Buprenorphine and the Treatment of Opioid Addiction

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Illicit opioid addiction, which is no stranger to the HIV-infected population, is a complex illness. It is characterized by compulsive, at times uncontrollable drug craving, seeking, and use that persist even in the face of extremely negative consequences. For many people, opioid addiction becomes chronic, with relapses possible even after long periods of abstinence.

Because opioid addiction has so many dimensions and disrupts so many aspects of an individual’s life, treatment for this illness is never simple. Effective drug abuse and addiction treatment programs typically incorporate many components, each directed to a particular aspect of the illness and its consequences.

Three decades of scientific research and clinical practice have found that opioid maintenance is a very effective approach to opioid-addiction treatment. Extensive data show opioid-addiction treatment to be as effective as treatments for most other similarly chronic medical conditions. However, for opioid-addiction treatment to be effective, it must be readily available. Because individuals who are addicted to opioids may be uncertain about entering treatment, taking advantage of opportunities when they are ready for treatment is crucial. Potential treatment applicants can be lost if treatment is not immediately available or is not readily accessible. In turn, there has been significant interest in incorporating opioid-addiction treatment into the primary care of individuals, particularly those being treated for HIV infection and/or other comorbidities.

With the passage of the Drug Addiction Treatment Act of 2000 and the recent approval of buprenorphine for the treatment of opioid addiction, primary care clinicians now have the ability to closely follow and treat their opioid-addicted patients. To help clinicians better understand this option, which has become a highly effective opioid-addiction treatment approach in France, Dr. Sharon Stancliff of the New York State Department of Health AIDS Institute was invited to the January 2004 PRN meeting to share her expansive knowledge of heroin addiction, methadone maintenance treatment, and the hopes of buprenorphine as a component of opioid addiction therapy.

Heroin

Heroin is processed from morphine, a naturally occurring substance extracted from the seedpod of the Asian poppy plant. Heroin is usually sold as a white or brown powder or as a sticky black substance and goes by a litany of street names, including “dope,” “smack,” “chiva,” “H,” “manteca,” “junk,” and “Mexican black tar.”

Heroin is usually injected, snorted, or smoked. Typically, a heavy heroin user may inject up to four times a day. Intravenous injection provides the greatest intensity and most rapid onset of euphoria (7 to 8 seconds), while intramuscular injection produces a relatively slow onset of euphoria (5 to 8 minutes). When heroin is snorted or smoked, peak effects are usually felt within 10 to 15 minutes. Although smoking and snorting heroin do not produce a “rush” as quickly or as intensely as intravenous injection, they are still addictive methods of heroin use.

Soon after injection (or inhalation), heroin crosses the blood–brain barrier. In the brain, heroin is converted to morphine and binds rapidly to opioid receptors. Abusers typically report feeling a surge of pleasurable sensation, a “rush.” The intensity of the rush is a function of how much drug is taken and how rapidly the drug enters the brain and binds to the natural opioid receptors. Heroin is particularly addictive because it enters the brain so rapidly. The rush is usually accompanied by a warm flushing of the skin, dry mouth, and a heavy feeling in the extremities, which may be accompanied by nausea, vomiting, and severe itching.

Following the initial euphoria, the user may go “on the nod,” a vacillating state of wakefulness and drowsiness. Mental functioning becomes clouded due to the depression of the central nervous system. Cardiac function slows. Breathing is also severely slowed, sometimes to the point of death in the event of an overdose. Heroin overdose is a serious risk on the street, particularly when people mix drugs or use it for the first time following a period of abstinence.

Long-Term Effects of Heroin Use

One of the most detrimental long-term effects of heroin is addiction itself. Addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use, and by neurochemical and molecular changes in the brain. Heroin also produces profound degrees of tolerance and physical dependence, which are also powerful motivating factors for compulsive use and abuse. “As with abusers of any addictive drug, heroin abusers gradually increase the amount of time and energy spent on obtaining and using the drug,” Dr. Stancliff said. “Once they are dependent, the heroin abusers’ primary purpose in life becomes seeking and using drugs.” At the same time, tolerance also develops and the user is rarely able to achieve the euphoria and is instead using the drug simply to avoid symptoms of withdrawal.

Physical dependence develops with repeated use of the drug. With physical dependence, the body adapts to the presence of the drug and withdrawal symptoms occur if use is reduced abruptly. Withdrawal may occur within a few hours after the last time the drug is taken. Symptoms of withdrawal include restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flushes with goose bumps (“cold turkey”), and leg movements. Major withdrawal symptoms peak between 24 and 48 hours after the last dose of heroin and subside after about a week. However, some users have shown persistent withdrawal signs for many months. Opioid withdrawal is not fatal to otherwise healthy adults, but it can cause death to the fetus of a pregnant woman dependent on licit or illicit opioids.

Medical consequences of heroin injection include scarred and/or collapsed veins, bacterial infections of the blood vessels and heart valves, abscesses and other soft-tissue infections, and liver or kidney disease. Lung complications—including various types of pneumonia and tuberculosis—may result from the poor health condition of the user as well as from heroin’s depressing effects on respiration. Many of the additives
Antagonist (Naloxone) for opioid addiction was serendipitously discovered by analgesic. The potential use of methadone as a treatment was developed prior to World War II in Germany as an analgesic. Methadone, an opioid, is a synthetic compound that essentially replaces the opioid receptors in the brain. Methadone occupies these receptors and is the stabilizing factor with weakness of the mind and spirit and everything to do with opiate receptors and endorphins.

Heroin releases an excess of dopamine in the body and causes users to need an opiate continuously occupying μ opioid receptors in the brain. Methadone occupies these receptors and is the stabilizing factor that permits methadone patients to change their behavior and to discontinue heroin use.

Taken orally once a day, methadone suppresses narcotic withdrawal for between 24 and 36 hours. The dose of methadone dispensed depends on the goal of administration, whether it’s detoxification or maintenance therapy. Withdrawal from methadone is much slower than from heroin. As a result, it is possible to maintain a patient on methadone without harsh side effects. Many methadone maintenance treatment (MMT) patients require continuous treatment, sometimes over a period of years (if not a lifetime).

According to the American Methadone Treatment Association, approximately 20% of the estimated 810,000 heroin-dependent persons in the United States receive MMT. At present, the operating practices of clinics and hospitals are bound by regulations established by the U.S. Food and Drug Administration that restrict the use and availability of methadone. Additionally, most States have laws that control and closely monitor the distribution of this medication.

**Methadone Maintenance**

Methadone, an opioid, is a synthetic compound that was developed prior to World War II in Germany as an analgesic. The potential use of methadone as a treatment for opioid addiction was serendipitously discovered by Drs. Vincent Dole and Marie Nyswander in the early 1960s (Payte, 1991). Attempting to treat six long-term heroin users, Drs. Dole and Nyswander found that methadone allowed the patients to function normally without mood swings that typically accompany heroin withdrawal. Subsequent investigations by Drs. Dole, Nyswander, and others found that, in sufficient doses, methadone was able to reduce cravings and to block the ability of heroin to produce euphoria, thereby making the use of heroin less desirable.

In essence, much of the opiate dependency research that was kicked off in the 1960s can be credited with a shifting of attitudes: that heroin addiction and its treatment is a medical problem, not a moral or political problem. This was also the first time anyone postulated that addiction was a metabolic disease, which ultimately led to the discovery—first by Drs. Dole and Nyswander—that addiction has little to do with weakness of the mind and spirit and everything to do with opiate receptors and endorphins.

**New York City has long been a hotbed of heroin activity in the United States.** According to Dr. Blanche Frank of the New York State Office of Alcoholism and Substance Abuse Services, the current prevalence of heroin use in New York State is approximately 200,000 users (Frank, 2000). For New York City, with approximately 80% of the State’s heroin users, the current estimate is about 160,000. “It’s believed that the prevalence of heroin use is actually increasing in New York State,” Dr. Stancliff added.

As stated above, heroin can be injected, snorted, or inhaled. While heroin has long been synonymous with injection drug use, the intranasal route has become a much more frequent mode of use in recent years. The availability of high-purity drug has encouraged intranasal use of the drug and allows users to avoid the transmission of diseases promoted by unsterile intravenous injections. There is also a reigning misperception that intranasal use of heroin, as opposed to intravenous use of the drug, is less addictive. According to data cited by Dr. Frank, injection of heroin declined from 71% to 39% between 1988 to 1998, whereas inhalation of heroin increased from 25% to 59% during this ten-year period.

Heroin use in the United States has historically gone through periods of rising and falling consumption. Since the early 1990s, not only has nationwide heroin use increased in terms of the total number of users, but use patterns have also changed. Heroin has spread from traditional markets in the inner city into wealthier suburbs and smaller cities and towns across the country. Particularly worrisome is the increase in the numbers of young people trying heroin, risking addiction. The combination of higher heroin purity, lower prices, and ready availability has brought an increase in the number of new, younger users. As has been seen in New York State, users throughout the United States are attracted by the purer heroin now available, which can be smoked or snorted instead of being injected.

The most recent estimate of the heroin-dependent population in the United States is 980,000. This figure was derived from data in a 1999 study sponsored by the Office of National Drug Control Policy that was designed to determine the expenditure habits of heroin users in the United States. Another estimate, extrapolated from data on overdose deaths, number of applicants for treatment, and number of heroin users arrested, places the heroin addicted population between 750,000 and 1,000,000.
The Office of National Drug Control Policy has reported that, among outpatients receiving MMT, weekly heroin use decreased by 69% (Office of National Drug Control Policy, 1998). Patients were no longer required to live a life of crime to support their habit, and criminal activity decreased by 52% among these patients. Full-time employment increased by 24%. In a 1994 study of drug treatment in California, researchers found that rates of illegal drug use, criminal activity, and hospitalization were lower for MMT patients than for patients in any other type of drug treatment program.

The Drug Abuse Treatment Outcome Study (DATOS) conducted an outpatient methadone treatment evaluation examining the long-term effects of MMT (Hubbard, 1997). The pretreatment problems consisted of weekly heroin use, no full-time employment, and illegal activity. One-year follow-up data showed a decrease in the number of weekly heroin users and a reduction in illegal activity after MMT.

The Office of National Drug Control Policy also reports that MMT costs approximately $13 per patient per day and is considered a cost-effective alternative to incarceration. In fact, MMT has a benefit-cost ratio of 4:1, meaning $4 in economic benefit accrued for every $1 spent on MMT.

MMT is not, however, a cure for heroin addiction. As explained by Dr. Stancliff, 80% to 90% of methadone patients who stop MMT will return to heroin use. “Methadone is a treatment, it is not a cure,” she said. “Heroin cravings persist long after successful detox and can kick in after a long period of methadone maintenance, if methadone is stopped.”

A noteworthy problem with MMT is its restricted access. MMT is one of the most monitored and regulated medical treatments in the United States. “Methadone is generally only available in methadone clinics,” Dr. Stancliff explained. “This often means daily trips to the clinic. And there are many parts of the United States where clinics are not available or do not have slots open to accept new patients. Where clinics and slots are open, many heroin users do not enter methadone programs, probably because of the restrictions.”

### Buprenorphine

**The drug addiction treatment act of 2000 (DATA 2000), a component of the Children’s Health Act of 2000, permits physicians who meet certain qualifications to treat opioid addiction with Schedule III, IV, and V narcotic medications that have been specifically approved by the Food and Drug Administration for that indication. Such medications may be prescribed and dispensed by waived physicians in treatment settings other than the traditional opioid treatment program (e.g., methadone clinics) setting (see sidebar on page 32 for information on how qualifying physicians may obtain a waiver to practice opioid addiction therapy using buprenorphine).**

The passage of DATA 2000 paved the way for buprenorphine to make its debut as an addition to methadone as a therapy for heroin addiction. Buprenorphine, a derivative of thebaine, is an opioid that has been marketed in the United States as the Schedule V parenteral analgesic Buprenex. In 2002, based on a reevaluation of available evidence regarding the potential for abuse, diversion, addiction, and side effects, the U.S. Drug Enforcement Agency reclassified buprenorphine from a Schedule V to a Schedule III narcotic.

In October 2002, England-based Reckitt Benckiser received FDA approval to market a buprenorphine monotherapy product, Subutex, and a buprenorphine/naloxone combination product, Suboxone, for use in opioid-addiction treatment. The combination product is designed to decrease the potential for abuse by injection. Subutex and Suboxone are currently the only Schedule III, IV, or V medications to have received FDA approval for this indication.

The FDA approval of these buprenorphine formulations does not affect the status of other medication-assisted opioid-addiction treatments, such as methadone and levo-alpha-acetyl-methadol (LAAM). [Editor’s note: Roxanne Laboratories, the manufacturer of LAAM, has notified the FDA of its plan to discontinue production of this product. Production was halted in January 2004, with distribution continuing until the inventory is depleted. Discontinuation was based on increasing reports of severe cardiac-related adverse events.] Only buprenorphine can be dispensed for the treatment of opioid addiction outside of an opioid treatment program; methadone must still be administered in the setting of an opioid treatment program.

Suboxone, a sublingual tablet, comes in two dosage forms: 2 mg buprenorphine/0.5 mg naloxone and 8 mg buprenorphine/2 mg naloxone. Subutex, also a sublingual tablet that does not contain naloxone, is available in 2 mg and 8 mg strengths.

Buprenorphine is an opioid partial agonist. While buprenorphine is an opioid—which can produce typical opioid agonist effects and side effects such as euphoria and respiratory depression—its maximal effects are less than those of full agonists like heroin and methadone. Buprenorphine produces sufficient agonist effect to enable opioid-addicted individuals to discontinue the misuse of opioids without experiencing withdrawal symptoms. The agonist effects of buprenorphine increase linearly with increasing doses of the drug until, at moderate doses, they reach a plateau and no longer continue to increase with further increases in dose—the “ceiling effect.” Thus, buprenorphine carries a lower risk of abuse, addiction, and side effects compared to full opioid agonists. In fact, in high doses and under certain circumstances, buprenorphine can actually block the effects of full opioid agonists and can precipitate withdrawal symptoms if administered to an opioid-dependent individual while a full agonist is in the bloodstream.

“Because buprenorphine is a partial agonist, it is expected to have a lower street value than either heroin or methadone,” Dr. Stancliff commented. “For a person who is dependent on an opioid and is high at the time of taking buprenorphine, symptoms of severe withdrawal will...”

### FIGURE 2. Bioavailability of Different Formulations of Buprenorphine

The absolute bioavailability of different formulations of buprenorphine. By definition, intravenous buprenorphine reaches 100 percent availability. In comparison, intramuscular buprenorphine reaches about 70 percent availability, and sublingual solution and tablets reach approximately 25 percent to 50 percent availability.

Source: The Danya Learning Center (http://www.danyalearningcenter.com)
kick in. However, for a person who is dependent on an opioid and is in withdrawal, sublingual buprenorphine provides relief. For the occasional opioid user, injecting buprenorphine can result in a high. The naloxone included in the tablet will be active if injected and it will attenuate the high.

Buprenorphine has poor oral bioavailability and moderate sublingual bioavailability. Formulations for opioid-addiction treatment are in the form of sublingual tablets. “If buprenorphine is swallowed, it has very poor activity,” Dr. Stancliff added. “Therefore, this drug is much safer to keep in a home with children who might inadvertently swallow it.”

Safety and Side Effects
Because of its Ceiling Effect and Poor Bioavailability, Buprenorphine is safer in overdose than opioid full agonists (e.g., methadone). The maximal effects of buprenorphine appear to occur in the 16 to 32 mg dose range for sublingual tablets. Higher doses are unlikely to produce greater effects.

Respiratory depression from buprenorphine (or buprenorphine/naloxone) overdose is less likely than from other opioids. There has been no evidence of organ damage with chronic use of buprenorphine, although increases in liver enzymes have been reported in a few instances. Likewise, there is no evidence of significant disruption of cognitive or psychomotor performance with buprenorphine maintenance dosing.

Information about the use of buprenorphine in pregnant, opioid-addicted women is limited; the few available case reports have not demonstrated any significant problems due to buprenorphine use during pregnancy. Suboxone and Subutex are classified by the FDA as Pregnancy Category C medications.

Side effects of buprenorphine are similar to those of other opioids and include nausea, vomiting, and constipation.

Therapy with Buprenorphine
Ideal candidates for opioid-addiction treatment with buprenorphine are individuals who have been objectively diagnosed with opioid addiction, are willing to follow safety precautions for treatment, can be expected to comply with the treatment, have no contraindications to buprenorphine therapy, and who agree to buprenorphine treatment after a review of treatment options. There are three phases of buprenorphine maintenance therapy: induction, stabilization, and maintenance.

The induction phase is the medically monitored startup of buprenorphine therapy. Buprenorphine for induction therapy is administered when an opioid-addicted individual has abstained from using opioids for 12 to 24 hours, depending on the half-life of the opioid used, and the individual is in the early stages of opioid withdrawal. If the patient is not in the early stages of withdrawal—if he or she has other opioids in the bloodstream—then the buprenorphine dose could precipitate acute withdrawal.

Induction is typically initiated as observed therapy in the clinician’s office and may be carried out using either Suboxone or Subutex, dependent upon the clinician’s judgment. “Observed therapy is preferred, but circumstances may vary,” Dr. Stancliff pointed out. “A test dose is given and follow-up, every one to three days, is necessary to titrate up to maintenance dosing.”

The stabilization phase begins when the patient has discontinued or greatly reduced the use of his or her drug of abuse, no longer has cravings, and is experiencing few or no side effects. The buprenorphine dose may need to be adjusted during the stabilization phase. “Most patients can be stabilized on 12 to 24 mg,” Dr. Stancliff said. “Because of the ceiling effect, few patients will be on a 32 mg or higher dose.”

Because of the long half-life of buprenorphine, Dr. Stancliff explained, “some patients can switch to buprenorphine dosed every two or three days.” Frequent medical visits are recommended, although the actual frequency of these visits is up to the clinician and the patient. “When clinicians are trained to prescribe buprenorphine and follow patients, urine testing for opioids is recommended but is not required by law,” she said.

The maintenance phase is reached when the patient is doing well on a steady dose of buprenorphine (or buprenorphine/naloxone). The length of time of the maintenance phase is individualized for each patient and may be indefinite. The alternative to going into (or continuing) a maintenance phase, once stabilization has been achieved, is medically supervised withdrawal, or detoxification. “Detoxification takes place over a period of four to eight days,” Dr. Stancliff pointed out. “The dose ranges from 4 to 16 mg a day. We might start the detoxification using 4 mg on the first day, up the dose to 8 mg on the second day, increase it to 10 mg on the third day, decrease it to 8 mg on the fourth day, and complete the detoxification course with 4 mg on the fifth day. Additional medications are usually not needed. But it is very important to note that no particular detoxification regimen has been shown to be more likely to lead to long-term abstinence.”

The Clinical Trials Experience
Buprenorphine has been evaluated as a treatment for opioid addiction in a number of clinical trials. In the first study reviewed by Dr. Stancliff, a Swedish study published last year in The Lancet, 40 volunteers who had been dependent on opioids for at least a year—but did not fulfill Swedish legal criteria for MMFR—were randomized to receive either daily buprenorphine (16 mg sublingually for 12 months) or a tapered six-day regimen of buprenorphine followed by placebo (Kakko, 2003). All patients participated in cognitive-behavioral group therapy to prevent relapse, received individual counseling sessions, and provided urine samples three times a week for analysis. The primary endpoint for the study was one-year retention in the treatment program.

One year after entering the study, 75% of the individuals receiving buprenorphine and 0% of the individuals receiving placebo were retained. Urine screens—looking for illicit opiates, stimulants, cannabinoids, and benzodiazepines—remained negative in 75% of the buprenorphine patients, compared to 0% of placebo recipients. Also of note, four patients in the placebo group, versus no patients in the buprenorphine group, died before the completion of the study.

Several studies in the United States have suggested that buprenorphine may be more effective for those patients who would be comfortable on lower doses of methadone (10 mg to 60 mg). But data have also been published by an Australian team that randomized 405 opioid-dependent individuals to receive either buprenorphine or methadone over a 13-week treatment period in a double-blind, placebo-controlled trial (Mattick, 2003). During the first six weeks of the study, patients were dosed daily. From weeks seven to 13, individuals in the buprenorphine group received double their initial dose on alternate days. The primary endpoints in this study were treatment retention and illicit opioid use as determined by urinalysis. Self-reported drug use, psychological functioning, HIV-risk behavior, general health, and subjective ratings were secondary outcomes.

Methadone was superior to buprenorphine in terms of retention over the 13-week period; approximately 10% fewer patients were retained on
buprenorphine compared to methadone. The authors of the study suggested that this poorer retention could be tied to too-slow induction onto buprenorphine. However, there were no significant differences in morphine-positive urines, or in self-reports of heroin or other illicit drug use, between the two groups. The majority (85%) of the buprenorphine patients transferred to alternate-day dosing were maintained on alternate-day dosing.

There is little data involving HIV-infected individuals receiving buprenorphine as a component of opioid-addiction treatment, although there was one such study conducted in France. Between October 1995 and May 1998, the Manif 2000 cohort study enrolled 467 individuals infected with HIV via injection drug use. All patients were at least 18 years of age and had CD4+ counts of at least 300 cells/mm3 prior to enrollment. Of the 164 patients taking antiretroviral therapy, 34.8% took buprenorphine for patients with drug users not receiving buprenorphine (65%). However, these observations were not significantly lower among non-adherent patients. After adjustment by logistic regression, non-adherence was associated with younger age, alcohol consumption, frequency of negative life events during the prior six months, and active drug use. However, injection drug users undergoing buprenorphine treatment reached higher levels of adherence (78%) than active injection drug users (42%) and former injection drug users not receiving buprenorphine (65%). However, these observed differences did not reach statistical significance.

There are important considerations to keep in mind when prescribing buprenorphine for patients with HIV and other comorbidities. For example, in one study discussed by Dr. Stancliff, increases in AST and ALT levels were documented in patients with hepatitis taking buprenorphine (Petty, 2000). Four cases of severe hepatitis have also been reported after injection of buprenorphine (Berson, 2001). There is also a possible relationship between buprenorphine and hyperlactatemia in HIV-infected individuals receiving antiretroviral therapy (Marceau, 2003). “However,” Dr. Stancliff noted, “this was a small study and did not control for concurrent HCV infection.”

As for buprenorphine-antiretroviral drug interactions, it’s important to note that buprenorphine is metabolized by the liver via the cytochrome P450 3A4 enzyme system. Unfortunately, few formal studies have been completed to date. “The fact that buprenorphine is metabolized by CYP3A4 suggests possible interactions with protease inhibitors and non-nucleoside reverse transcriptase inhibitors,” Dr. Stancliff said. According to one in vitro study reviewed by Dr. Stancliff, ritonavir (Norvir) is the most potent inhibitor of buprenorphine metabolism, followed by indinavir (Crixivan), and saquinavir (Invirase; Fortovase) (Iribarne, 1998). In light of the suggestive but limited data, Dr. Stancliff stressed that clinicians need to be alert for potential interactions, especially with boosted protease inhibitor regimens employing ritonavir.

Conclusion
IN SUMMARIZING HER REVIEW OF BUPRENORPHINE, DR. STANCLIFF reiterated that it is the first modality of its kind to move addiction treatment into the primary care setting. “This is a very important distinction that sets buprenorphine apart from other approaches, such as methadone maintenance therapy. This could translate into greater access to addiction treatment for those who need it, particularly those who don’t have access to or are reluctant to join a program at a methadone clinic. It may also bring patients into care before various comorbidities have an impact. Finally, it may increase the use and response to HIV treatment.”

So, You Want to Prescribe Buprenorphine?

The Drug Addiction Treatment Act of 2000 (DATA 2000) enables qualifying physicians to practice medication-assisted opioid addiction therapy with Schedule III, IV, or V narcotic medications that have been approved by the FDA, specifically for this purpose (e.g., buprenorphine). To practice opioid addiction therapy with buprenorphine, physicians must meet certain criteria and must notify the Center for Substance Abuse Treatment—CSAT, a component of the Substance Abuse and Mental Health Services Administration (SAMHSA)—of his or her intent to begin dispensing or prescribing this treatment. This Notification of Intent must be submitted to CSAT before the initial dispensing or prescribing of opioid therapy.

The Notification of Intent must contain information on the physician's qualifying credentials and other requirements, including the capacity to refer patients for appropriate counseling and that no more than 30 patients are to be treated with buprenorphine at one time. To practice buprenorphine-assisted opioid-addiction therapy, a licensed physician (MD or DO) must meet any one or more of a number of qualifying criteria. These include: Holding a subspecialty board certification in addiction psychiatry from the American Board of Medical Specialties (ABMS); holding an addiction certification from the American Society of Addiction Medicine (ASAM); holding a subspecialty board certification in addiction medicine from the American Osteopathic Association (AOA); or completing no fewer than eight hours of training that is provided by the ASAM, the American Academy of Addiction Psychiatry, the American Medical Association, the AOA, the American Psychiatric Association, or any other organization deemed appropriate for this purpose.

The criteria and procedures for filing a Notification of Intent, along with a comprehensive review of buprenorphine-assisted opioid-addiction therapy, are available through the SAMHSA website: http://buprenorphine.samhsa.gov/bwns.

References