*): You'll then come to our office to meet a study physician who will review your medical history and perform a physical exam. You will also view a series of pictures. Some of the pictures may be pleasant, such as photos of puppies, tasty foods, exciting sports moments, and romantic scenes without nudity. Some pictures may be unpleasant, such as photos of accident victims, persons with disfiguring diseases, victims of violence, disgusting scenes (e.g., a dirty toilet), and fear-producing photos such as an aggressive dog, a snake, and someone holding a gun. Some are scenes with alcohol. These pictures are commonly used in the field of human emotion research and their content, while strong, is consistent with photos published in such news magazines as *TIME* and *Newsweek*. While viewing each picture, you will be asked to rate each picture on craving, pleasantness and arousal.

After the screening, you can be in the study only if all of the following things are true.

- ✓ You want to be in the study
- ✓ We decide that you're right for the study
- ✓ Your parent/legal guardian allows you to be in the study (if you're younger than 18 years old)

❖ AFTER YOU START THE STUDY

First Office Visit (*about 4 hours long*): If you qualify for this study, you'll come to our office to learn specific instructions for being in the study, provide another urine sample for a drug test and, if you're female, a pregnancy test, and answer more questions about your mental health now and in the past. The interview about your mental health will be audio taped to ensure the accuracy of the assessment. Audio tapes will be destroyed after being reviewed. You will complete several questionnaires and tests during this visit. You'll also do an alcohol breathalyzer test. If your alcohol level is above 0.0% you'll be asked to wait until it is 0.0% or to return to complete the session the next day. During this session, you will have your heart rate and blood pressure recorded while you relax and again while you look at non-alcoholic beverage cues (sight and smell of a non-alcoholic drink) and while you look at alcoholic beverage cues (sight and smell of an alcoholic drink). During this time you will be asked to answer questions about your urges to drink alcohol. We will also get your reaction to a series of pictures (see description of pictures above). While you view these pictures you'll have surface sensors attached to your face to measure eye muscle movements. Before, during, and after viewing the pictures, you'll hear brief, fairly loud noises through earphones. After viewing all of the pictures, you'll be asked to rate each picture on craving, pleasantness, and arousal.

You'll also receive and learn how to use a small handheld computer that's similar to a Blackberry®, but without a useable cell phone. You will use this device to keep a record of what you do, how you feel, and your alcohol use. The handheld computer will send the information you recorded to us each day using secure wireless technology.

Practicing with the Handheld Computer (*7 days*): You will then practice with the handheld computer for 7 days and we will check in with you by telephone to discuss how you're doing and to answer any questions. If necessary, we will visit you to help you learn how to use it, or you can come back to the lab for further training. If you're not able to use it correctly, you won't be able to continue in the study.

Taking Medication Capsules (*8 weeks*): After you've practiced using the handheld computer successfully, you'll take medication capsules for 8 weeks. You will take medication capsules

that contain either Topamax® (up to 200 mg per day) or a placebo 2 times each day, 1 capsule in the morning and 1 at bedtime. We decide if you'll take Topamax® or placebo by using a process that guarantees each adolescent has an equal chance (50/50) of getting either one. Once it's decided which type of capsule you'll take, however, you'll take that type during the whole study. If you take Topamax®, the dose will start at 25 mg per day and increase over time to a dose of 200 mg per day. You won't know which type of capsule you're taking. Only the study doctors will know whether you're taking Topamax® or placebo. We will call you daily to help you remember to take your medication capsules and to ask about how you're feeling.

Using the Handheld Computer (*4 weeks*): You will not use the handheld computer for the first 4 weeks you are taking the study medication. During the last 4 weeks you are on the medication, you will carry the handheld computer around with you at all times and answer questions on it every day.

- You'll answer questions on the handheld computer when:
  - You wake up each day
  - You use alcohol (if you use any)
  - When it beeps (about 4 times per day). You can shut it off when you're sleeping or busy and can't respond, and when you're driving, operating machinery, or in other situations where it would be unsafe to use the device

- You'll use the handheld computer to report:
  - Where you are and what you're doing
  - How you're feeling
  - Urges to drink alcohol
  - Number of alcoholic drinks you had recently

Checkup Visits (*8 weekly visits, each between 30 and 90 minutes long*): You'll attend 8 weekly checkup visits at our office. During these visits, we'll answer all your questions and give you more medication capsules. You'll also take a urine drug test and, if female, a pregnancy test, and have your blood pressure, pulse, weight, and temperature recorded.

At two of these checkup visits you'll have your blood taken (approximately 2 teaspoons) at our offices or a nearby laboratory to test for whether you're taking the medication capsules. At any time during the study, including during these visits, you can meet with the study physician to review how you feel while taking the capsules.

During 4 of the checkup visits we'll also talk with you about your alcohol use, including your thoughts about cutting down your use, how your alcohol use compares to other adolescents, and how alcohol use is harmful. We'll help you set goals for monitoring and cutting down your drinking. Everyone in this study will get this counseling regardless of how much he or she uses alcohol.

Laboratory Session (*About 4 hours long*): After taking medication capsules and using the handheld computer for at least 49 days you'll come to our office for a laboratory session. At the beginning of the session, you'll do an alcohol breathalyzer test. If your alcohol level is above 0.0% you'll be asked to wait until it is 0.0% or to return to complete that session on another day. You'll also provide a urine sample to test for drugs and, if female, pregnancy, and we'll record your blood pressure, pulse, weight, and temperature. We'll also ask about the study medication, alcohol, other drug use, and how you're feeling.

During this session, we will record your heart rate and blood pressure while you relax, while you look at and smell a non-alcoholic drink, and while you look at and smell an alcoholic drink. During this time you will be asked to answer questions about your urges to drink alcohol. You will also be asked to complete a series of tests during this session. We will also get your reaction to a series of pictures using the same procedures as in the First Office Visit.

Slowly Stopping the Medication (*14 days*): After you're done taking medication capsules for 8 weeks, we'll reduce your medication dose over 14 days. It's important that you stay in contact with us while you're coming off the medication. We'll still call you daily to remind you to take your medication capsules and to ask about how you're feeling.

Follow-up appointments (*2 hours for the first follow-up, 1 hour for the second*): Six (6) months after finishing the medication, we will schedule you for a follow-up appointment. During this appointment, we will ask about your alcohol and drug use and you will complete a series of tests.

Twelve (12) months after finishing the medication, we will schedule you for another follow-up appointment. During this appointment, we will ask about your alcohol and drug use.

C. Financial Considerations

- There will be no cost to you for being in this study. You'll receive all payments during your office visits in the form of gift certificates to local stores. All participants will be paid in gift certificates, not cash. You'll receive payment for any part of the study you complete, even if you decide to stop the study early for any reason.

Schedule of Sessions and Payment – Adolescent

Study Phase	Payment Schedule
Screening Appointment	**$20** (regardless of study participation)
Physical Exam & Lab Tests	**$20**
First Office Visit	**$25**
EMA Practice Period	**$5** per day for using the handheld computer (up to $35 per week**)**
Week 1	**$20** for completing an office visit
Week 2	**$20** for completing an office visit
Week 3	**$20** for completing an office visit
Week 4	**$20** for completing an office visit
Week 5	**$5** per day for using the handheld computer (up to $35 per week**)** **$20** for completing an office visit
Week 6	**$5** per day for using the handheld computer (up to $35 per week**)** **$20** for completing an office visit
Week 7	**$5** per day for using the handheld computer (up to $35 per week**)** **$20** for completing an office visit
Week 8 + Lab session	**$5** per day for using the handheld computer (up to $35 per week**)** **$50** for completing laboratory session
6 Month follow-up appointment	**$20** for completing an office visit
12 Month follow-up appointment	**$20** for completing an office visit
Bonus	**$75** bonus for completing the entire study and returning the handheld computer and medication bottle
Total Possible Payments =	**$545**

Schedule of Sessions and Payment – Parent/Legal Guardian (if adolescent is less than 18 years old)

Study Phase	Payment Schedule
Screening Appointment	**$50** (regardless of adolescent's study participation)
Total Possible Payments =	**$50**

D. Risks or Discomforts and Potential Benefits

❖ POSSIBLE RISKS OR DISCOMFORTS OF BEING IN THIS STUDY

The risks of this study include:

- Possible side effects from Topamax®
- Topamax® can reduce the effectiveness of oral contraceptives
- Emotional discomfort from answering questions in the assessment
- Emotional discomfort from viewing the photographic slides
- Discomfort associated with drawing blood and other medical tests
- Risk of coercion
- Breach of confidentiality

Possible Side Effects From Topamax®

Most Common Side Effects	Numbness & tingling, tiredness, dizziness, sleepiness, loss of appetite, difficulty with memory or word finding, difficulty with coordination or balance, nausea, and runny nose, sinus problems, or sneezing.
Less Common Side Effects	Weight loss, difficulty concentrating, nervousness, slow thinking, change in sense of taste, abnormal vision, confusion, and language problems Kidney stones are another less common possible side effect and are potentially serious. Drinking adequate amounts of nonalcoholic fluids is recommended and may reduce risk of kidney stones. Occasionally, depression and mood problems have been reported and some patients have had suicidal thoughts or actions. If your mood changes or if you feel depressed or feel you may harm yourself, contact your doctor immediately. Robert Swift, M.D., Ph.D. or Thomas Chun, M.D. (the study physicians), Robert Miranda, Ph.D. (a clinical psychologist), or another designated licensed mental health professional, will monitor your mood during the study. You will be given a list of mental health resources available in Rhode Island. If you need a psychiatrist, a study doctor or your primary care doctor will refer you to a mental health agency in your local area.
Rare But Serious Side Effects	Metabolic acidosis (increased acidity in the blood) can cause symptoms such as tiredness and loss of appetite, or more serious conditions including irregular heartbeat or coma. Long-term metabolic acidosis can result in thinning of the bones (osteoporosis) with an increased risk for fractures. In children, this condition may reduce growth rates which may eventually decrease maximum height achieved. Metabolic acidosis may increase the risk for kidney stones. Decreased sweating is a rare but serious side effect. Activities such as exercise or exposure to warm temperatures while taking Topamax® may increase the risk of heat-related side effects, such as heat stroke. Drinking plenty of fluids is recommended. A medical condition consisting of sudden worsening of vision and an elevation of fluid pressure in the eyes called acute secondary glaucoma, has been described in patients

	taking Topamax®, usually occurring in the beginning of their treatment. If you have sudden, significant worsening of vision, blurred vision, or eye pain, contact your doctor immediately.
Rare & Isolated Cases	Liver failure/hepatitis and blistering skin rashes have also been reported.
Issues with Pregnancy	Pregnant women and nursing mothers cannot participate in this study. Topamax® increases the risk of birth defects such as cleft lip and cleft palate in infants born to mothers taking this medication, and any woman who should become pregnant while in this study will be removed from the study. Because of this risk, any females who become pregnant while in this study must tell us immediately.
Effects on Other Medications	Topamax® may cause a change (increase or decrease) in the effect of some other medications. If you are taking other medications while you're in this study, your study doctor will explain whether Topamax® may have an effect and if necessary, may adjust your study medication dose. It is very important for you to speak to the study doctor about the use of other medications during the course of the study to evaluate the possibility of interactions. You must inform a study doctor of all medications you are taking because certain medications are not allowed while participating in this study.

The risk of cognitive impairment includes such difficulties as fuzzy thinking and word-finding issues. Research shows that these difficulties, if experienced, reverse once off the study medication. In addition, Topamax® can reduce the effectiveness of oral contraceptives. Females who use oral contraceptives are at increased risk of pregnancy while taking Topamax®. Topamax® also increases the risk of birth defects such as cleft lip and cleft palate in infants born to mothers taking this medication. Therefore, females who refuse to use a reliable barrier method of birth control (e.g., condom) cannot participate in this study.

As with any new medication, you may experience an allergic reaction to Topamax®. In addition, as with any medication, there may be risks related to taking Topamax® that are not now known. You'll be told of any important new findings that may affect your willingness to continue in the study.

Due to the possibility of dizziness or drowsiness, you must be cautious when operating a vehicle or heavy equipment while in this study, until you have experience using Topamax®.

If you stop taking Topamax® too quickly and without medical supervision, there is a risk that you may have a seizure. Therefore, it is important that you take the medication capsules as instructed during the study and that you stay in contact with us while you're coming off the medication. If you want to stop being in the study before it's over, it's important to tell us so a study physician can decide the best way for you to come off the medication. If necessary, you may be asked to sign a release of health care information form to allow a study physician to speak with your primary care physician and/or psychiatrist.

If you choose to participate in this study, you'll be given an alert card to carry on your person at all times, explaining the study and the effects of Topamax® along with a 24 hour phone number for a physician you could call in case of an emergency.

Emotional Discomfort from Answering Questions in the Assessment

The questions we ask in this study are commonly used in research with adolescents and when adolescents see a doctor. You may feel uncomfortable discussing mental health issues. You may also be concerned about other people finding out the results. Any information we get as part of this study that can be identified with you will remain confidential, or private. That is, it will not be shared with anyone else. It will be identified only by a code number.

Discomfort Associated with Drawing Blood and other Medical Tests

Although complications from drawing blood occur very rarely, all, some, or none of the following may occur: a bruise or lump at the puncture site, local bleeding, local infection, and lightheadedness. The amount of blood loss is about 2 teaspoonfuls, which is considered very small.

If something is learned about you during this study that may be important for your medical heath, for example discovering that you're pregnant, this information (called an incidental finding) will be discussed with you by Dr. Miranda or another qualified member of the research team in a timely fashion. This communication will be made verbally to allow you to have any questions answered. If you provide a signed release of information, such findings could be disclosed to your personal physician.

Emotional Discomfort from Viewing the Photographic Slides
There is risk of possible discomfort from viewing the series of pictures, some of which may be pleasant, some may be unpleasant, some are scenes with alcoholic beverages, and some are scenes with marijuana. Discomfort from viewing these pictures is unlikely because these are standard procedures used across many populations, including adolescents, without complication. At the end of the study, however, you will have the opportunity to ask questions about your participation and to discuss the pictures. This will ensure that you have the opportunity to discuss any lasting effects of the procedures.

Risk of Coercion
The risk of coercion (i.e., pressuring you in any way to be in the study) usually happens when the payment that adolescents get for being in a study is large. Coercion is not likely because payments are reasonable for the amount of time and effort required and similar to other studies with adolescents in this area, and there will be no other incentives (for example, rewards or payments). In addition, each adolescent will get payment for any time he or she participates, even if he or she decides to stop the study for any reason.

Breaking of Confidentiality (Privacy)
This study will ask private and sensitive information about you and your alcohol and drug use. Every attempt will be made to keep this information confidential, or private. However, it is possible that your confidentiality may be violated. Please read Section F of this form for specific information about how we will keep information about you private.

- POSSIBLE BENEFITS OF BEING IN THIS STUDY

The benefits of participating in this study are considered minimal, but include:

- **Four individual counseling sessions where you discuss your alcohol use**
  As described above, all participants, regardless of how much he or she uses alcohol, will receive 4 individual counseling sessions about their alcohol use. These sessions will focus on increasing your motivation to change your alcohol use, as well as providing feedback about how your drinking compares to other adolescents and how alcohol use is harmful to adolescents. During these sessions, we will help you set goals for changing your use.

- **The chance to contribute to research that may prove beneficial to you or to others in the future.**

E. Alternative Procedures

- If you decide that you should not be in this study, we do not offer any other study. However, there are treatment programs in Rhode Island and you will be given a list of those treatment providers.

F. Confidentiality

- This study will request potentially sensitive information about your alcohol and drug use. Every attempt will be made to keep this information confidential. All reasonable efforts will be made to protect the confidentiality of your participation in the study. However, it is possible that your confidentiality may be violated. In order to protect your confidentiality, all your records will be kept in a locked file under a code number rather than your name. Your name will not be publicly disclosed at any time, and the records will be strictly maintained according to current legal requirements. Instances when information will not be kept confidential involve reports of child abuse, or threats to harm yourself or others. If you report suicidal or homicidal intent or ideation or child or elder abuse, the principal investigator, clinical psychologist, or study physician will be notified immediately. If you're less than 18 years old, your parent/legal guardian will be contacted immediately. A report will be filed with the appropriate agency if abuse is reported.

- To help keep information about you confidential or private, we have obtained a Certificate of Confidentiality from the U.S. Department of Health and Human Services (DHHS). The Confidentiality Certificate will protect the investigators from being forced, even under a court order or subpoena, to release information that could identify you. We may release identifying information in some circumstances, however. For example, we may disclose medical information in cases of medical necessity. We will take steps (notifying the authorities) to protect you or someone else from serious harm, including child abuse and threats to harm oneself or others. Also, because this research is sponsored by DHHS, staff from that institution may review records that identify you only for audit or program evaluation. They can't report anything that would harm the research subjects. This Certificate, however, does not imply that the Secretary, DHHS, approves or disapproves of the project.

- You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation and obtains your consent to receive research information, then the investigator may not use the Confidentiality Certificate to withhold this information. This means that you and your family must also actively protect your own privacy.

- If you give us your permission by signing this document, information, which does not identify you by name, may be used for medical and scientific purposes, including teaching and/or publication. Because of the investigational nature of this study, the Food and Drug Administration, the Department of Health and Human Services, the Offices of Inspector General and Civil Rights, (or regulatory agencies from other countries) have the right to review patient records. Your information will be kept confidential to the extent of the law.

- Your research records will be treated as private information and will be protected according to Brown University's privacy practices and policies that are based on state and federal law. In particular, federal law requires us to get your permission to use or disclose (release to someone outside Brown University) your health information for research purposes. If you sign this form you agree to be in this research study and permit the use and disclosure of your health information as we described. This permission has no expiration date.

G. Refusal/Withdrawal

- Participation is voluntary, which means you can decide not to be in this study for any reason. Even if we decide you're right for this study and you agree to be in this study, you can then decide not to continue in the study for any reason. If you want to stop, it is important to notify study staff so that they can arrange to get the remaining medication, medication bottle, and handheld computer from you. If you have already begun taking the study medication, the study physician will decide the best way for you to come off the medication. You should not stop taking the study medication before talking with us so that we can plan the healthiest way for you to stop taking the medication.

H. Medical Treatment/Compensation in Case of Injury

- We do not expect any unusual risk in this research project. Emergency care will be provided if necessary, but Brown University and the investigators assume no responsibility to pay for such care or to provide financial compensation for emergency or non-emergency health services.

I. Who to Contact with Questions about the Study

- Please ask any questions you may have now. If at any time you have further questions about this project, please feel free to ask the investigator, Dr. Miranda (401-863-6658) who is available during normal business hours. At all other times, you may call 401-456-2000 and ask to have Dr. Robert M. Swift paged.

J. Who to Contact if you have Complaints Regarding the Study

- If you have any complaints regarding participation in this study, or would like more information about the rules for research projects, or the rights of people who take part in research, please contact the Brown University Human Research Protection Program at (866) 309-2095 or (401) 863-3050.

K. Potential Conflict of Interest

- One of the researchers on this project has a financial relationship with a company (not the sponsor of this study) that is developing drugs to be used in the treatment of alcohol abuse.

L. Research Participant's Rights

- I have read and have had read to me all of the above. _____ has explained the study to me and answered all of my questions. I have been told that the researchers of this project are unable to provide me with other research opportunities and that this study is not meant to be treatment. The results of this study may be published, but my records will not be revealed unless required by law. The Institutional Review Board at Brown University may monitor my records for quality assurance purposes.

M. ClinicalTrials.gov

- 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.

Parent/Legal Guardian Completes:

I give my teenager, (Name: _____), permission to participate in this research study.

_____
Parent/Legal Guardian's Signature* Date
*Must have signature if adolescent is less than 18 years old and if parent agrees to participate in the research study

Adolescent Completes:
I acknowledge that the above explanation of this project has been read to me and that all of my questions have been satisfactorily answered. I will receive a copy of this form.

I (Print Name: _____), agree to participate in this research study.

_____
Participant's Signature Date

Adolescent & Parent/Legal Guardian (If adolescent is less than 18 years old) Completes:
I agree to be re-contacted for future studies:

□ Yes □ No _____ (Adolescent's initials)

_____ (Parent/Legal Guardian's initials)

Researcher Completes:
I certify that I have explained fully to the above individual the nature and purpose, procedures, and the possible risks and potential benefits of this research project.

_____
Researcher's Signature Date

Witness Completes:
I acknowledge the process and/or signature or statement set forth above.

_____
Witness' Signature Date