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# MOTIVATIONAL INCENTIVES FOR ENHANCED DRUG ABUSE RECOVERY: METHADONE CLINICS

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# 1 LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| BSI | Brief Symptom Inventory |
| CRF | Case Report Form |
| CTN | clinical trial node |
| CTP | community treatment program |
| HIV | human immunodeficiency virus |
| IRB | Institutional Review Board |
| NIDA | National Institute on Drug Abuse |
| RA | research assistant |
| SUR | substance use report |
| THC | tetrahydrocannabinol |

## 2 PROTOCOL SUMMARY

**STUDY OBJECTIVES:** The purpose of the proposed research is to implement and systematically evaluate, in community treatment settings, motivational incentive procedures that have been well researched and have proven efficacious in a variety of treatment research clinics. The study will determine if motivational incentives along with standard care therapy is more effective than standard therapy alone for the treatment of patients using cocaine or methamphetamine and entering a substance abuse treatment program.

**STUDY POPULATION/ELIGIBILITY CRITERIA:** The study population will be drawn from patients entering methadone maintenance treatment and remaining in treatment for at least one month. Primary eligibility criteria for study entry is evidence of stimulant use (cocaine or methamphetamine) as determined by urinalysis test results. Eligible patients must submit at least one cocaine or methamphetamine positive urine within the two weeks prior to study entry.

**STUDY DESIGN:** The study utilizes a two group random assignment design. Thus, interested and eligible participant volunteers will be assigned to receive usual care or usual care supplemented by a motivational incentive program. The study lasts for 12 weeks, with follow-up interviews scheduled at 1, 3 and 6 months after study enrollment.

**USUAL CARE TREATMENT:** Those assigned to usual care will receive standard counseling procedures used at the CTP for 12 weeks. Participants assigned to the usual care condition will be expected to meet with the RA twice weekly to give urine samples and to participate in follow-up interviews, as scheduled.

**INCENTIVE PROCEDURES:** In addition to usual care services, those subjects in the motivational incentive group will be given the opportunity to receive tangible incentives twice weekly based on drug-free urine test results. Each time a participant tests negative for the primary target drugs cocaine, methamphetamine, amphetamines, and alcohol (via breathalyzer), they will be able to make recovery picks from the abstinence bowl. Some picks will result in no incentive award. Some picks will result in receipt of a “small” incentive such as a soda, candy bar or toiletry item. Yet other picks may result in receipt of a larger incentive such as a radio, walkman or gift certificate to a local restaurant, grocery or retail store. Clients and clinic staff will determine the specific incentives to be awarded within monetary guidelines specified in the protocol. The number of recovery picks escalates with consecutive weeks in which urine tests are negative for all 4 primary target substances. Bonus picks are also available at each incentive opportunity for urines that test negative for opiates. The maximum cash value of tangible incentives awarded to participants who remain continuously abstinent from all tested drugs will be approximately $400 per subject. Actual payout is expected to average $200 per subject or less, depending on the percentage of drug-free urines submitted.

**EFFICACY ASSESSMENTS:** Treatment retention of study subjects will be tracked and mean retention duration compared for the two study groups. Regular urine testing conducted during treatment will also be used to compare performance of incentive and control participants, as will data on counseling utilization. Primary source of data for establishing efficacy will be obtained from during treatment drug use data (percent stimulant-free urines submitted and longest

duration of stimulant-free testing). Follow-up interviews and urine testing will also be obtained from all subjects who sign informed consent, whether or not they stay in treatment for 12 weeks ("intent-to-treat" sample). Subjects will be assessed at all follow-up visits (1, 3, and 6 months) for: 1) drug use via full screen urinalysis and alcohol breathalyzer, 2) drug use via self-report, 3) HIV risk exposure, 4) employment status, 5) criminal activity, 6) gambling behavior, and 7) psychiatric symptoms. It is predicted that outcomes for those assigned to receive incentives in addition to standard care will be better than outcomes for those who receive standard care only. Specifically, those who receive incentives will have less drug use and criminal activity, more employment and fewer psychiatric symptoms.

**SUBJECT BENEFITS:** All study participants will receive compensation of $25 for each follow-up assessment completed. All participants may benefit from stopping their drug use during treatment and working toward life-style changes that are needed to sustain long-term abstinence. Those in the incentive condition may experience enhanced motivation to abstain and may benefit from the tangible incentives received.

## 3 BACKGROUND AND SIGNIFICANCE

Cocaine dependence is associated with high rates of unemployment, psychiatric disturbances, and criminal activity. Intravenous drug use is a leading cause of the spread of AIDS and other infectious diseases (Curran et al., 1988; Hser et al., 1993). Although substance abuse treatment can be effective in reducing drug use and related problems, treatment programs tend to have high rates of attrition and frequent relapses (Tims and Leukefeld, 1993). The implementation of effective, research-based treatments into standard clinical practice is central to our efforts to decrease illicit drug use and reduce the spread of AIDS.

One technique that is effective in improving outcomes of substance abusers is contingency management, or motivational incentives. The central tenets of this treatment are to: (a) arrange the environment such that substance use is readily detected; (b) provide tangible incentives when abstinence is demonstrated; and (c) extinguish drug use by withholding incentives when drug use is detected. Methadone programs sometimes employ incentives such as take-home privileges to reinforce abstinence. In treatment programs that do not use substitution medications, motivational incentive approaches have provided money (Shaner *et al.*, 1997) or vouchers, exchangeable for retail goods and services, upon submission of drug-free urine samples (Higgins *et al.*, 1993, 1994).

A series of studies have demonstrated that these motivational incentive procedures are more effective than standard treatments including disease-model therapy or intensive behavioral counseling without incentives. First, motivational incentive procedures that provide positive rewards tend to retain clients in treatment for longer periods of time than does counseling alone. For example, 75% of cocaine-dependent outpatients assigned to a voucher condition completed a 24-week trial compared with 40% in a no voucher condition (Higgins *et al.*, 1994). This study was conducted in a research-funded treatment program, and all clients received intensive (2 days per week) individualized counseling. A recent study found incentive procedures to be an effective add-on for enhancing retention of clients in community-based treatment programs as well. Twenty-two percent of clients completed 8 weeks of standard, outpatient treatment consisting of 12-step oriented groups, relapse prevention, coping skills training, daily planning, and recreational and vocational training. In contrast, 84% of clients who received the same standard treatment plus an opportunity to win prizes contingent upon non-drug behaviors completed treatment (Petry *et al.*, 2000). Thus, providing incentives retains clients in treatment.

Motivational incentive procedures are also effective in reducing drug use. Higgins *et al.* (1994) demonstrated that 55% of cocaine-dependent clients who received behavioral therapy plus vouchers for submitting negative urine samples achieved over 2 months of continuous cocaine abstinence in a 24-week trial. Only 15% of clients assigned to a behavioral therapy-only group maintained this period of abstinence. In randomized, controlled trials of opioid-dependent clients, money, voucher incentives or other clinic privileges provided contingent upon objective indicators of drug abstinence significantly reduced illicit drug use (Bickel *et al.*, 1997; Hall *et al*., 1979; Higgins *et al.*, 1986; Iguchi *et al.*, 1988; Kidorf & Stitzer, 1996; Magura *et al.*, 1988; McCaul *et al*., 1984; Milby *et al*., 1978; Silverman *et al*., 1996a; Stitzer *et al.*, 1980, 1982, 1984, 1986, 1989, 1992). For example, when submission of drug-negative urine samples was

reinforced with methadone take-home doses, 42% of urine specimens were drug-free, compared with an average of 8% during a baseline study phase (Iguchi *et al.*, 1988).

Motivational incentive procedures also are beneficial for reducing use of marijuana (Budney *et al.*, 1991), alcohol (Bigelow *et al*., 1975; Griffiths *et al.*, 1978; Miller *et al*., 1974; Miller, 1975; Petry *et al*., 2000), nicotine (Crowley *et al*., 1991; Roll *et al*., 1996; Schmitz *et al.*, 1995; Shoptaw *et al.*, 1996; Stitzer & Bigelow, 1982, 1983, 1984) and benzodiazepines (Stitzer *et al.*, 1982, 1992).

Importantly, Silverman and colleagues (1996b) and Higgins *et al.* (2000) by including control patients who received tangible goods independent of urine test results, have demonstrated that contingent delivery of the reinforcer, rather than just access to the reinforcer or greater retention in treatment, engenders reductions in drug use. Silverman *et al*. (1996b) randomly assigned cocaine-abusing methadone clients to one of two treatment conditions: (a) vouchers contingent upon submission of cocaine-free urine specimens, or (b) vouchers regardless of urine toxicology results. Clients in the non-contingent voucher group received the same overall amount of vouchers as those in the contingent group, and retention rates were similar for both groups. Of clients in the contingent voucher group, 47% achieved at least six weeks of continuous cocaine abstinence compared with 6% in the non-contingent group. Higgins *et al.* (2000) report similar results in cocaine-dependent outpatients; 42% of clients receiving vouchers contingent upon submission of cocaine-free urine samples achieved 10 or more weeks of continuous abstinence, compared with 17% of clients in the control condition.

Although voucher incentive programs are effective interventions for treating substance use disorders, community-based treatment programs have yet to implement these procedures. A number of criticisms of this approach have been raised, and one of the primary criticisms is cost. Voucher incentive treatments, the intervention with the most empirical support, are expensive to employ and manage. For example, in the Vermont and Johns Hopkins voucher-based programs (Bickel, 1997; Higgins *et al*., 1991, 1993, 1994; Silverman *et al.*, 1996b), each client can earn over $1,000 worth of goods during treatment, and average earnings are approximately $600 (Higgins *et al*., 1994; Silverman *et al*., 1996a, 1996b). These costs may preclude the use of this procedure in many community-based clinical settings.

Several strategies have been utilized to apply less costly incentives, rather than vouchers (see Petry, 2000, for review). Changes in methadone dose (Calsyn and Saxon, 1987; Stitzer *et al*., 1986), take-home privileges (Stitzer *et al.*, 1992), and continued treatment as opposed to administrative discharge (Dolan *et al*., 1985; McCarthey and Borders, 1985) have been used as reinforcers in methadone programs. While these reinforcers are not costly, they are only applicable within the context of settings that utilize substitution pharmacotherapies. Other strategies that have been proposed are to provide public assistance (Shaner *et al*., 1995), reduce fees for service (Amass *et al*., 1998), or establish a representative payee for clients receiving disability or other public support (Jerrel and Ridgley, 1995; Reis and Dyck, 1997; Spittle, 1991) and allow greater latitude in management of the individual's own finances when abstinence is achieved and maintained. While such techniques may be inexpensive once implemented, they require substantial involvement with each state's individual public welfare system and/or with each individual HMO or insurance carrier. Therefore, they may take several years to negotiate.

Another inexpensive approach is to specify an aversive consequence, such as informing an employer, legal authority or licensing board if drug use is detected. This technique has been found effective in maintaining long-term abstinence of substance-abusing health care professionals (Anker and Crowley, 1982; Crowley, 1984, 1986). However, it may be applicable only if the client is employed or is under legal supervision. Some individuals who may benefit from such a system may be unwilling to commit to it voluntarily. Other procedures are to have clients pay a large fee upon treatment entry, which is refunded if treatment is completed and abstinence maintained (Boudin *et al.,* 1977). This technique, however, is unlikely to entice substance abusers into treatment and is impractical in a primarily underprivileged population. In summary, these techniques, while innovative and effective, may not be readily applicable.

A benefit of vouchers is that, except for the issue of cost, they seemingly could complement any existing treatment structure. A strategy for making the voucher system less costly would be to provide lower amounts of incentives. A few studies have examined whether magnitude affects outcomes. Stitzer and Bigelow (1983, 1984) found that nicotine abstinence increased as a function of the magnitude of the reinforcer, ranging from $0 up to $12 per day for reduced carbon monoxide readings. Silverman *et al.* (1997) found that clients who were "treatment-resistant" at the standard voucher amounts achieved abstinence if the voucher amounts were increased approximately 10-fold.

A feature of the voucher incentive system that significantly increases the cost is the escalating nature of the vouchers. As clients achieve longer periods of abstinence, the amount of the voucher increases. By the end of the 12-week treatment period in Higgins' studies, for example, clients can earn up to $20 for a single drug-free urine specimen, plus a $10 bonus for every third consecutive negative specimen. Eliminating this escalating and bonus system and providing a constant rate of reinforcement may make the voucher system less expensive. However, a study by Roll and colleagues (1996) compared the escalating system to one that provided a constant rate of reinforcement. Both procedures provided equivalent total reinforcement. Although both schedules engendered greater abstinence than a yoked control condition, the escalating system resulted in longer periods of continuous drug abstinence. These results suggest that an escalating system is necessary for promoting the clinically relevant goal of continuous drug abstinence.

Escalating systems that incorporate a variable ratio schedule of reinforcement may be able to engender similar beneficial results while reducing costs of the incentive system. Petry and colleagues (Petry *et al.,* 2000) have recently completed a study which showed that a variable ratio schedule of reinforcement may be effective in retaining clients in treatment and reducing drug use. Rather than earning vouchers for each drug-free urine submitted, clients earned the chance to pick from a bowl and win incentives of varying magnitudes. The incentives that can be won range from small $1 items (choice of bus tokens, VA or McDonald's coupons) to large $20 items (choice of walkmans, gift certificates, watches, and phone cards), and jumbo items (choice of small televisions, stereos, and VCRs). This system is less expensive than the standard voucher system as only a proportion of qualifying drug-free urine samples are reinforced. This variable ratio schedule of reinforcement system appears to be a relatively inexpensive expansion of the voucher system, and one that may be well-suited to standard treatment settings.

## 4 STUDY OBJECTIVE

The purpose of this study is to implement and systematically evaluate in methadone community treatment settings, motivational incentive procedures that have been well researched and have proven efficacious in a variety of treatment research clinics. Specifically, the study will determine whether an incentive procedure that utilizes a variable ratio schedule of reinforcement will be effective in enhancing retention in treatment and reducing drug use across a range of drug-free community-based treatment programs. Based on existing research, we anticipate that the intervention will be highly effective and will produce impressive and clinically meaningful improvements in treatment outcome. Thus, the study will demonstrate the utility of contingent reinforcement to community-based practitioners and teach a new and useful therapeutic approach.

## 5 SUSTAINABILITY WITHIN THE CTP'S

Sustainability is one of several criteria that were considered in selecting protocol concepts for implementation in the Clinical Trials Network (CTN). Sustainability is an important consideration, given that one over-arching goal of the CTN is to improve treatment services nationwide by disseminating research-based interventions. The protocol described may not be fully sustainable as proposed, since cash-valued incentives will be offered that a typical community-based treatment program may not be able to afford to incorporate into their operating budget. Nevertheless, there are several ways in which this particular project should have sustainable impact that will improve services delivery.

First, the project will teach staff how to conceptualize and implement incentive models. Treatment staff will learn how to define and measure appropriate outcome targets and they will learn the principles that have been used for effective incentive intervention, such as immediacy and consistency of the procedure. Further, counseling and other treatment staff will be able to observe directly both the operation and the effectiveness of this approach with their clients. The role of incentive value or amount will be discussed with staff in terms of both efficacy and sustainability in order to stimulate creative thinking about development of lower cost incentives.

Second, the project will provide direct technical assistance for operation of a variable ratio incentive protocol. Programs will retain both the knowledge and the mechanics to continue operating such a program after the study ends. The technical assistance includes a user-friendly computer program that accepts urine data input, automatically tracks the duration of sustained abstinence from targeted drugs and outputs results of an escalating incentive schedule ideal for promoting sustained abstinence. Programs can keep and continue to use these items after the research program ends, when they may choose to offer affordable incentives of their own selection.

Third, it is expected that CTN research and training staff will work with community providers during the first research project in order to develop sustainable lower-cost incentive menus that can be implemented and tested in a subsequent study. This experience and input from the community clinics will be invaluable for developing such lower-cost alternatives.

Finally, the issue of sustainability will be addressed by cost-effectiveness analysis planned as part of the study evaluation, in which the cost effectiveness of incentive procedures will be compared with that of usual care. These analyses may provide guidance regarding patient subsets for whom incentive interventions are a more cost-effective strategy compared with usual care.

## 6 STUDY DESIGN

This initial study will utilize a parallel 2-group design, as shown below. Considerations in selection of this design for the first study were simplicity and relative ease of implementation. If this study supports feasibility and effectiveness of incentive interventions in community clinics, later studies may utilize more complex designs (e.g. 3-groups) to further explore the parameters of motivational incentive therapies.

**Group 1: No incentive** **Group 2: Drug abstinence incentive**

### 6.1 Primary Drug targets

**Primary incentive targets: cocaine, amphetamine, methamphetamine and alcohol**

Cocaine and methamphetamine were originally selected as the primary drug targets for the intervention, as these are arguably the most prevalent drugs in current use nationwide. Amphetamine is added because this is a closely related drug that will be included in commercial 5-panel test cups. In order to enhance acceptability and make the study more congruent with existing clinical practice, alcohol (i.e. negative breathalyzer reading) was also added as an additional primary drug target.

### 6.2 Bonus incentive targets: opiates

In methadone clinics, only opiates will be used as the bonus drugs. Clinicians will receive information on marijuana use by their patients, but marijuana is not included as a bonus drug for methadone settings. This is because marijuana is not traditionally included in these settings when determining drug-free status for clinic privileges such a take-home medication.

Testing positive on a bonus drug does not preclude receipt of incentives for primary drug targets.

## 7 CTP ELIGIBILITY CRITERIA:

In order to enter the study, clinics must have:

1. Projected average intake rate of at least 2 eligible study clients per week.
2. Projected minimum of 100 study clients to be enrolled at the site within one year.
3. Adequate space to accommodate research assistants and study protocol procedures including on-site urinalysis collection and testing.

4. Able to provide records of counseling attendance by individual clients (or institute system to obtain these data).

## 8 STUDY PARTICIPANTS

**Inclusion criteria:**

1. Recent admission to an opioid substitution (methadone maintenance) CTP.

   • Completed at least 4 weeks of maintenance at time of study entry

2. Evidence of cocaine or methamphetamine use

   • Minimum of one documented positive urine within 2 weeks of study entry.

   • For those exiting a controlled environment, any stimulant use within two weeks of entering the controlled environment

**Exclusion criteria:**

1. Unable to give informed consent (fails simple consent quiz)

2. Answers yes to question: "Are you in recovery from gambling? That is, have you stopped gambling because of previous gambling problems?"

## 9 PROJECTED STUDY SAMPLE SIZE: 400

One perspective on sample size was obtained by conducting a power analysis based on data from Piotrowski et al. (1999). This study implemented a complex incentive intervention at a community VA methadone clinic that targeted multiple drugs of abuse. Although the specific intervention was quite different from the one proposed in the current CTN protocol, this was an incentive study conducted in a community clinic with considerable variability in outcome. With probability of a Type I error set at 0.05 (alpha) and a Type II error set at 0.20 (Power = 0.80), and using a two-tailed test, it was determined that 130 subjects would be needed in the incentive and control groups, respectively, to obtain statistical significance on the measure percent drug negative urines (28.5% versus 16.3% during months 5 and 6).

Additional sample size estimates have been calculated based on two recently published voucher incentive studies, one of which did (Preston et al., 2000) and one of which did not (Downey et al., 2000) detect statistically significant effects of the voucher intervention being tested. Effect sizes for the primary outcome variable percent drug-free urines ranged from .16 to .19 with a mean of .18. This yielded sample size estimates of 110-153. In addition, these estimated sample sizes have been adjusted based on 10% to 20% increases in variability due to multi-site testing. As shown in the appended table, our projected sample size of 200 per group should allow us to detect between group differences of the magnitude previously observed with power = .80 and alpha =.05, even with a 20% increase in variability over single-site studies.

The projected sample size should allow us to detect a between-group difference of approximately 10-15 percentage points in percent drug negative urines at the 12-week follow-up. Base rates of cocaine or methamphetamine positive urines are likely to differ in methadone versus drug-free clinics. Studies in the literature suggest that rates of cocaine negative urines in study-eligible methadone patients will range from 20-35% (Downey et al., 2000; Preston et al., 2000; Silverman et al., 1998). In contrast, rates of cocaine and methamphetamine-free urines are likely to be 50% or greater for those who remain in drug-free treatment (Carroll et al., 1994; Hersh et al., 1998; Higgins et al., 1994; Rawson et al., 1995). This suggests that it will be especially important to meet study enrollment expectations in the drug-free clinics, since there may be greater outcome variability in drug-free than in methadone clinics associated with lower retention rates and higher absolute rates of drug-free outcomes in those participants who remain in treatment.

Actual total sample size will depend on the number of clinics who choose to participate as well as number of subjects recruited per site, and may be larger than 200 per group.

## 10 STUDY INTAKE RATE; SAMPLE SIZE PER CLINIC; ENROLLMENT PERIOD

In order to allow for the possibility of analysis at the individual clinic level, it is desirable that each participating clinic enrolls at least 100 subjects. (However, if more than 8 sites volunteer to participate, fewer subjects per site would be acceptable.)

The rate of intake into the study has implications for the study enrollment period and for workload management. If subjects are enrolled into the 12 week study at a rate of 2 per week, RA's will eventually be managing a study "workload" of 24 subjects and it will take approximately 1 year to enroll 100 subjects. At an intake rate of 3 clients per week, the study workload will be 36 clients and 144 study clients could be enrolled in one year. At an intake rate of 4 per week, the workload would be 48 and nearly 200 subjects could be enrolled in one year.

A one-year enrollment period seems reasonable, with sample size per clinic determined by subject availability. Projected enrollment at each clinic is 100 subjects.

## 11 STUDY PROCEDURES

### 11.1 Timeline

A time and events schedule of study activities is shown in Table 1. An outline of the study timeline follows:

1. Determination of study eligibility and randomization

2. Study intervention: 12 weeks

3. Follow-up evaluation: 1, 3 and 6 months after study intake.

## Table 1. Motivational Incentives Time and Events Schedule

| Activity | Screening | Enrollment | Treatment (week) | | | | | | | | | | | | Follow-up (months) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 6 |
| Standard treatment[1] | | | | | | | | | | | | | | | |
| Informed consent | X | | | | | | | | | | | | | | |
| Urine test (test-cup) | X | X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | |
| Alcohol Breathalyzer | | X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | X |
| Incentive Drawing | | X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | 2X | |
| Usual care urine testing[2,3] | | X | | X | | X | | X | | X | | X | | X | X |
| Drug-use[4] | X | X | | | | X | | | | | | | | X | X |
| BSI | | X | | | | X | | | | | | | | X | X |
| HIV risk exposure | | X | | | | X | | | | | | | | X | X |
| Gambling behavior | | X | | | | X | | | | | | | | X | X |
| Employment status[4] | | X | | | | X | | | | | | | | X | X |
| Criminal activity[4] | | X | | | | X | | | | | | | | X | X |
| HIV status | | X | | | | | | | | | | | | | |
| Demographics; DSMIV checklist | | X | | | | | | | | | | | | | |
| Contact information | | X | | | | | | | | | | | | | |
| Treatment history | | X | | | | | | | | | | | | X | X |
| Counseling utilization[3] | | | | | | | | | | | | | | | |
| Follow-up urine testing | | | | | | X | | | | | | | | X | X |

1. Occurs during the entire 12-week study.
2. Performed on alternative weeks during the treatment. May be started in week 2 and performed in weeks 4, 6, 8, 10, and 12.
3. Documented throughout the treatment according to participation.
4. From ASI at enrollment and follow-up CRF at other time-points

**11.2 Study intake procedures for methadone clinics**

Methadone clients will not begin the study until week 5 of treatment or later. It is anticipated that regular (at least biweekly) urinalysis results will be available during this time. Those eligible for the study will have at least one cocaine or methamphetamine positive urine documented during the two weeks prior to study intake.

Clients are approached for study intake by RA's or counselor. The study opportunity will be described to eligible enrollees. Those interested in participation will be escorted to the study intake site. RA or designated counselor will perform the following procedures:

1. Describe study

2. Obtain informed consent

3. Conduct common assessment intake battery (see section 14)

4. Conduct stratification

   Subjects will be stratified on two variables prior to random assignment:

   a) presence versus absence of any target stimulant drug in urine

   b) presence versus absence of bonus drug (opiate) in urine.

5. Conduct randomization

   Randomization will take place at each site independent of other sites. Thus, stratification by site is not necessary. Stratification and random assignment will be computerized using the dynamic balanced randomization procedure (Signorini et al., 1993).

6. Conduct incentive procedure for those clients assigned to incentive condition who test drug-negative at intake. Remind these clients when they will be eligible for their next recovery pick

7. Discuss urine results in relation to study procedures:

   Those in incentive condition testing drug negative will be encouraged to remain negative and reminded of the subsequent recovery pick opportunities.

   Those in incentive condition testing drug positive will be encouraged to stop using so they can earn recovery picks as soon as possible and reminded that they can begin earning picks the next time they come into the clinic.

Those in no incentive condition will be encouraged to become or remain drug-free in order to take full advantage of their time in treatment .

8. Allow clients to choose one large incentive for intake bonus.

9. Initiate caserecord for new participant; enter intake data

Whenever possible, all procedures will be completed on the day the client is approached about study participation. If necessary, clients can return the following day to finish intake. In this case, another urine will be collected for use as the first study urine, and this will be counted as the study intake day.

**11.3 Study drop-out criteria**

Clients will be considered active in the study throughout the three months following study intake independent of clinic attendance frequency, provided they remain enrolled at that clinic. Subjects assigned to the incentive condition are eligible for incentive procedures whenever they come in to the clinic so long as they are currently enrolled for treatment in that clinic. Thus, clients may come to the clinic to leave a urine and participate in incentives even if they do not participate in counseling. Research staff will make every reasonable attempt to notify counselors that a particular client who they want to see has come in.

Clients who have been discharged or terminated from treatment cannot participate in incentive procedures. A uniform drop-out criteria will be adopted by participating clinics. It is anticipated that this criteria will be no face-to-face contact for 30 days (subject to approval by CTP's).

**11.4 Sample collection and testing procedures**

***On-site urine testing***

Study participants will be expected to give urines twice weekly throughout the 12-week study (total of 24 urines including intake urine). It is recommended that the first urine be collected on Monday and the second on Thursday.

Clients who are absent on the day of scheduled urine collection can give a sample the next time they come to the clinic. Any two samples given within a week on non-consecutive days will qualify for participation in incentive procedures. Special arrangements for urine collection on unscheduled days can be arranged for individuals who have excused absences or emergencies.

***Sample validity***

It is recommended that all urine collections be observed by a same-sex observer. However, it is recognized that this will not always be possible. The test cups to be used for urine testing have temperature strips included. Criteria for a valid urine will be indicated by the

temperature strip (e.g. above 92 and below 98 degrees Fahrenheit). A further validity check will be provided by Adultacheck, a commercially available test strip that indicates normal ranges for creatinine, pH, gluteraldehyde and nitrates.

Participants whose urine does not pass validity checks will need to give a second sample, if they wish. Otherwise, the sample will be counted as missing (and positive for purposes of incentive procedures).

***Testing methods***

Urine testing methods will be uniform across clinics, as specified by the protocol. A 5-panel test cup will be utilized. The drug panel includes cocaine, amphetamine, methamphetamine, morphine and marijuana (THC). Purchase of urine testing supplies will most likely be responsibility of Node study coordinators under pricing structure negotiated by the CTN. Aside from incentive procedures, no clinical decisions will be based on these test results.

***Breathalyzer testing***

Breathalyzer testing will be performed at each study visit. If the clinic owns a breathalyzer and routinely conducts testing, this equipment may be utilized. In most cases, a new breathalyzer will be purchased as part of research support. Those qualifying for incentive must read 0.00.

**11.5 Variable ratio incentive procedures**

Clients randomly assigned to the incentive condition will be able to participate in an incentive procedure each time they test negative for cocaine, amphetamine, methamphetamine and alcohol. Two methods are described below- an abstinence bowl and a computer-based incentive award procedure. It is preferable for all study clinics to use the same method. Therefore it is anticipated that . It is preferable for all study clinics to use the same method. Therefore it is anticipated that a choice will be made prior to protocol implementation of one method or the other after discussion with participating CTP's.

The primary advantage of the computer-based method is that it may reduce the association between abstinence incentive procedures and other gambling behaviors in which clients may participate. Another advantage is that it should reduce the "carnival" atmosphere that has been a focus of objection by some nodes. A third significant advantage is that use of the computer simplifies protocol implementation and avoids any potential problems with client manipulation or tampering.

The primary advantage of the abstinence bowl method is that it minimizes distrust on the part of the participant since s/he directly participates in determining outcome of the incentive procedure. A second advantage is that it may facilitate a positive celebratory atmosphere surrounding the otherwise grim and difficult process of drug abuse recovery.

***Characteristics of the abstinence bowl***

Node study coordinators will be responsible for purchasing appropriate vessels for recovery picks. These can be any glass or plastic container of suitable dimensions.

***Contents of the abstinence bowl***

CTN will supply coded chits for use in recovery picks. There will be 500 chits supplied for the abstinence bowl. Fifty percent of the chits will say "good job" and will not result in an incentive award. 41.8% of the chits will result in a small incentive, 8% will result in a large incentive and only a very small percentage (0.2%) will result in a jumbo incentive. Chits should be placed on a table in the sequence drawn and remain there until all recovery picks are completed and data has been entered. Chit replacements can be obtained from national study coordinator should any be lost or damaged.

***Security of the abstinence bowl***

To prevent tampering, the bowl should be kept in a locked cabinet along with the tangible incentives overnight and whenever it is not in use.

Study coordinator should inventory chits once per month to ensure the proper number, probability distribution and coding.

***Recovery pick methods***

Study subjects should pick a chit from the bowl the appropriate number of times for each drug-free urine submitted. A computer program supplied by CTN will assist staff in determining the correct number of recovery picks based on history of drug-free tests. Whenever possible, these recovery pick events should take place in the presence of the study client's counselor. RA or designated counselor is responsible for recording the results of the pick procedure, for delivering the appropriate incentive and for recording the incentive(s) selected. Clients initial or sign for each incentive received.

***Computer-based incentive method***

For this option, the data management software will be programmed to simulate the incentive probability schedule utilized for the abstinence bowl. Thus, client will press a button the appropriate number of times, as calculated on the basis of urine testing history, and the computer will determine (using random probability schedules) and show results of each simulated recovery pick opportunity.

***Escalating Schedule of recovery picks for primary drug abstinence***

Clients in the incentive group will earn at least one recovery pick for each sample submitted that tests negative for the primary drugs: cocaine, amphetamine, methamphetamine and provided a negative breath alcohol reading is obtained. The number of picks allowed at each

urine collection will escalate with consecutive week of negative testing on primary drugs. Specifically, an additional recovery pick is added for each consecutive week that the participant tests negative for cocaine, amphetamine, methamphetamine and alcohol.

| Study week | Number of recovery picks for primary drug abstinence |
|---|---|
| 1 | 1 |
| 2 | 2 |
| 3 | 3 |
| 4 | 4 |
| 5 | 5 |
| etc | |

Missing or positive samples result in reset to 1 in number of recovery picks for the next negative sample submitted.

The escalating schedule is designed to sustain long periods of abstinence, and as such, the highest rates of reinforcement are scheduled late in the protocol for continuously abstinent participants. In order to counteract discouragement from the low reinforcement rate expected early in the escalating draw protocol, a single $20 bonus incentive will be given after two consecutive weeks of abstinence from primary target drugs. This bonus incentive can only be received once during the study; if a client re-sets and starts the escalating schedule over again, no bonus incentive will be available.

***Bonuses for drug-free panel - opiates.***

Bonus recovery picks will be available at each testing opportunity. This is in addition to the escalating number of recovery picks for the primary drugs described above. As previously described, the bonus pick is based on opiates for methadone maintained participants. Participants can earn two bonus picks for each urine free of bonus target drug (opiates). To earn a bonus pick, clients must also test negative for all of the primary target drugs (cocaine, amphetamine, methamphetamine and alcohol) that day.

***Storage and display of tangible incentive***

Tangible incentives will be stored in a durable locking cabinet. Size of the cabinet should be suitable to display items listed below. CTN will provide information about cabinet options; these will be purchased by node coordinators. RA or designated counselor(s) is responsible for keeping cabinet full, keeping inventory of contents, tracking expenditures and incentive awards to individual clients. and soliciting suggestions from clients and counselors on cabinet contents.

***Suggested content of tangible incentives- number, type***

The tangible incentives represent part of the active ingredient of this intervention, and thus need to be defined in the protocol. However, CTP's also have latitude in selecting specific

incentives to offer. Guidelines are given below as to the value and content of small, large and jumbo incentive categories. Each study site will be expected to keep an inventory of their incentive stock and incentive awards; this inventory will be facilitated by a computer software program that will be linked to protocol management software.

Jumbo incentive items (average $80 value)
Generally consist of electronic goods, small appliances or larger valued gift certificates to desirable restaurants, grocery stores and retail outlets. 2-3 jumbo prizes should be on display at all times.

Large incentive items (average $20 value)
Generally consist of watches, walkmans, gift certificates to a variety of local restaurants and retail stores, clothing items, an AA Blue Book, etc.
10-15 should be on display at all times.

Small incentive items (average $1 value)
Generally consists of bus passes, candy bars, food items, sodas, toiletries and gift certificates to food outlets (Dunkin Donuts, McDonalds, Subway). 75 should be available at all times. . It is also recommended that some incentives with $5 value be stocked and that clients who receive multiple $1 awards be allowed to take a $5 prize in exchange.

***Maximum earnings***

The maximum cash value of tangible incentives awarded to participants who remain continuously abstinent from all tested drugs will be approximately $400 per subject. Actual payout is expected to average $200 per subject or less, depending on the percentage of drug-free urines submitted.

## 12 ROLE OF COUNSELORS IN THE PROTOCOL

It is the intent of the protocol to involve counselors wherever possible in order to provide additional support for participation and success of their study clients. Specific roles will be determined at individual CTP's. Among the possible roles are the following:

- Witness the informed consent procedure whenever possible.
- Include study urine testing results in clinical feedback and treatment planning
- Be present at recovery picks whenever possible
- Receive regular reports on client progress in the study
- Encourage clients to continue providing urine samples and to remain abstinent from all chemical substances during treatment
- Suggest tangible incentives for the cabinet.
- After appropriate training, operate the incentive program in order to provide backup coverage to RA's
- Work with clients to build life-style changes during periods of abstinence

- Provide suggestions regarding very low or no-cost incentives that may be implemented after the study ends.

## 13 FOLLOW-UP PROCEDURES

Follow-ups will be conducted at 1, 3 and 6 months after study intake on an intent-to-treat sample of those who were randomized into study conditions. A brief assessment battery will be administered (see below) and a urine collected. Participants who complete these procedures will receive compensation at a rate of $25 for each interview.

**Successful follow-up will require active subject tracking procedures.**

Contact information will be obtained at intake- names, addresses and phone numbers of 3 people who "will know where we can reach you".

A reminder letter will be sent two weeks prior to scheduled interview requesting the participant call the office.

If person fails to call prior to scheduled day, contacts are telephoned repeatedly in an attempt to talk to the participant and messages are left for the participant to call or come in.

If no contact has been made by the scheduled date, then additional letters are sent to contact addresses and attempts to contact by telephone continue as well and additional information sought as to their whereabouts.

Individuals who have moved or have been difficult to contact may be interviewed over the phone. At that time, those who still reside in the area should be reminded that they can get their money if they come in to give a urine sample. This often results in an in-person contact.

These procedures have resulted in 95% interview completion rates.

## 14 STUDY ASSESSMENT BATTERY

A battery of information will be collected at intake and at each follow-up contact. Intake battery will include the ASI Lite, Methadone treatment information, DSM IV Checklist, Services Utilization Report, Health Risk Behavior Survey, Gambling behavior survey and Brief Symptom Inventory. Shown below is the information to be collected in CRF's; information to be collected at intake only is so indicated.

***Demographics*** (intake only)
Age, Gender, Race, Educational attainment, Marital status,

***Methadone Treatment Information***
Methadone dose at study entry, Days in treatment at study entry,
Methadone dose on last day of study participation

***DSMIV Checklist*** (intake only) To characterize drug dependence profile**.**

***Contact information*** (intake only)

Names, addresses and phone numbers of 3 people who will know where to find you and who we can contact to get messages to you.

***Services Utilization Report*** *(administered at intake, 3 and 6-month follow-ups only)*

Treatment episodes in past 3 months
- days of methadone maintenance
- days of outpatient drug-free
- days of residential treatment
- days of outpatient detoxification
- days of residential detoxification
- Number of visits to an emergency room

***Recent drug use***

Urine testing:

Test cup result (opiates, cocaine, amphetamine, methamphetamine); breathalyzer reading.

Self-report: Days of use in the last 30 (from ASI lite)
- opiates, cocaine, methamphetamine, alcohol, marijuana, sedatives

***HIV status*** (intake only; note that clinics may be exempted from asking this question if local laws require reporting)
- Positive, negative, don't know

***HIV risk exposure*** (12-item HIV Risk Behavior Survey)

***Employment*** (from ASI lite at enrollment or follow-up CRF)
- Current employment status (full time; part time)
- Days of work in the past 30
- $ earned for work in past 30

***Criminal activity*** (from ASI lite at enrollment or followup-CRF)
- Days of criminal activity in past 30 (drug dealing included)
- Money earned for criminal activity in past 30 days

**Medical, family/social and psychiatric status** (ASI lite; intake only)
- Days troubled by problems

***Gambling behavior***
- Days spent money on gambling in past 30 (state lottery included)
- Amount of $ spent on gambling in past 30 days

***Psychiatric symptoms*:** Brief Symptom Inventory (BSI)

## 15 OTHER PRE-STUDY AND DURING STUDY DATA TO BE COLLECTED

### 15.1 Pre-study client retention and drug use

Research staff will be charged with obtaining from clinic records information about overall clinic retention rates during the 6 months prior to study start. When possible, information about drug use profiles of entering clients will also be obtained in order to calculate stratified retention rates by drug use characteristics. This information will be used to determine whether overall clinic retention rates change over time as research is introduced.

### 15.2 Counseling utilization

The research assistant, in collaboration with project coordinator and clinic staff, will be charged with setting up a system to track counseling utilization. The data desired is number of individual (15 minutes or more) and group counseling contacts per week for each study subject. Ideally, the clinic will already have a system for tracking this utilization data. In cases where a utilization tracking system is not currently in place, models will be suggested based on systems used in other participating CTP's.

## 16 ANALYSIS PLAN

This section enumerates outcome measures and presents the statistical approaches that will be used to describe the data set and test study hypotheses.

### 16.1 Primary during-study outcomes

Because the intervention targets stimulant drug use, the most sensitive measures for detecting intervention effects are likely to be measures of stimulant drug use observed during treatment. Therefore, two primary outcome measures will be defined:

a) Percent of submitted urines cocaine, amphetamine and methamphetamine-free

b) Longest duration of abstinence from primary target drugs (cocaine, amphetamine, methamphetamine, alcohol)

### 16.2 Secondary during study outcomes

A variety of additional outcome measures will be collected during treatment and analyzed for between-group differences. These measures include:

**Retention**

Time from initial intake until last face-to-face contact censored at 12 weeks

**Urinalysis**

Percent of scheduled urines submitted during 12 week study period
Percent of breathalyzer tests reading 0.01 or higher
Percent of submitted urines free of opioids and marijuana
Longest duration of totally drug-free testing

Percent of patients achieving 4 and 8 weeks of abstinence:
a. from primary target drugs
b. from all tested drugs

**Counseling utilization**

Total number of group and individual sessions received
Mean number of group and individual sessions per week during weeks of participation

### 16.3 Follow-up outcomes

The primary follow-up outcome is abstinence from stimulant drugs (cocaine and methamphetamine in the intent-to-treat sample at 1, 3 and 6 month follow-up time points.). Abstinence is defined as no stimulant use reported in the past 30 days and a stimulant negative urine. In addition, percent of stimulant negative urines alone will be used as an outcome measure at these time points.

Additional outcomes derived from urine testing and ASI interviewing data obtained at each follow-up time point include:

Percent of patients abstinent (negative urine/breath test and no reported use in the past 30 days) from alcohol, from opiates, from marijuana, and from all targeted drugs of abuse.

Days of use in the past 30 for each drug and for alcohol
Days of criminal activity in the past 30 days
Days paid for work in the past 30 days
Days spent money on gambling in past 30 days
HIV risk exposure score
Psychiatric symptom score(s)

### 16.4 Data analysis plans

**Descriptive statistics**

Frequencies will be run and examined for evidence of sparseness for categorical data and for non-normality (using plots, examination of skewness, kurtosis etc.) for continuous variables. Where sparseness exists in categorical variables, we will collapse as necessary to produce sufficient cell sizes. Where non-normality is evident, variables may be transformed. Outliers may be recoded or omitted if necessary. Wherever the statistics that are proposed below assume normality, we recognize that non-parametric alternatives may be necessary.

**Time-to-event variables**

Survival analysis will be used to assess "time to an event" variables, for example, treatment retention. Survival analysis can be used to assess whether the incentive or usual care group differ in assessing time to the last face-to-face contact. We define the "event" of interest as "leaving treatment." Leaving treatment is defined as occurring whenever a subject fails to complete the entire treatment period. The log rank test or Cox proportional hazard models will be used to identify a difference between the treatment and control groups. Cox regression will be used to test whether other independent variables affect retention. The primary statistic of interest will be hazard ratios with 95% confidence intervals.

**Continuous and dichotomous summary variables**

For summary variables using continuous data (e.g. percent of negative urines; longest duration of abstinence), we will use t-tests for simple analyses and multiple regression if it is necessary to control for baseline or other covariate differences. For summary variables using dichotomous data (e.g., percent of patients achieving 30-day abstinence at follow-up or achieving 4 or 8 weeks of abstinence during treatment), we will use chi square with relative risks and 95% confidence limits for simple comparison of treatment groups. If it is necessary to control for covariates, logistic or Poisson regression will again be used.

**Repeated measures variables**

For continuous variables that are measured either during treatment (e.g. at each follow-up time point), classical repeated measures analysis of variance would be possible if missing data is non-existent or minimal. If missing data is a problem, then methods of analysis used for mixed linear models will be used. These methods allow for missing data with repeated measures. For continuous or dichotomous variables measured at several time points (e.g. follow-up outcomes), we propose using GEE. GEE is a powerful analytic method that is used to correct for correlation among observations within subjects in a repeated measures design. Odds ratios and 95% confidence limits will be produced to represent differences between the treatment groups and to estimate the effects of other variables. It may be possible that there is decay over time in treatment effects. Focusing on only one time point (e.g. end-of-treatment), we propose to compare treatment and control groups using chi square and compute relative risk and 95% confidence limits. To adjust for covariates and possible site differences, logistic regression analysis will be used to assess treatment effects. While logistic regression provides accurate estimates of statistical significance, the method tends to produce inflated estimates of risk when prevalence of an outcome is high. Poisson regression may be used to produce more accurate estimates of risk relative risk).

## 16.5 Other statistical issues

**Replacement of missing data**

In general, data replacement should not be necessary since statistical techniques have been selected that accommodate data sets with missing data. For the measure "longest duration of abstinence", a single missed urine/breath test will be tolerated and replaced by a negative result if both surrounding tests for that drug are negative. In all other cases (one or both surrounding tests are positive for that drug or more than one consecutive test is missing), the sample result is replaced by a positive.

**Baseline Comparability of Sites**

It is important to evaluate the comparability of sites with respect to potential confounders. Categorical methods of analysis (e.g. cross tabulations, chi-square) will be used to compare sites for qualitative data. ANOVA will be used to test for homogeneity of the sites for continuous data. If a statistically significant difference is found, a "site" term will be included in any subsequent analysis. If sufficient power exists, we may perform stratified analysis by sites.

**Baseline Comparability of Treatment and Control Groups**

Categorical methods of analysis (e.g. cross tabulations, chi-square) will be used to compare treatment and control groups for qualitative data. T-tests will be used to test for homogeneity of the treatment groups for continuous data. If a statistically significant difference is found, terms representing the covariate will be included in any subsequent analysis.

## 17 STUDY HYPOTHESES

### 17.1 Primary hypotheses: During treatment data

1) Incentive participants will have a higher percentage of urines testing negative for cocaine and methamphetamine than no incentive (as percent of urines collected; as percent of expected urines).

2) Incentive participants will have longer average durations of documented cocaine and methamphetamine-free urines than no incentive participants.

### 17.2 Primary hypothesis: Follow-up data

A higher percentage of incentive than no incentive participants will have verified abstinence from cocaine or methamphetamine (negative urine and no use reported in past 30 days)

### 17.3 Secondary hypotheses: During treatment data

1) Incentive participants will have longer treatment retention than no incentive participants.

2) Incentive participants will have a higher percentage of urine and breath tests negative for all other drugs of abuse (opiates, marijuana, and alcohol combined) during the study compared with no incentive (as percent of urines collected; as percent of expected urines)

2) Incentive participants will receive a higher mean number of counseling hours per week than no incentive participants.

### 17.4 Secondary hypotheses: Follow-up data

1) A higher percentage of incentive than no incentive participants will test negative for all drugs of abuse and alcohol
2) Incentive participants will report less HIV risk exposure than no incentive
3) Incentive participants will report less criminal activity than no incentive.
4) Incentive participants will have lower scores on the BSI.
5) Incentive participants will have greater utilization of outpatient treatment services.
6) Incentive participants will have less utilization of detoxification and ER services.
7) There will be no differences between groups on measures of gambling.
8) There will be no differences between groups on measures of employment.

## 18 HUMAN SUBJECTS

A minimum of 400 and as many as 1000 individuals applying for treatment at community drug abuse clinics will participate in this study. Recruitment for the study will take place during the clinic intake process. Inclusion criteria ensure that the study sample are cocaine or methamphetamine users. The sample is inclusive of community treatment participants; the only exclusion criteria proposed is inability to comprehend the consent form, based on clinical judgement of acute psychosis or intoxication.

### 18.1 Risks

The risks of this study are minimal and are described below. Adverse events will be reported only for death, hospitalization and increase in gambling behavior, as defined below.

Dissatisfaction with study assignment. One risk is that participants randomly assigned to the no incentive condition will be dissatisfied with their assignment. This is a risk common to many randomized clinical trials, particularly where interventions cannot be blinded. The risk is explained as part of the consent procedure, and those unwilling to take the risk of assignment to control condition can refuse to participate. Experience of the Co-lead Investigator, who has conducted similar trials in community clinics, is that assignment dissatisfaction has not been a major problem.

Drug use following receipt of large prizes. Participants randomly assigned to the experimental incentive group will be able to earn small, large and jumbo incentive items under a variable ratio schedule as rewards for submitting drug-free urines. There is some risk that clients who have been abstinent would return to drug use following receipt of a large ($20) or jumbo ($80) prize. This is included as a risk due to concern that study patients may sell prize items and use the money to purchase drugs. The percentage of large and jumbo prize awards that are followed by drug use (i.e. a positive urine at the next study visit) will be reported, and compared if possible with return to drug observed on occasions when only small prizes or no prizes have been received. It should be noted that any detrimental effect of the protocol with regard to stimulating relapse is self-limiting, as clients can no longer earn incentives while actively using drugs.

Marked increase in gambling behavior. The variable ratio schedule proposed includes an element of chance, and there is some concern that this will stimulate gambling behavior in those who have a problem with this type of impulsive behavior. It should be noted that there is no evidence to support such a concern. Further, the variable ratio incentive procedure itself could not be defined as gambling. It does not require the volunteers to put up their own money, nor is there any chance that volunteers could benefit excessively or lose their own money as a result of participating successfully in the incentive program. There is a chance that an individual with a gambling problem in remission could be stimulated to resume gambling. For this reason, compulsive gambling in remission has been added as a study exclusion criteria. There is also a chance that individuals who tend to engage in excessive gambling and who abstain from drug use during the study would have more disposable income to spend on gambling. For this reason, gambling behavior will be monitored at study follow-up points. A substantial increase in self-reported gambling behavior at 1, 3 and 6 months compared with baseline will be reported as an adverse event. The changes needed to trigger an adverse event evaluation is an increase of 10 days or more per month on which gambling occurred (e.g. from 10 to 20 days), a 50% or greater increase in the reported amount of money spent on gambling and an absolute amount spent of at least $100 per month. Any subject who meets these criteria will be given a clinical interview regarding their gambling behavior in relation to other changes in life circumstances. The adverse event report will include a judgement by the clinician regarding the extent to which the behavior change might have been protocol-related. Information about gambling behaviors reported by study subjects will be provided to counselors so that they can work on this independent behavior problem with their clients, as appropriate. Subjects may be withdrawn from the study protocol and referred for specialized gambling treatment if clinically indicated.

Hospitalization. An adverse event will be reported for any hospitalization episode. Drug overdose requiring medical intervention will be tracked separately. Overdose is a serious risk among drug abusers in general, but may be of particular concern when patients have abstained for any substantial period of time.

### 18.2 Benefits

All study participants will benefit by receiving intensive urine monitoring during the study and participation in paid follow-up interviews. Those assigned to the incentive condition may benefit by stopping their drug and alcohol use during treatment. As a consequence, they may be better able to make the life-style changes that will sustain abstinence beyond the study.

### 18.3 Informed consent

The study will be described by research or counseling staff and informed consent will be obtained prior to participation. The consent form will be witnessed by a member of the clinical or research staff.

### 18.4 Confidentiality

In order to make the study useful to clinical staff, some information collected by researchers including urine test results may be made available to clinical staff at the program

where the volunteer is enrolled. If the CTP decides to share information, this should be stipulated in the consent form. Information collected about study participants will not be available outside the treatment clinic. The confidentiality of data transferred to node or national data management sites will be protected by using only unique study number identifiers; no names will be included in data files. Study number codes linking names with numbers will be retained at the local treatment sites and central data management sites. Any hard copy data or name-number codes stored at any sites will be kept in locked filing cabinets. Research staff will not reveal the identity of participating clients to anyone outside the treatment clinic. Data and identifying information will be further protected by a NIDA Certificate of Confidentiality.

**18.5 Risk/benefit ratio**

Overall, the risk/benefit ratio appears highly favorable for this study.

## 19 SIGNATURES

### INVESTIGATOR (S)

I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol; deviations from the protocol are acceptable only with a mutually agreed upon protocol amendment with the IRB approval. I also agree to report all information or data in accordance with the protocol.

| **Typed Name** | **Signature** | **Date** |
|---|---|---|
| _____ | _____ | _____ |
| Primary Investigator | | |
| _____ | _____ | _____ |
| Subinvestigator | | |
| _____ | _____ | _____ |
| Subinvestigator | | |
| _____ | _____ | _____ |
| Subinvestigator | | |

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