SCRIPPS IRB

CONSENT TO PARTICIPATE IN RESEARCH

Mifepristone Treatment of Alcohol Use Disorder

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Before you start reading about this research, please read the California Experimental Subjects' Bill of Rights, which is page 10 of this form.

Why is this research being done?
This research is being done to find out if mifepristone will help prevent a return to drinking in persons with an alcohol problem who have recently quit drinking.

You have been asked to participate because you have an alcohol problem and agree to stop drinking for at least 4 days before starting our study medication. Investigators at The Scripps Research Institute hope to learn how effective mifepristone (Korlym®) is in comparison to a placebo pill for prolonging the time that you go without drinking alcohol and for helping to reduce the severity of any relapse (return) to drinking. A "placebo" looks like study drug but does not contain real drug.

Mifepristone is a drug that has not been approved by the US Food and Drug Administration (FDA) to treat alcohol dependence but is approved for a different purpose (to control high blood sugar in patients with Cushing syndrome and also to end a pregnancy that is less than 7 weeks along when taken in combination with misoprostol). The dose of mifepristone to be used in this study is 1200 mg per day to be taken orally for 7 days.

The investigators hope that the current drug under investigation, mifepristone, will be better than available drugs for prolonging abstinence and relieving symptoms following alcohol withdrawal. There are three oral drugs that are supposed to help people with alcohol problems stay abstinent and they are

naltrexone (oral or injectable long acting formulations), disulfiram (Antabuse®), and acamprosate (Campral ®).

Naltrexone (ReVia®) decreases the risk of relapse to heavy drinking in alcoholics. Disulfiram (Antabuse®) makes people who drink violently ill. Some people with an alcohol problem who take Antabuse® find that it reduces their risk of relapse because they know that drinking will make them sick. Acamprosate (Campral®) has been approved for the maintenance of abstinence following alcohol withdrawal.

These drugs work differently than the drug used in this study. The investigators think mifepristone will reduce craving for alcohol in people with alcohol dependence by helping to normalize their brain activity, thereby reducing craving.

The sponsor, the company that pays Scripps and the study doctor to do the study, is the National Institute on Alcohol Abuse and Alcoholism. Up to 150 people will be in this study, all of them here at Scripps.

How long is the study?
If the study suits you and you agree to join, you will be in it for 12 weeks.

What will happen to me?
You will first come to The Scripps Research Institute for a screening visit. During that visit, which will last about 3.5 hours, you will be asked questions regarding your alcohol use and health. Blood and urine samples will be collected. You will then fill out some questionnaires.

At the next visit, a doctor will examine you. This examination and the medical care you will receive in the study is not the same as seeing your regular doctor. You will then fill out some questionnaires and take some computer and pencil-and-paper tests that test your memory, attention and concentration.

Some procedures and tests would be done to determine your eligibility, even if you did not join the study. They are:

- Answer questions about your medical, alcohol, smoking, mood, and sleep history
- Electrocardiogram (ECG) to measure your heart rate and rhythm
- Urine sample for kidney function test and drug screen
- Blood chemistry
- An examination by a study physician

These procedures and tests will be done at some visits (see schedule below):

Blood sample: The medical assistant will draw a blood sample (2-4 teaspoons) from your vein for lab tests of your body functions. If you are female, you will also be tested to be sure that you are not pregnant.

Genetic Studies: Blood samples and a saliva sample will be collected for genetic testing, including DNA. The reason for this genetic testing is that we want to look at various genes that might explain why some people become addicted to substances while others may not, or predict your response to study procedures.

Urine sample: You will be asked to give a urine sample to test how your kidneys work and to screen for drugs of abuse and to verify abstinence from alcohol. If your urine shows you have used any disallowed drugs you will not be able to proceed with the study and you will not be paid for the visit. If you are female, you will also be asked to provide a urine sample at Weeks 0, 2 and 3 for a pregnancy test.

Vital Signs: Your blood pressure, heart rate, temperature and weight (vital signs) will be measured.

Breath Samples: Samples of your breath will be collected at each study visit. You will be asked to blow into two small tubes for up to 15 seconds. This is done to measure alcohol and carbon monoxide levels in your body.

ECG: Self-stick pads will be placed on your chest, arms and legs. Wires will be attached to the pads and to a machine that will record the electrical activity of your heart. An electrocardiogram (ECG) is a tracing of your heart's activity. The ECG will be performed at randomization and again at Week 2.

Exam: A physician will examine you. This exam is not meant to take the place of your regular medical care.

Behavioral counseling is a part of this research study (Weeks -1-8, see schedule). The counseling hopes to explore the reasons why you drink, increase your motivation to stop drinking, and encourage you to keep the study-related visits.

If your test results are acceptable, you will be randomized to a treatment group by chance, to get either the study drug, mifepristone (1200 mg/day), or placebo. A "placebo" looks like study drug but has no real drug, it does not contain the active ingredient. You have a 1 in 2 chance of taking the study drug and a one in two chance of receiving a placebo pill. You won't know which you are taking and neither will the study doctor or staff. The study doctor could find out in an emergency.

Study drugs will be dispensed in a container with sections for each day and time. You will take your first dose of the study medication, after you have been medically cleared, during your study visit at the lab. You will be asked to take the drug as directed and to return your medication packages and any unused medication at your Week 1 study visit. Three days after you begin taking the study drug, study staff will contact you by telephone to see how you are tolerating the medication and answer any questions you might have about the study medication. You will be compensated $10.00 for participating in this brief telephone call.

Follow Up: After you finish the behavioral counseling portion of the study, you will have three weekly follow-up telephone calls scheduled as part of your study participation (Weeks 9-11). Your final visit of the study will occur 4 weeks after study completion at Week 12.

Schedule of Procedures for Study Visits

Scheduled Procedures Week	S	R	1	2	3	4	5	6	7	8	12
Informed consent, demographics, medical and alcohol history, DSM-V	X										
Alcohol Dependence Scale; Fagerstrom Test for Nicotine Dependence; Illicit Drug Use Index; Childhood Trauma Questionnaire; Treatment Goals Checklist	X										
BAC, vital signs, Adverse events, Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test[1]	X	X		X	X						
Clinical Institute Withdrawal Assessment-Revised (CIWA)	X	X									
CBC w/diff, blood chemistry, UA	X		X								
GGT, UDS	X		X			X				X	X
ECG, Physical exam		X		X							
Plasma cortisol, ACTH		X	X	X		X				X	X
Mifepristone plasma concentration, return study medication			X								
Alcohol Craving Questionnaire (ACQ); Timeline Follow Back Interview (TLFB); Pittsburg Sleep Quality Index (PSQI); Beck Depression Inventory-II (BDI-II), State-Trait Anxiety Inventory (STAI), Pain Scale Concomitant Psychosocial Therapy, Clinical Global Impression (CGI)	X	X	X	X	X	X	X	X	X	X	X
End of Treatment Evaluation			X							X	
Neurocognitive Assessment		X								X	
Blood for pharmacogenetics		X	X								X
Saliva sample, dispense study drug, EtG/EtS		X									
Manual-guided counseling	X	X	X	X	X	X	X	X	X	X	

S=Screening Visit, R=Randomization Visit

[1] Females of child-bearing potential only, with serum pregnancy at Screening Visit and *urine at Randomization Visit, Week 2 and Week 3.*

Could I experience any side effects or discomforts?

Abnormal test results may cause you to experience anxiety and to seek additional medical services, and therefore may be a potential risk of your research participation.

All drugs can cause reactions or side effects. The most commonly occurring side effects reported in clinical trials using mifepristone are:

- Headache
- Dizziness
- Indigestion

These side effects are usually mild and of brief duration.

In the week after medication cessation, some subjects have developed a skin rash. The skin rash may be localized on a certain area of the body or it may be generalized. It may clear without treatment or may be treated with over-the-counter antihistamines and usually resolves within a few days. Please call your Study Physician to be evaluated if a rash occurs.

Although unlikely with one week of treatment, the package insert for long-term use of mifepristone lists adrenal insufficiency as a potential risk. Therefore, we are providing you with a study participant information card to keep in your wallet in case of medical emergency during your study participation.

There could be other side effects that we just don't know about yet and we do not know if the same side effects will occur, or if new side effects will emerge in persons who have a problem with alcohol

dependence. Since this is an investigational drug for alcohol dependence there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

There are no known allergic reactions from mifepristone but allergy is possible.

You should be cautious about operating machinery, including automobiles, until you are certain that taking mifepristone does not affect your ability to drive or work with machinery.

The placebo pill will be a pill that looks like real drug, but contains no active drug. Study drugs may contain lactose. People who are unable to digest lactose properly are called lactose intolerant. If you are lactose intolerant you might experience side effects such nausea, abdominal cramping, bloating or gas, after taking study drugs. These side effects are usually not dangerous and will stop when the medication is stopped. Please let the study coordinator know if you are lactose intolerant.

Alcohol Withdrawal
If you choose to join the study, you must agree to take study medication as prescribed and abstain from alcohol for four days in a row prior to starting study medication. This could put you at risk for alcohol withdrawal symptoms. If you do have alcohol withdrawal symptoms, you will be referred to a local detoxification center. The costs of detoxification will be your responsibility. If you are under the influence of alcohol at your appointment, which will be checked by an intoximeter, you will have to either stay in our office until your blood alcohol level goes down to .000, call someone to pick you up, or call a taxi to take you home at your own expense. If you are found to be impaired by alcohol at your study visit, the visit will have to be rescheduled for another time, and you will not be paid for that visit. Because your blood alcohol level may remain elevated for a period of time after drinking, it is recommended you do not drink the night before your appointment in order to attain a reading of .000.

Is there anything else I should know?

- If you are female, you will have a pregnancy test at screening, randomization and at the end of medication. You can't be in the study if you are pregnant or plan to get pregnant. Therefore, to participate in the study you must agree to use an effective form of birth control for the study duration and for 4 weeks thereafter.
- If you have been in another research study in the last month, you should tell the study doctor.
- You can't use any drugs or supplements without asking the study doctor.
- You can't give the drug to anyone else and you should keep it away from children.
- We may use information you give us to help find you in case you move. Any information (like your address or phone numbers) will be used only to help find you for follow-up studies.

Blood Sampling: You may feel pain or discomfort when the needle pokes your skin. There may be bruising, swelling, pain, or infection later at the puncture site, although this is unlikely. Dizziness and fainting are possible, but very unlikely. If you have ever felt dizzy or fainted while having blood drawn, you should tell the person drawing your blood. You might not get dizzy if you lie down. If these problems occur, you will be given proper treatment until you recover.

Abnormal Medical Test Results: Medical testing performed during your participation may increase the possibility of receiving an abnormal test result, for example, high blood sugar or elevated liver enzymes.

Medical tests performed within the protocol are for research purposes and are not intended to, and may not be suitable for, diagnosing a medical problem. Your medical results will be reviewed by a study physician. Abnormal results will be communicated to you by a research team member. If you decide to pursue medical follow-up, we will release the results to your physician with your written permission. In order for the Certificate of Confidentiality to protect sensitive information, the identity of the study will not be released to your physician along with the abnormal test results. If you do not have medical insurance, we will supply you with a list of medical service providers in the San Diego area that can be accessed for free or at little cost to you.

Abnormal test results may cause you to experience anxiety and to seek additional medical services, and therefore may be a potential risk of your research participation.

www.ClinicalTrials.gov

A description of this study is 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.

What's in it for me?

You may feel better after receiving study medications or counseling, but we cannot promise that you will. Other people who stop drinking may have better treatments someday because of your research participation.

Will I get paid?

Yes, you will be paid $25 for completing the screening visit, that amount will increase by $5.00 for each consecutive visit attended, but will return to $25 if a visit is missed and not rescheduled. The 4 weekly phone calls will be compensated at a flat rate of $10.00 each. Perfect attendance and participation in 4 phone calls will result in a total of $590.00 over the 12 weeks of study and follow-up. As part of our referral bonus system, you will be given 3 unique referral cards with your research ID number on them. Every individual you refer to this study that is successfully randomized into this study, will result in you earning a $50.00 bonus. All the person you refer has to do is bring the unique referral card you gave them to their first in-person visit so that we can associate their entry into the study with your referral. If you make 3 successful referrals, you stand to earn $150.00 in bonus money. It is important to know that these referral cards cannot be replaced if you happen to lose them or if you refer an individual who decides to not follow through with study participation. For this reason, it will be important for you to be careful with your cards and to refer people who you think are appropriate and interested in study participation. This referral system is completely voluntary and you do not have to participate in it if you are in any way uncomfortable with it. With the referral bonus system, you may receive up to a total of $740.00 over the course of the study.

Will it cost anything to be in the study?

Everything in the study is provided at no cost to you. If you choose to pursue medical follow-up for abnormal medical test results, the financial costs will not be paid by The Scripps Research Institute, they will be your responsibility.

What if I end the study early?
If you quit the study or are taken out early, you will not be paid for visits you have not completed. You may be asked to return for tests to be sure your health has not changed during the study.

The investigator can take you out of the study if you fail to follow study procedures or for other reasons

What other treatments could I take?
Instead of being in this study, you could take naltrexone (ReVia®), disulfiram (Antabuse®) or acamprosate (Campral®). These three drugs are the only FDA-approved oral medications for alcohol dependence.

What are my rights?

- You can call the staff to ask any questions about this study. The telephone number is listed at the top of this form.
- You can decide not to be in this study or you can quit after starting. Whatever you do, your medical care at Scripps will not be affected.
- If you have any questions about your rights, call the Scripps Office for the Protection of Research Subjects at (858) 678-6402. You should also read the *Experimental Subject's Bill of Rights,* which is the last page of this form.
- You do not have to be in this study. You still have all your legal rights whether you join the study or not.

What are my responsibilities if I join?
If you are in this study, you are expected to:

- Follow the instructions of the research staff
- Report any serious or unusual side effects to the study doctor
- Take study drugs as directed
- Keep your study appointments

What about confidentiality?
We have several ways to protect electronic data, in both technical ways, as well as by rules and physical security, just as we control access to your paper medical record. Using technology, we hide our computers on the network so that unauthorized viewers can't see them, and the computers that can be seen can only be accessed with unique passwords and authorization using "security certifications," data encryption in some instances and passwords. We also keep track of who opens what computer files. We give access to members of our research staff on a case-by-case basis for the specific purposes of having them enter data or to help us with your care and our research. We grant this access according to the same level staff would have to look at your medical and research paper files. Thus, we impose a set of standards to protect your information as it resides in our computers. In the very unlikely case that your genetic information was discovered by someone outside The Scripps Research Institute, there could be some risk of being identified as someone who has used abused alcohol. We will use every safeguard available to protect your confidentiality. We will keep your genetic information for approximately 10 years. However, you may withdraw from the study at any time and you may request that your sample be permanently removed if it has not already been used.

With our referral bonus system, we have taken every step to preserve your confidentiality. Referral cards will only have your research ID number on them, so if they are ever lost by you or the person you referred, there is no direct way of linking you to the card. Additionally, study staff will not discuss the relationship of participants in any way, and will not confirm the participation of an individual in this study. Finally, referral connections will be tracked by study staff for reimbursement purposes using only a participant's research ID number to preserve confidentiality and anonymity. Even with these safeguards in place, if you choose to participate in this referral system, you are disclosing your knowledge of this study to the individuals you chose to speak about it or refer to this study. In this way, we are not able to assure your confidentiality will be preserved by the individuals you chose to disclose your connection to this study with.

A new Federal law, called the **Genetic Information Nondiscrimination Act (GINA)**, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- This new Federal law ***does not*** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

There also may be other privacy risks that we have not foreseen.

The study doctor, the research staff, and the funding institution will keep your personal information confidential. Your medical records could be reviewed by agencies within the Department of Health and Human Services who evaluate and monitor research studies for their accuracy of findings as well as your safety and welfare. These agencies included the Office of Human Research Protection, the Food and Drug Administration (FDA) and National Institutes of Health (NIH).

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local, civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: disclosure that a child is being abused, or an indication of intent to hurt yourself or others.

What if I get hurt in the study?
You may call Dr. Shadan at (858) 752-2913 or call Dr. Beneze at (858) 271-2557 Monday through Friday, 8:00 a.m. to 5:00 p.m., if you get sick or injured while on this study, or have any questions about the medication (mifepristone). If you get sick or injured or have questions about the medication at night or on a weekend, you should page Dr. Shadan at (858) 752-2913 or seek treatment at an Urgent Care or Emergency Room facility. If you feel you need immediate attention, you should call 9-1-1. If you need

either medical care or urgent medical treatment as a result of your participation in the study, TSRI general liability insurance will cover these costs.

No money is available to pay you for time off from work. You are not giving up any of your legal rights by being in this study.

What's in it for the institution and the researchers?
The Scripps Research Institute and the study doctor are being paid to do this study by the National Institute on Alcohol Abuse and Alcoholism

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I agree to participate.

I have read the explanation of the study and understand it. The study has also been explained to me by Dr. Mason or a member of her research staff. I have had a chance to ask questions and have them answered to my satisfaction. I agree to take part in this study. I have not been forced or made to feel obligated to take part.

*I have read the attached **Experimental Subject's Bill of Rights**, which contains some important information about research studies. I must sign this consent form, the **Experimental Subject's Bill of Rights** and will be given a signed copy of each to keep.*

Printed Name of Subject	*Signature of Subject*	*Date*

Signature of person conducting the informed consent discussion	*Date*

Role of person named above in the research project

*EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

If I am asked to consent to be a subject in a research study involving a medical experiment, or if I am asked to consent for someone else, I have the right to:

Learn the nature and purpose of the experiment (also called "study" or "clinical trial").

Receive an explanation of the procedures to be followed in the study, and any drug or device to be used.

Receive a description of any discomforts and risks that I could experience from the study.

Receive an explanation of any benefits I might expect from the study.

Learn about the risks and benefits of any other available procedures, drugs or devices that might be helpful to me.

Learn what medical treatment will be made available to me if I should be injured as a result of the study.

Ask any questions about the study or the procedures involved.

Quit the study at any time, and my decision will not be used as an excuse to withhold necessary medical treatment.

Receive a copy of the signed and dated consent form.

Decide to consent or not to consent to a study without feeling forced or obligated.

If I have questions about a research study, I can call the contact person listed on the consent form. If I have concerns about the research staff, or need more information about my rights as a subject, I can contact the Scripps Office for the Protection of Research Subjects, which protects volunteers in research studies. I may telephone the Office at (858) 678-6402, 8:00 a.m. to 4:00 p.m. weekdays, or I may write to the Scripps Office for the Protection of Research Subjects c/o Scripps Clinic, Mail Stop CPB200, 4275 Campus Point Court, San Diego, CA, 92121.

By signing this document, I agree that I have read and received a copy of this Bill of Rights.

_____ _____

Signature of Subject or Legal Representative Date

*California Health & Safety Code, Section 24172