JOINT MEETING OF THE ANESTHETIC AND LIFE SUPPORT DRUGS ADVISORY COMMITTEE AND THE DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

October 21 and 22, 2010

Background Package:
Postmarketing Studies of OxyContin (oxycodone ydrochloride controlled-release) Tablets and Embeda (morphine sulfate extended-release with a sequestered naltrexone hydrochloride inner core) Capsules to Assess Whether Product-Specific Properties Intended to Discourage Misuse and Abuse Actually Result in a Decrease in the Risks and Their Consequences

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FDA CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF ANESTHESIA, ANALGESIA, AND RHEUMATOLOGY PRODUCTS

M E M O R A N D U M

DATE: September 23, 2010

FROM: Bob A. Rappaport, MD
Director
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II, CDER, FDA

TO: Chair, Members and Invited Guests
Anesthetic and Life Support Drugs Advisory Committee (ALSDAC)
Drug Safety and Risk Management Advisory Committee (DSaRM)

RE: Overview of the October 21-22, 2010 ALSDAC and DSaRM meeting to discuss postmarketing epidemiological studies for NDA 22-272 reformulated OxyContin (Oxycodone hydrochloride controlled-release) tablets and for NDA 22-321 Embeda (morphine sulfate extended-release and naltrexone hydrochloride) capsules.

At this joint meeting of the ALSDAC and DSaRM, we will be discussing the design and conduct of postmarketing epidemiological studies intended to assess the impact on abuse of new opioid drug products that have been formulated specifically to deter abuse. The FDA and our federal, state and local partners, as well as numerous professional societies and the pharmaceutical industry, have long recognized that one approach to reducing the abuse of opioid drug products and its consequences, overdose, addiction and death, while maintaining access to these drugs for the patients who need them, would be to develop new formulations specifically designed to prevent or mitigate abuse. Thus far, the Agency has encouraged the development of novel formulations and has provided guidance for evaluating abuse-deterrent products based on the input from previous advisory committees:

The evaluation of abuse-deterrent products falls into three areas:

1. In vitro data from studies designed to evaluate the product's resistance to attempts to defeat the abuse-deterrent properties. These studies should be based on information from abusers, and must be scientifically rigorous and blinded.

2. Pharmacokinetic data from studies that evaluate the effects of different methods of physical manipulation identified in the in vitro studies on the pharmacokinetic profile of the abuse-deterrent formulation.

3. Clinical data from studies of opioid-experienced drug abusers to evaluate the likability and euphorigenic effects of manipulated and intact abuse-deterrent product compared to a formulation of a formulation of the same drug substance that was not designed to be abuse-deterrent.

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Thus far, we have reviewed applications for products designed to be abuse-deterrent that have included:

- formulations with physico-chemical barriers to tampering,
- combination products of an agonist and an antagonist intended to reduce the euphoria associated with the opioid agonist when the antagonist is released during inappropriate use, e.g. injection of an oral preparation, and
- formulations that include non-analgesic ingredients that cause unpleasant side effects when the product is used inappropriately, e.g. a substance that causes irritation when the oral product is crushed and snorted.

While both products that will be discussed during this meeting have been developed to deter abuse, the reformulated OxyContin was designed to have more tamper resistant properties compared to the original formulation of OxyContin, whereas Embeda was designed as a combination product containing morphine sulfate and a sequestered opioid antagonist, naltrexone hydrochloride. Consistent with the Agency's current position that the final evidence of the ability of a drug product to provide abuse deterrence can only come from appropriately designed epidemiological studies, with the approval of each of these products the manufacturers were required to conduct postmarketing studies to assess whether the abuse-deterrent features of their products actually resulted in a decrease in abuse in the community.

The current approach to measuring abuse and its outcomes relies heavily on the data collected in the existing surveillance systems. Some of these systems collect data primarily related to abuse patterns (e.g. National Drug Survey on Use and Health, Monitoring the Future Survey from the National Institute on Drug Abuse, National Network of Abuse Treatment Programs), while others collect data on abuse and misuse outcomes (e.g. Drug Abuse Warning Network, Treatment Episode Dataset, National Vital Statistics, National Poison Data System). Each of the systems has its strengths and limitations, and measuring trends within each system may also present considerable challenges. During this meeting you will hear presentations describing the available data

resources in order to assist you in your discussions. You will also hear an expert perspective on the design of observational studies aimed to measure abuse. Finally, Purdue and King Pharmaceuticals will present their epidemiological study proposals for the reformulated OxyContin and Embeda products.

You will be asked to discuss the currently available databases and surveillance systems and recommend which specific databases should be used for obtaining data, not only for Oxycontin and Embeda, but for all products intended to be abuse deterrent. It is important to note that this meeting is not intended to evaluate the quality of the Purdue and King protocols from a regulatory standpoint, for two reasons. The first reason is that the companies have provided only early drafts, and the second reason is that they have not had a chance to receive even initial feedback from the Agency on these drafts. As such, we will not be asking you to vote on the adequacy of these proposals. Instead, we will be asking you to include the proposals in your overall discussions as examples of possible study designs, metrics and outcomes, as you address a number of discussion points intended to define a current gold-standard study (or studies) for the evaluation of the impact of products designed to be abuse deterrent on actual abuse in the community.

As mentioned in the FDA draft guidance document "Assessment of Abuse Potential of Drugs" published in January 2010, the Agency currently views the concept of abuse deterrence as the introduction of some limits or impediments to abuse, as opposed to the outright elimination of abuse. Although any incremental changes to reduce abuse are valuable, when designing a large epidemiological study it is essential to understand what degree of decrease in abuse and its consequences would be sufficient to conclude that the product is actually abuse deterrent in the community. To this end, you will be asked to discuss what degree of decrease in the measurable outcomes of abuse would be sufficient to label a product as abuse deterrent. Labeling becomes a key issue as we move forward with possible approvals for abuse deterrent products. It is essential that the product labeling is accurate and that promotion by the manufacturer be based on explicit or implicit language in that labeling that is not misleading. The consequences of misleading the medical and patient communities regarding the abuse potential of a drug product are likely to result in a worsening of our existing public health crisis.

We are grateful for your participation and thank you for your assistance in providing your expertise and insights to us as we move forward with decisions regarding the design and interpretation of postmarketing epidemiological studies for abuse-deterrent formulations. When appropriately designed, such studies will hopefully provide the necessary data to assess whether the introduction of a product intended to be abuse deterrent actually results in a decrease in the serious adverse outcomes associated with abuse and, ultimately, whether the development of these types of products will provide a viable aid to solving the growing national problem of prescription opioid drug abuse.

FOOD AND DRUG ADMINISTRATION

Center for Drug Evaluation and Research

Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and Drug Safety & Risk Management Advisory Committee

October 21-22, 2010

Draft Discussion Points for the Committee

1. Considering the measures and databases currently available, which are likely to be the most effective and efficient metrics and surveillance systems for use in evaluating the impact on abuse and misuse in the community of the introduction of abuse-deterrent opioid formulations?

2. Are new surveillance systems needed in order to evaluate the effect of abuse-deterrent formulations on abuse and misuse? If so, describe what types of systems are needed.

3. Abuse of opioids encompasses several populations at risk including patients, household contacts and individuals unrelated to patients. Abuse of these products may also involve more than one route or method of administration. Discuss how to incorporate these different aspects of abuse and misuse into the evaluation of the effects of the abuse-deterrent formulations.

4. It is unlikely that abuse-deterrent formulations will completely prevent abuse and misuse of opioids. There may be different degrees of change across the measures used to assess abuse and misuse. Can a minimal reduction in abuse and misuse necessary to support a finding of abuse deterrence be determined a priori for these measures?

5. For some drugs, the abuse-deterrent formulations and the non-abuse- deterrent formulations of the same active drug substance will both be on the market at the same time.

    a. In this situation, discuss whether non-abuse-deterrent formulations with the same active drug substance as the abuse-deterrent formulation represent appropriate comparators.

    b. Is there any situation in which it would be considered useful to compare the indicators of abuse and misuse from products with different drug substances?

6. In some instances, the abuse-deterrent formulation will replace the non-abuse-deterrent formulations that were previously marketed.

a. In this situation, would it be appropriate to limit the evaluation of abuse deterrence to comparisons with the older products?

b. Would it be necessary or possible to take into account changing patterns in abuse of other drug substances over time?

7. Discuss how a novel analgesic that is introduced to the market in an abuse-deterrent formulation could be evaluated for abuse-deterrent properties?

8. Discuss what constitutes an adequate duration of observation for postmarketing studies of abuse deterrence.

    a. How should market penetration be taken into consideration?

    b. Discuss how sustainability of the effects of an abuse-deterrent product can be assessed over time

9. The products included to help elucidate the discussion today represent two very different approaches to the development of abuse-deterrent formulations:

    a. physicochemical resistance to manipulation, and

    b. incorporation of an opioid antagonist.

    They also represent two different marketing paradigms:

    c. one in which the original product is removed from the market, and

    d. one in which the original formulation without abuse-deterrent properties will remain on the market at the same time as the product with the abuse- deterrent properties.

    Discuss which aspects of Purdue's proposed studies and King's proposed studies would be potentially useful in the assessment of the abuse-deterrent effects of products, in general, that have been developed to be abuse-deterrent. Please take into consideration the proposed methodologies, outcome measures, study populations, duration of studies and comparators.

M E M O R A N D U M

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research

Date: September 22, 2010

To: Bob Rappaport, M.D., Director
Division of Anesthesia, Analgesia and Rheumatology Products (DAAP)

Through: Michael Klein, Ph.D., Director
Controlled Substance Staff (CSS)

From: Silvia Calderon, Ph.D., Pharmacology Team Leader
Controlled Substance Staff (CSS)

Subject: NDA 22,272 - OxyContin (oxycodone hydrochloride controlled release tablets - Reformulated OxyContin)
NDA 22,321 EMBEDA (Morphine sulfate extended-release with sequestered naltrexone hydrochloride)

Indication: Management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

Company: Purdue Pharma L.P. and King Pharmaceuticals

Summary

FDA approved EMBEDA and reformulated OxyContin on August 13, 2009, and April 5, 2010, respectively. Each Sponsor proposed plans for postmarketing epidemiological studies to assess the abuse, misuse, overdose and addiction for their products, per DAAP requirements. As these plans will be reviewed by the Joint Meeting of the Anesthetic and Life Support Drugs and the Drug Safety and Risk Management Advisory Committees on October 21-22, CSS provides below general information on the kinds of studies submitted in NDAs in support of *abuse deterrent* claims and reviewed by the FDA.

Background

The concept of *abuse deterrence* is described in FDA/CDER's draft *"Guidance for Industry Assessment of Abuse Potential of Drugs." Abuse deterrence* is viewed as the introduction of some limits or impediments to abuse in a drug product formulation, as opposed to the outright elimination of abuse.

As stated in the draft guidance, formulations that deter abuse may be useful in ensuring access to drugs for purposes of medical treatment while limiting abuse and the consequences

of abuse. Several different types of abuse deterrent formulations have been proposed in the scientific literature, including formulations with physical barriers to tampering, combinations of an agonist with an antagonist, components that cause adverse events, and alternative methods of administration.

A new formulation that is designed with a possible claim of abuse deterrent qualities should be studied for its relative abuse potential.

A three tier approach is usually followed when evaluating the abuse potential of formulations claimed to be abuse deterrent. These three areas of testing (tier approach) are:

1. Laboratory-based in vitro "manipulation" and extraction studies
2. Pharmacokinetic/Pharmacodynamic studies, and
3. Human abuse potential studies.

The results of the first level of studies will influence the design of the pharmacokinetic/pharmacodynamic studies, and these studies will impact the design and goals of the human abuse potential studies, as well as the need for these types of studies.

All of these studies must be conducted on the to-be-marketed formulation (intact, manipulated or both) and require the use of an appropriate positive control as a comparator drug. The positive control in these studies may be an immediate release product, an extended-release product, and possibly a "manipulated" form of a formulation that is known to be abuse.

The laboratory-based in vitro "manipulation" studies, which are designed to evaluate procedures on how to defeat the deterrent mechanism[s], is the first step in understanding the characteristics of the formulation. Methodologically, this in vitro manipulation study should be designed with knowledge of the physicochemical properties of the formulation and knowledge of the methods available and known to abusers. These studies not only should identify mechanisms by which abusers can deliberately overcome the abuse deterrent properties of the product, but also should identify ways that patients may unintentionally alter the formulation, consequently changing the amount of drug released; as an example, dose dumping may occur when taking the novel formulation with alcohol. In addition, when evaluating the various ways to overcome the abuse deterrent mechanism[s], we need to consider the degree of effort required to bypass the deterrent mechanism. Bypassing the deterrent properties of a formulation by using extraction methods to obtain a limited amount of the active pharmaceutical ingredient (API) is a different concept than bypassing the deterrent mechanism by ingesting a meal.

The extraction studies assess various mechanical and chemical means, ranging from the simple to the sophisticated, to defeat or partially compromise the controlled release of the API, as well as an antagonist, if present. Commonly available items ranging from spoons to coffee grinders are used in an attempt to crush, cut, grade or grind the product formulation. Extractability and solubility studies should be designed to determine whether any of the drugs present in the combination might be differentially solubilized and extracted,

and thus separated from the API. The ease of extracting the API from intact and manipulated product is determined using a variety of solvents ranging from water to beverages, and other solvents such as ethanol, rubbing alcohol, ethyl acetate, methylene chloride, vinegar, bicarbonate solution and others. Effects of temperature and pH on solvent extraction are also determined. Methods are explored for manipulating the product physically and chemically to prepare samples for abuse by snorting, smoking, and intravenous injection. This topic has been discussed at prior meetings of the Anesthetic & Life Support Drugs Advisory Committee and Drug Safety & Risk Management Advisory Committee (*NDA 22-272*, *OxyContin*, May 5, 2008, and September 24, 2009)

Clinical pharmacokinetic studies evaluate the pharmacokinetic profiles of the "manipulated" formulations, through one or more routes of administration, as well as provide data to determine if food and alcohol alter the pharmacokinetic parameters, such as Cmax, and can result in an increased abuse potential, as well as other serious adverse events. The most common route of abuse of the API deserves attention. Some formulations might be designed to limit abuse by a specific route of administration, but the overall evaluation of an abuse deterrent formulation should take into consideration the most common route of abuse for the active ingredient. For example, a label claim of abuse deterrent for a product by the intranasal route would not be relevant and maybe confusing if the drug is primarily and almost solely abused by the oral route. Survey data and studies published in the scientific literature indicate that the oral route is the most common route of abuse of prescription opioids, followed by, to a lesser degree, snorting and injection (TEDS, 2009, Butler *et al*., 2010 and 2008, Katz *et al*, 2008, McCabe *et al*., 2007, Hays *et al*. 2003). Therefore the major route of abuse needs to be the focus of these studies.

In the event that in vitro studies and pharmacokinetic studies suggest that selected manipulations (physical or chemical) of a product defeat or partially compromise the controlled release mechanism, human abuse potential studies are conducted to provide a pharmacodynamic measure (subjective reinforcing effects as well as other effects) to evaluate the impact of the product manipulation. In terms of design, these studies are crossover, randomized, and positive controlled, conducted in non-dependent subjects with a prior history of opioid abuse. Comparisons are made between the intact product, the manipulated product, an immediate release product and, in some cases; researchers may want to consider the use of an extended-release product, either intact or manipulated, to determine the relative abuse potential of the novel formulation.

Traditionally, the data from human abuse potential studies have contributed to determining the appropriate level of control of a drug under the Controlled Substances Act (CSA) by assessing the relative abuse potential of a new drug to a known drug of abuse. When evaluating abuse deterrent formulations, these studies are conducted with the goal of characterizing the abuse potential of the formulation and incorporating the findings into the product label for product differentiation.

Though the three approaches outlined above provide empirical data to characterize the abuse potential of novel formulations claimed to be abuse deterrent, the predictive value of these studies must be validated with data from epidemiological studies.

Conclusions

1. Results of in vitro manipulation assays, pharmacokinetic/pharmacodynamic studies and the human abuse potential studies are submitted in NDAs to support claims of abuse deterrence for new products. The abuse potential of the new formulation needs to be compared to a previously approved product that serves as a positive control. Results of these studies allow only a prediction, but not a definitive conclusion, on the relative abuse liability of the products once on the market.

2. Post-marketing epidemiological studies are necessary to determine whether the abuse deterrent properties are meaningful after marketing.

Recommendations

Companies developing drug products claimed to have abuse-deterrent properties need to work with the FDA to develop and implement postmarketing epidemiological study programs to assess the extent to which their products are actually abused after marketing.

References

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/s/

SILVIA N CALDERON
09/22/2010

MICHAEL KLEIN
09/22/2010

Drug Abuse Warning Network

The Drug Abuse Warning Network (DAWN) provides information on some of the most serious medical consequences of substance use, misuse, and abuse as manifested in visits to hospital emergency departments and in deaths investigated by medical examiners/coroners.

DAWN Emergency Department Surveillance

DAWN records substances associated with drug-related emergency department visits; provides a means for monitoring drug misuse and abuse patterns, trends, and the emergence of new substances; assesses some of the morbidity associated with drug misuse and abuse; and generates information for national, State, and local drug policy and program planning. DAWN is also a tool that is increasingly being utilized for postmarketing surveillance and risk management for the pharmaceuticals regulated by the Food and Drug Administration (FDA). DAWN is the responsibility of the Office of Applied Studies, a Federal statistical unit within the Substance Abuse and Mental Health Services Administration (SAMHSA).

DAWN relies on a national probability sample of non-Federal, short-stay, general hospitals that operate 24-hour emergency departments (EDs). The DAWN sample is designed to produce estimates and trends for the United States overall, and for individual metropolitan areas (12 in 2008). To achieve this, the selected metropolitan areas are oversampled. The oversampled hospitals and a supplementary sample of hospitals outside those areas together capture ED visits in all 50 states and the District of Columbia. Based on data from sampled units, national estimates of drug-related emergency department visits for the U.S. are produced annually.

DAWN estimates for 2008 are based on data submitted by 231 hospitals. The overall weighted hospital response rate was 32.9% (response rates have been stable from year to year). In 2008, DAWN recorded 351,697 drug-related ED visits. Response rates for the oversampled metropolitan areas ranged from 26.8% in Houston to 83.1% in Detroit. Estimates reflect adjustments for the stratified sample design, unit nonresponse, and nonresponse within a facility. At this time, comparisons over time are available for 2004 – 2008.

To collect the data, each hospital emergency department that participates in DAWN has one or more trained DAWN reporters who review emergency department medical records retrospectively to find DAWN cases. Cases reported to DAWN include emergency department visits caused by or related to drug use for patients of any age. The drug use must be recent; chronic effects and history of drug abuse are not reportable. Visits related to drugs used for therapeutic purposes, as well as drug misuse and abuse, are all included. Information that would directly identify a patient (such as name, address, social security number) is never collected. All data are submitted electronically over a secure connection, and automated processes review case data to identify potential errors. Statistical process control (SPC) is used on an ongoing basis to monitor visit, chart, and case counts and case type distribution from participating facilities.

For each reportable visit, demographic, visit, and diagnosis, and drug characteristics are abstracted from the medical record. DAWN captures substance misuse and abuse, drug-related suicide attempts, patients who are seeking detoxification or substance abuse treatment services,

underage alcohol use (whether or not another drug was involved), adverse reactions to pharmaceuticals taken as prescribed or as directed on the label, overmedication (i.e., when the prescribed or recommended dose of a prescription or over-the-counter medication or dietary supplement was exceeded), malicious poisonings (i.e., drug-facilitated assault), and accidental ingestions (i.e., when a drug was used accidentally or unknowingly). Data tables containing annual estimates and trends are produced on most of these types of visits, as well as these analytic categories:

- All Drug Misuse and Abuse (all ED visits that involved an illicit drug, or alcohol, or the nonmedical use of a pharmaceutical),
- Nonmedical use of Pharmaceuticals (visits that involved the patient taking more than the prescribed dose of a prescription pharmaceutical or more than the recommended dose of an over-the-counter pharmaceutical or supplement; taking a pharmaceutical prescribed for another individual; deliberate poisoning with a pharmaceutical by another person; and documented misuse or abuse of a prescription drug, an over-the-counter pharmaceutical, or a dietary supplement),
- Illicit Drugs,
- All Alcohol-related Visits, and
- Underage Drinking (alcohol was involved and the patient was younger than 21 years)

The analytic categories follow a standard format and include information on patient gender, age, and race/ethnicity, the number of drugs involved, the disposition of ED visit, and characteristics of the drugs.

DAWN captures very detailed drug information. Up to 16 drugs plus alcohol can be reported for each DAWN case. Drug-related emergency department visits often include multiple drugs, on average, 1.6 drugs per visit. For adults, alcohol is reportable only when present with another reportable drug; for minors, alcohol is always reportable. Drug information is captured at the level of detail present in the medical record. The same drug may be reported to DAWN by brand, generic, chemical, street, or nonspecific name, depending on the completeness and specificity of information in the medical record. Training and automated rules prompt DAWN reporters to use all available documentation in the medical chart to record drugs by their most specific names (e.g., OxyContin, when documented as such, instead of oxycodone), not to record the same drug by different names (e.g., marijuana and weed), and to exclude current medications unrelated to the visit. Estimates are published at the generic level (e.g., acetaminophen-hydrocodone), for specific ingredients (e.g., dextromethorphan), or by drug category (e.g., opiates/opioids, benzodiazepines). Estimates attributed to particular brand or trade names (e.g., Concerta®) are not published.

Since data for DAWN are extracted from a retrospective review of medical records, no patients, family members, or health care providers are interviewed. Off-site "satellite" EDs associated with participating hospitals are included, but other units within the hospital are not. Although each drug report has an associated indicator for whether the drug was confirmed by toxicology testing, specific laboratory findings are not recorded for DAWN cases. The source of the drug is not collected because it is so rarely available in medical records. Repeat visits by the same individual cannot be linked together. Visits due to chronic conditions associated with a history

of drug abuse are explicitly excluded. While DAWN does not collect direct identifiers, such as patient name, the content of the case data could potentially render the data individually identifiable, and individually identifiable data are protected by Federal law from disclosure without consent.

DAWN does not measure the prevalence of drug abuse in the population, and external factors unrelated to the level of drug abuse in the population may contribute to the likelihood that a person presents to a hospital emergency department for a drug-related problem. For example, the availability of health insurance and/or other sources of care may influence whether an individual seeks care in an emergency department. Purity, experience, or other factors related to the physiological effects of drugs may affect whether a condition occurs to give rise to an emergency department visit.

DAWN Mortality Surveillance

DAWN also collects data on drug-related deaths reviewed by medical examiners and coroners (ME/Cs) in selected metropolitan areas and selected States. The death investigation jurisdictions that participate in DAWN do not constitute a statistical sample of the U.S.; as a result, extrapolation of drug-related deaths to the Nation as a whole is not possible. Because most metropolitan areas contain multiple jurisdictions, totals for a metropolitan area are only possible when every jurisdiction participates. The number of jurisdictions that participate in DAWN varies from year to year. In 2008, there were 544 participating ME/Cs who identified and reported to DAWN on all deaths referred to their offices that met the DAWN criteria for being a drug-related death. These ME/Cs represent the larger metropolitan and micropolitan areas in 36 states and, collectively, cover one third of the nation's population. In 12 States, DAWN had 100% coverage.

The case criteria and data collection procedures for drug-related deaths mirror those used in emergency departments. Causes and manner of death are captured, in lieu of case type and diagnoses.

Summary of National Survey on Drug Use and Health (NSDUH)

NSDUH is the primary source of statistical information on the use of illegal drugs, alcohol, and tobacco in the civilian, non-institutional population of the United States aged 12 or older. Conducted by the Federal Government since 1971, the survey collects data by administering questionnaires to a representative sample of the population through face-to-face interviews at the respondent's place of residence. The survey is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services, and is planned and managed by SAMHSA's Office of Applied Studies (OAS). Data collection is conducted under contract with RTI International, Research Triangle Park, North Carolina.[1]

NSDUH collects information from residents of households and non-institutional group quarters (e.g., shelters, rooming houses, dormitories) and from civilians living on military bases. The survey excludes homeless persons who do not use shelters, military personnel on active duty, and residents of institutional group quarters, such as jails and hospitals.

Since 1999, the NSDUH interview has been carried out using computer-assisted interviewing (CAI). Most of the questions are administered with audio computer-assisted self-interviewing (ACASI). ACASI is designed to provide the respondent with a highly private and confidential means of responding to questions to increase the level of honest reporting of illicit drug use and other sensitive behaviors and problems. Less sensitive items are administered by interviewers using computer-assisted personal interviewing (CAPI).

In addition to questions about the use of tobacco and alcohol, the survey obtains information on nine different categories of illicit drug use: use of marijuana, cocaine, heroin, hallucinogens, and inhalants; and the nonmedical use of prescription-type pain relievers, tranquilizers, stimulants, and sedatives. In these categories, hashish is included with marijuana, and crack is considered a form of cocaine. Several drugs are grouped under the hallucinogens category, including LSD, PCP, peyote, mescaline, mushrooms, and "Ecstasy" (MDMA). Inhalants include a variety of substances, such as nitrous oxide, amyl nitrite, cleaning fluids, gasoline, spray paint, other aerosol sprays, and glue. The four categories of prescription-type drugs (pain relievers, tranquilizers, stimulants, and sedatives) cover numerous pharmaceutical drugs available by prescription and drugs within these groupings that may be manufactured illegally, such as methamphetamine, which is included under stimulants. Respondents are asked to report only "nonmedical" use of these drugs, defined as use without a prescription of the individual's own or simply for the experience or feeling the drugs caused. Within the pain reliever category, specific questions about nonmedical use of Oxycontin are asked. Use of over-the-counter drugs and legitimate use of prescription drugs are not included.

Questions assessing substance use disorders, based on DSM-IV criteria, are included, as well as items on treatment for substance use problems. Mental health status and treatment are also covered in NSDUH.

[1] RTI International is a trade name of Research Triangle Institute.

The 2008 NSDUH employed a State-based design with an independent, multistage area probability sample within each State and the District of Columbia. The eight States with the largest population (which together account for 48 percent of the total U.S. population aged 12 or older) were designated as large sample States (California, Florida, Illinois, Michigan, New York, Ohio, Pennsylvania, and Texas). For these States, the design provided a sample sufficient to support direct State estimates. For the remaining 42 States and the District of Columbia, smaller, but adequate, samples support State estimates using small area estimation (SAE) techniques. The design oversampled youths and young adults, so that each State's sample was approximately equally distributed among three age groups: 12 to 17 years, 18 to 25 years, and 26 years or older.

Nationally, 142,938 addresses were screened for the 2008 survey, and 68,736 completed interviews were obtained. The survey was conducted from January through December 2008. Weighted response rates for household screening and for interviewing were 89.0 and 74.4 percent, respectively.

Although the design of the 2002 through 2008 NSDUHs is similar to the design of the 1999 through 2001 surveys, there are important methodological differences that affect the comparability of the 2002-2008 estimates with estimates from prior surveys. In addition to the name change, each NSDUH respondent completing the interview is now given an incentive payment of $30. These changes, implemented in 2002 and continued subsequently, resulted in an improvement in the response rate, but also affected respondents' reporting of items that are the basis of prevalence measures produced each year. Comparability also may be affected by improved data collection quality control procedures that were introduced beginning in 2001 and by the incorporation of new population data from the 2000 decennial census into NSDUH sample weighting procedures**.** Analyses of the effects of these factors on NSDUH estimates have shown that 2002 and later data should not be compared with 2001 and earlier data from the survey series to assess changes over time.

A comprehensive set of tables, referred to as "detailed tables," is available through the Internet at http://www.oas.samhsa.gov. The tables are organized into sections based primarily on the topic, and most tables are provided in several parts, showing population estimates (e.g., numbers of drug users), rates (e.g., percentages of population using drugs), and standard errors of all non-suppressed estimates. Additional methodological information on NSDUH, including the questionnaire, is available electronically at the same Web address.

Annual summary reports, brief descriptive reports and in-depth analytic reports focusing on specific issues or population groups are produced by OAS. A complete listing of published reports from NSDUH and other data sources is available from OAS. Most of these reports also are available through the Internet (http://www.oas.samhsa.gov). In addition, OAS makes public use data files available to researchers through the Substance Abuse and Mental Health Data Archive (SAMHDA, 2007) at http://www.icpsr.umich.edu/SAMHDA/index.html. Currently, files are available from the 1979 to 2008 surveys. The 2009 NSDUH public use file will be available by the end of 2010.

Treatment Episode Data Set

The Treatment Episode Data Set (TEDS) provides information on the demographic characteristics and substance abuse problems of clients admitted to treatment for abuse of alcohol and drugs in the United States. The information in TEDS is compiled from State administrative systems and is collected by the States from those treatment facilities that they monitor or fund. TEDS records represent admissions rather than individuals, as a person may be admitted to treatment more than once. Approximately 1.9 million admissions records are submitted to TEDS each year. TEDS is maintained by the Center for Behavioral Health Statistics and Quality (formerly the Office of Applied Studies), Substance Abuse and Mental Health Services Administration (SAMHSA).

TEDS, while comprising a significant proportion of all admissions to substance abuse treatment, does not include all such admissions. TEDS is a compilation of facility data from State administrative systems. The scope of facilities included in TEDS is affected by differences in State licensure, certification, and accreditation practices, and disbursement of public funds. For example, some State substance abuse agencies regulate private facilities and individual practitioners, while others do not. In some States, hospital-based substance abuse treatment facilities are not licensed through the State substance abuse agency. Some State substance abuse agencies track correctional facilities (State prisons and jails), while others do not.

In general, facilities reporting TEDS data receive State alcohol and/or drug agency funds (including Federal Block Grant funds) for provision of alcohol and/or drug treatment services. Most States are able to report all admissions to all eligible facilities, although some report only admissions financed by public funds. States may report data from facilities that do not receive public funds, but generally do not because of the difficulty in obtaining data from those facilities. TEDS generally does not include data on facilities operated by Federal agencies (the Bureau of Prisons, the Department of Defense, and the Veterans Administration). However, some facilities operated by the Indian Health Service are included.

TEDS data on treatment admissions include:

- demographic information
- primary secondary and tertiary substances of abuse, their route of administration, frequency of use, and age at first use
- source of referral to treatment
- number of prior treatment episodes
- service type, including planned use of methadone.

Among the substances of abuse collected in TEDS are opiates. This category is further broken down into three subcategories: heroin, non-prescription methadone, and other opiates/synthetics. “Other opiates” is comprised almost entirely of opioid analgesics. While admissions involving use of “other opiates” represent a very small proportion of total TEDS admissions (5.6% in 2008), in the past decade, there has been a dramatic

increase in the admissions for drugs in this category. Most of this growth has occurred since 1997. From 1997-2008, total admissions increased 19%, admissions in which heroin was the primary substance of abuse increased 14% and admissions in which "other opiates" were the primary substance increased 603%.

	1997		2008	
	N	%	N	%
Total admissions	1,586,485	100.0	1,882,083	100.0
Primary heroin admissions	235,114	14.8	267,895	14.2
Primary other opiate admissions	15,057	0.9	105,857	5.6

Admissions for "other opiates" are primarily white and somewhat more likely to be male than female (53.5% versus 46.5%). The increase in admissions for "other opiates" between 1997 and 2008 were greatest among the youngest age groups, especially 18-20 years, 20-24 years and 25-29 years.

TEDS is an exceptionally large and powerful data set. Like all data sets, however, care must be taken that interpretation does not extend beyond the limitations of the data. Limitations fall into two broad categories: those related to the scope of the data collection system, and those related to the difficulties of aggregating data from the highly diverse State data collection systems. Limitations to be kept in mind while analyzing TEDS data include:

- TEDS is an admission-based system and TEDS admissions do not represent individuals. An individual admitted to treatment twice within a calendar year would be counted as two admissions.
- TEDS attempts to enumerate treatment episodes by distinguishing the initial admission of a client from his/her subsequent transfer to a different service type (for example, from residential treatment to outpatient) within a single continuous treatment episode. However, States differ greatly in their ability to identify transfers; some can distinguish transfers within providers but not across providers. Some admission records may in fact represent transfers, and therefore the number of admissions reported probably overestimates the number of treatment episodes.
- The number and client mix of TEDS admissions does not represent the total national demand for substance abuse treatment, nor the prevalence of substance abuse in the general population.

- The primary, secondary, and tertiary substances of abuse reported to TEDS are those substances which led to the treatment episode, and not necessarily a complete enumeration of all drugs used at the time of admission.