# COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

## YALE UNIVERSITY SCHOOL OF MEDICINE
## THE APT FOUNDATION
## Central Medical Unit

**Study Title:** Pilot study of galantamine and CBT4CBT to reduce post-taper relapse for MAT
**Principal Investigator:** Kathleen M. Carroll, Ph.D.

**Funding Source:** National Institute on Drug Abuse

**Invitation to Participate and Description of Project**

You are invited to take part in a research study designed to evaluate the effects of the medication *galantamine and computer based training for cognitive behavioral therapy CBT4CBT* to help prevent relapse to opioid use following taper off of methadone or buprenorphine among people with opioid use disorder. Galantamine has been approved by the Food and Drug Administration (FDA) for use in adults for other uses, but has not been approved by the FDA for treatment of opioid dependence or withdrawal. The use of galantamine is investigational for the purpose of this study, meaning that we are studying whether or not this medication is effective for helping to prevent relapse following a taper from methadone or buprenorphine. You have been asked to take part because you are an adult who has voluntarily requested to taper off from methadone or buprenorphine.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

**Description of Procedures**

Galantamine is a medication that has been approved for the treatment of mild cognitive problems (such as learning and memory in older adults with memory problems) and may improve response to CBT4CBT, a computerized cognitive behavioral therapy, that has been proved to be effective in several studies.

Treatment in this study will last for 8-10 weeks, with follow up visits 2 weeks, 1 month and 3 months after the end of the treatment part of the study and will take place at the Central Medical Unit (CMU) of the APT Foundation. Your participation will include: 1) the screening visit and physical exam, 2) a pretreatment evaluation, 3) taper off of methadone or buprenorphine over a 4 to 6 week period, 4) study medication daily during taper off methadone or buprenorphine (4-6 weeks) and for 4 weeks after you successfully complete the taper for a total of 8 – 10 weeks, 5) weekly meetings with the research team, 6) weekly CBT4CBT session for 8-10 weeks which you are free to complete on site at CMU or at home, 6) follow-up visits at 2 weeks, 1-month and 3-months following completion of the study.

If you agree to take part in this study, the following will happen:

***Screening Visit and Physical Examination****:* You will come in for a screening visit to see if you qualify for the study. This visit will include a review of the consent form and opportunity for you to ask questions. If you are willing to participate in this study and sign this consent form, you will be asked to complete questionnaires about your drug use and craving and to provide a urine and breath specimen for drug and alcohol testing. You will also be examined by Dr. Julia Shi, Medical Director of the CMU who will take a brief medical history and perform a physical exam. An electrocardiogram (to examine the health of your heart) and urine screening tests will be performed to aid the study physician in the decision as to whether it is safe for you to participate. The urine sample will be used for drug testing and pregnancy screening. We will also check your pulse, blood pressure, height and weight. If you are eligible we will schedule you for a Pretreatment Evaluation. This may occur immediately following your screening appointment.

***Pretreatment Evaluations***
Eligible individuals will meet with the Research Assistant to complete a baseline interview and self-report scales. You will be asked questions about your substance use (and cigarette smoking) as well as about your mood, your nerves, and current medications. You will also be asked to complete questionnaires about your drug use and craving.

***Randomization***
Following final confirmation of eligibility by Dr. Shi, you will be randomly assigned (using a computerized urn randomization program to balance treatment conditions) to receive either placebo (sugar pill) or galantamine for 4- 6 weeks during your taper off methadone/ buprenorphine and 4 weeks after completing taper for a total of 8-10 weeks. This is a double blind study, this means that neither you nor any member of the research team, including Dr. Shi, will know which medication you are receiving.

***Initiation of Taper*****:** Your doctor will begin to reduce your methadone/buprenorphine dose per standard CMU procedure. The taper will last from 4 to 6 weeks depending upon your methadone or buprenorphine dose at the beginning of the study.

***CBT4CBT Program****:* At the start of taper, you will be offered weekly CBT4CBT sessions. CBT4CBT is a computer-based program that teaches skills for stopping drug use and increasing coping skills, such as how to understand patterns of drug use, how to cope with cravings for drugs, how to refuse offers of drugs, and so on. The program consists of movies, quizzes, and other strategies for teaching these skills. You will receive a unique username and password to access the program and will be taught how to use the computer program by a staff member and will be asked to spend about 7 hours using the program (approximately one hour per week). Staff will be available at all times while you are using the program at the clinic if you have any concerns or questions about the computer program. A member of the research staff will check-in with you each week should you have questions or concerns. You will also be given the option to use this program at home or other locations on a secure website instead of using it at the clinic. You should be aware that access to the CBT program via wifi is free of charge, but if you choose to use a device (i.e., tablet, etc.) on a data plan outside of wifi you may accrue billable charges

which you will be responsible for. We will remind you via text to complete your computer modules on a weekly basis.

***Study Medication Phase:*** As you begin your taper off methadone or buprenorphine, you will begin the study medication. You will be randomly assigned to receive either placebo (a sugar pill) or galantamine (starting at 8 mg per day with an option to increase to 16 mg per day) for 8 – 10 weeks. It is important to take your study medication daily as prescribed. You will come to the clinic weekly to receive a week supply of your study medication, to complete brief questionnaires as well as urine and breath screening for drugs and alcohol. On the last day of your taper off methadone or buprenorphine there will be a blood draw to measure inflammatory markers and we will ask you to complete research questionnaires. You will continue to come to the clinic weekly for the next 4 weeks to meet with the research team, and receive weekly supply of study medication. At the end of the study medication phase there will be another blood draw and we will ask you to complete an endpoint interview. The medication you are taking will not change during the 8 – 10 weeks of treatment. Participation in this study includes taking the study medication (placebo or galantamine 8 or16 mg) by mouth, once a day, for a total of 8–10 weeks.

***Follow-Up Visits***: Two weeks, one month and again three months following the end of the 8-10 week study you will be asked to complete questionnaires, discuss your progress with study personnel and give a urine and breath sample. These visits will take about 1 hour.

The research team will use several methods of contact to keep in touch with you. We will ask you to provide us with phone numbers, e-mail addresses, current home and work addresses, and contact information of family and friends who may know how best to reach you, or to pass you a message to contact us. If we need to contact those individuals, the research team will not reveal any information about the study or your treatment (we will not ask about drug use or other problems).

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.

**Duration of Study**

Participation in this study will last approximately 8-10 weeks. After completion of the screening and physical exam visit, the pretreatment visit will be scheduled. If you are eligible, you will begin to taper off of methadone or buprenorphine following standard clinic procedures, this typically takes 4-6 weeks. When you start the taper, you will begin taking study medication and meet with a member of the research team weekly. Following completion of the taper, for the next 4 weeks, you will continue taking study medication and come to the clinic weekly to meet with a member of the research team. During this time you will complete weekly CBT4CBT computerized sessions. At completion of the taper and again after completion of the study medication phase you will have an endpoint interview. You will then be contacted at 2 weeks, 1 month and 3 months after completing study medication to have a follow-up visit.

The screening and physical exam visit will last about 2 hours. The pretreatment visit will last about 2 hours. Completion of CBT4CBT computerized sessions will take approximately 1 hour/week. Weekly visits during the 8 -10 weeks of study medication will last about 30 min.

Interviews at the end of taper and on the last day of study medication will take about two hours each. The follow-up visits, at 2 weeks, 1-month, and 3-months will last about an hour each.

**Risks and Inconveniences**

There are several risks involved with participating in this study, including risks associated with galantamine, study procedures, and loss of confidentiality.

All medications may cause side effects and there are several known risks and discomforts associated with galantamine. Your condition will be monitored closely by Dr. Shi, the Medical Director of the CMU, and other CMU medical staff. If Dr. Shi, CMU medical staff or you decide to stop your participation in the study due to unwanted experiences or side effects, you will receive appropriate follow-up care as determined by CMU staff.

1) Adverse Effects of galantamine

In this study, you may be taking galantamine, 8 or16 mg orally (by mouth). Galantamine is a generally well-tolerated medication and has a good safety profile in related populations at the 8 - 16 mg doses as proposed here. The most common side effects of galantamine are: include loss of appetite, weight loss, diarrhea, nausea, vomiting, light-headedness, fainting, or headache (generally in 5-15% of people). Other less common adverse events include slow or uneven heartbeat, heart failure, bloody or black, tarry stools, or vomiting of blood or material that looks like coffee grounds, severe stomach pain, and seizures (less than 2% of people).

For women of childbearing age: Since this research may have bad effects on a fetus and should not be done during pregnancy, it is necessary that a pregnancy test be done first. If the test is positive, you will not be included in this study. During your study participation, we will also do monthly urine pregnancy tests. Prior to entering the study, we will discuss with you, in detail, the need to avoid becoming pregnant and what precautions you should take. You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study. If you change your mind about becoming pregnant or regarding how you will avoid becoming pregnant, we ask you to notify us immediately.

2) Blood draws

Over the course of the study you will have a total of 3 blood draws, one at the time of your physical exam, one after you complete your taper and one when you complete the study medication. Each blood draw will be less that 50cc's and there will be no restrictions with regard to future blood donation. The blood drawing may cause some pain, bruising or rarely infection

3) Risk of Loss of Confidentiality

There is a chance that your personal information may inadvertently not be kept confidential. Some answers you give during the research visits (like whether you use illegal drugs) or results of your urine drug tests may put you at risk if other people find out. We will make every effort to insure your confidentiality. To keep what you say private, your study records will use a code number instead of your name. We will further protect your records by keeping all your materials in locked file cabinets only accessible by research staff and all computer files will be secure password-protected files only accessed by research staff. Your research records are kept separate from clinic records and will not be shared with any clinical program you are involved with. Only research staff will have access to your private information.

**Benefits**

You may benefit from participation in this study. However, given the investigational nature of this study, benefit cannot be guaranteed or promised. Information gained from this study may help other investigators have a better understanding of the treatment of substance dependence.

**Economic Considerations**

There are no costs to you for your participation in this study.

You will receive a $25 gift card for completing the screening visit and physical exam, a $25 gift card for completing the pretreatment visit. You may also choose to complete a CANTAB computer assessment for an additional $20 per timepoint (see below), however you must complete the first CANTAB in order to be considered for the other two timepoints. You will also receive $10 per week, during the 8 – 10 weeks while you are taking the study medication, for completing research questionnaires and $10 per week for urine toxicology screen, for a total of $160 - $200, $30 for completing the interview at the end of your taper, $35 for completing the interview at the end of the study medication, $40 for completing the 2-week follow-up visit, $45 for completing the one-month follow-up visit and $50 for completing the three-month follow up visit. If you are not able to complete a visit you will not be paid for that visit. You may receive up $510 in cash or gift cards if you complete all visits.

Subject Compensation Schedule

| Activity | Compensation Available | Form of Payment |
|---|---|---|
| Screening | $25 | Gift Card |
| Pretreatment | $25 | Gift Card |
| Optional CANTAB 1 | $20 | Cash |
| Weekly visits | $80 - $100 Total (@$10 a visit)<br>$80 - $100 Total @$10/urine drug screen | Cash |
| End of Taper Interview | $30 | Cash |
| Optional CANTAB 2<br>(Only if 1 is completed) | $20 | Cash |
| End of Study Medication | $35 | Cash |
| Optional CANTAB 3<br>(Only if 1 is completed) | $20 | Cash |
| Two-week Follow-up | $40 | Cash |
| One Month Follow Up | $45 | Cash |
| Three Month Follow Up | $50 | Cash |
| Total Available | $470 - $510 | |

**Treatment Alternatives/Alternatives**

You have the option of declining to participate in this study. Alternative treatments for opioid dependence are available. You are free to choose not to participate, and if you do become a subject, you are free to withdraw from the study at any time. If you withdraw it will not adversely affect your relationship with this clinic or the clinicians or doctors here. If you decide to withdraw, you will be referred to the regular evaluation and intake procedures and will receive treatment as usual at this clinic

**Investigator Conflict of Interest**

The Principal Investigator of this study, Kathleen Carroll, PhD, has been involved in the development, creation and testing of the CBT4CBT program. Therefore, she has a financial interest in the CBT4CBT program. This will not affect your treatment here or use of this program. If you have any questions or concerns regarding Dr. Carroll's financial interest you are encouraged to contact Dr. Carroll at (203) 737-1544 or the Human Research Protection Program (HRPP) office of Yale University at (203) 785-4688.

**In case of injury**

If you develop any mental or physical problems as a direct result of being in this study, we will refer you for treatment or provide it for you at the Central Medical Unit (CMU) of the APT Foundation. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. Your legal rights are not waived by signing this consent form.

**Confidentiality and Privacy**

If you decide to take part in this research study, you will be required to give us information about your substance use. Any of your identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission, with the following exceptions: We will disclose to appropriate authorities known or suspected abuse of a child or elderly person, or if you become a danger to yourself or others. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and address. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator, Kathleen Carroll, PhD. will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. All personal information will be coded and stored in a locked cabinet and any data stored on a computer will be password protected to further protect your confidentiality. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for the 1 year follow up period after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form for a minimum of 3 years after the study has ended and then will be destroyed.

The information about your health that will be collected in this study includes:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Information obtained during this research about:

- Laboratory test results
- The diagnosis and treatment of a mental health condition

Information about you and your health, which might identify you, may be given to

- Yale University School of Medicine
- APT Foundation
- Clinical Science Labs
- National Institute of Health (NIH). The research sponsor
- Members of the Human Investigations Committee or ethics Committee(s)
- Key Investigators
- Key Study Personnel
- Data and Safety Monitoring Board and others authorized to monitor the conduct of the study
- The US Food and Drug Administration (FDA); This is done so that the FDA can review information about the use of the drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

The research team can only give information about you to others for research with your permission. We will make every effort to insure your confidentiality. In all records of the study you will be identified only by a number. Your name will not appear in any publication or be released to anyone without your written consent. However, you should understand that there is a risk that you will be recognized by other participants or staff involved in the study, but this is no greater than the usual risk of identification that occurs in our usual treatment in this clinic. If you find this risk unacceptable you should not sign this consent form.

If you decide to take part in this research study, you will be required to give us information about your substance use and we will test you for drug use. This research is covered by a Certificate of Confidentiality (CoC) issued by the NIH. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The

researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The protection offered by the CoC does not stop us from voluntarily reporting information about suspected or known sexual, physical, or other abuse of a child or older person, or a participant's threats of violence to self or others. If any member of the research team is given such information, he or she will make a report to the appropriate authorities.
Because this research is sponsored by the Department of Health and Human Services through NIDA, staff from that and other DHHS agencies may review records that identify you only for audit or program evaluation. They cannot report anything that would harm you or other research subjects.

Even when a CoC is in place, you and your family members must still continue to actively protect your own privacy. If you voluntarily give your written consent for anyone to receive information about your participation in the research, then we may not use the CoC to withhold this information.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, by deciding to take part in a single or double blinded treatment study and sign this permission form, you will not be allowed to look at or copy your study related information until after the research is complete.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

**Voluntary Participation and Withdrawal**

You are free to choose not to participate, and if you do become a participant, you are free to withdraw from the study at any time. If you withdraw it will not adversely affect your relationship with this clinic or the clinicians or doctors here. If you decide to withdraw we can refer you to a clinic or doctor who can offer you treatment.

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments

The researchers may withdraw you from participating in the research if necessary only for not coming in for treatment or if you show signs of clinical deterioration and need more intensive care. Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital.

*Withdrawing Your Authorization to Use and Disclose Your Health Information*

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to Kathleen Carroll, PhD; 40 Temple Street., Suite 6C; New Haven, CT 06511. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

**Questions**

Please feel free to ask about anything you do not understand and please consider this research and the consent form carefully before you decide whether or not to participate. You may take as much time as necessary to think it over.

**Authorization and Permission**

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Printed Name of Subject:_____

Signature:_____

Date:_____

_____ _____
Signature of Person Obtaining Consent Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator Kathleen Carroll, PhD at (203) 737-1544. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.