U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Substance Abuse and Mental Health Services Administration

*Center for Substance Abuse Treatment*

# Approval and Monitoring of Narcotic Treatment Programs

## A Guide on the Roles of Federal and State Agencies

*Technical Assistance Publication Series*

12

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This publication was prepared under contract no. 270-91-004 from the Substance Abuse and Mental Health Services Administration (SAMHSA). Robert Lubran, M.S., M.P.A., served as the Government project officer.

The opinions expressed herein are the views of the authors and do not necessarily reflect the official position of CSAT or any other part of the U.S. Department of Health and Human Services (DHHS).

DHHS Publication No.
(SMA) 94-2082
Printed 1994

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**Exhibits**

# Foreword

The Center for Substance Abuse Treatment (CSAT) of the Substance Abuse and Mental Health Services Administration (SAMHSA) is pleased to present this document *Approval and Monitoring of Narcotic Treatment Programs: A Guide on the Roles of Federal and State Agencies.* Narcotic treatment programs are the most heavily regulated substance abuse services. Treatment program staff and management, as well as State agency officials, sometimes find Federal regulatory procedures complex and confusing. This guide was developed to address some of the questions asked by State agency officials, program administrators, and sponsors as they begin working with Federal agencies.

The guide is one of several products recently developed by the CSAT Methadone Treatment Improvement Project (MTIP) to provide basic information to prospective direct care providers. It presents information about State and Federal application requirements for program approval and compliance with ongoing regulatory standards. It may also serve as a reference for Federal agencies and State authorities involved in program oversight, management, and technical assistance.

Information contained herein was prepared in collaboration with staff from the Food and Drug Administration (FDA), Drug Enforcement Administration (DEA), National Institute on Drug Abuse (NIDA), and the National Association of State Alcohol and Drug Abuse Directors (NASADAD). We wish to thank these agencies and their staff for collaborating in this effort.

**Nothing in this guide should be construed as authorizing or permitting any person to perform an act that is not permitted under the regulations governing narcotic treatment programs as cited throughout the guide, or by any other Federal and State laws.**

# Executive Summary

The role of Federal and State agencies in approving, monitoring, and setting policy for narcotic treatment programs is sometimes confusing to individuals who want to sponsor the establishment of a narcotic treatment program. After reviewing some of the history of the involvement of Federal and State regulatory agencies in the treatment of opioid addicts, the guide offers a step-by-step overview of what to expect from Federal and State agencies during the process of program approval and monitoring.

The term "narcotic treatment," which is uniformly used throughout the guide, is intended to refer to the use of a narcotic drug as the primary element of treatment. While methadone treatment is only one intervention in a spectrum of services available to persons with opioid addiction, it is currently the most frequently used substitution therapy. Thus the approval and monitoring procedures reviewed in this guide are applicable to methadone treatment; however, the same procedures are expected to be used by Federal and State regulatory agencies to approve programs using other opioid medication therapies, as they are approved by the Food and Drug Administration (FDA).

Given that there are many Federal and State agencies involved in regulating, monitoring, researching, funding, and providing assistance to narcotic treatment programs, "who does what" can be very confusing. Yet, understanding the roles of the various agencies is the key to operating your program according to the established standards. The responsibilities for approving and disapproving, monitoring, and setting standards for narcotic treatment programs are shared by the State and Federal agencies.

State approval and monitoring regulations must be at least as restrictive as the Federal regulations, but States may have any other regulations that fall within the authority of State law, as long as there is no conflict between Federal and State laws that prevents the two from standing together. For instance, many States have developed standards more stringent than the Federal regulations alone.

To permit a narcotic treatment program to operate in a State, that State is required by the FDA methadone regulations to designate a State Authority (SA) whose major role is to review each program application and determine the need for approving and disapproving narcotic treatment programs within the State. The need for a program is based on its proposed proximity to other programs and service need in the proposed location.

The SA collaborates with FDA and the Drug Enforcement Administration (DEA) to ensure that a proposed program meets minimum quality standards. SA representatives are allowed to inspect programs for compliance with regulatory standards and, if necessary, to recommend revocation of approval to FDA. In addition, FDA and DEA cannot approve an application unless the SA concurs.

In partial fulfillment of its responsibilities under the Federal Food, Drug, and Cosmetics Act, FDA, which is situated within the Department of Health and Human Services (DHHS), must ensure the safety and effectiveness of narcotic drugs. Within FDA this responsibility is delegated to the Center for Drug Evaluation and Research. Day-to-day responsibilities are conducted by the Division of Scientific Investigations, Regulatory Management Branch, which is responsible for confirming that all programs using narcotics are in compliance with Federal narcotic treatment regulations for maintenance and detoxification. It is this entity within the FDA that has the authority to approve or disapprove an application to establish a narcotic treatment program. Using procedures developed specifically for narcotic treatment programs, FDA field investigators monitor program services by conducting periodic inspection site visits.

Like FDA, DEA, under its Office of Diversion Control, will conduct program site visits to monitor compliance with controlled substance laws. DEA is situated within the Department of Justice and with the Narcotic Addict Treatment Act of 1974, became responsible for registering narcotic treatment programs that use methadone (or other approved narcotic drugs) in the treatment of narcotic addiction. DEA also ensures

that programs are in compliance with controlled substance laws and requires registration of all programs in addition to the usual registration of physicians and pharmacists to prescribe, compound, or dispense controlled substances.

A further result of the 1974 Narcotic Addict Treatment Act was the collaboration of the National Institute on Drug Abuse (NIDA) and FDA to develop medical standards for using narcotic medications to treat narcotic addiction. Now a part of the National Institutes of Health (NIH), NIDA's role is to conduct research on the effectiveness of narcotic drugs for maintenance and detoxification, and quality-of-service issues. NIDA then makes the information on these research findings available to the other Federal agencies. In this way, NIDA-supported research contributes to revisions of standards that are made in the interest of improving the quality of treatment services.

Improving treatment services for individuals who abuse drugs is the principal function of the Center for Substance Abuse Treatment (CSAT) of the Substance Abuse and Mental Health Services Administration (SAMHSA). As with FDA, DEA, and NIDA, CSAT works with SAs and other Federal agencies to identify programmatic and systemwide issues that require technical assistance or training interventions. CSAT provides financial support through several different grant programs to meet the local or regional needs of targeted areas and special populations. In addition, CSAT has undertaken a number of initiatives designed to assist interested parties in developing and evaluating narcotic treatment services and in improving the quality of existing programs.

Copies of the pertinent Federal regulations are provided in this guide as appendices, along with sample forms. These exhibits are included to assist the reader in understanding the regulations and application process. However, **nothing in this guide should be construed as authorizing or permitting any person to perform an act that is not permitted under the regulations governing narcotic treatment programs as cited throughout the guide, or by any other Federal and State laws.**

# Introduction

The roles of Federal and State agencies in approving, monitoring, and setting policy for narcotic treatment programs are sometimes confusing to individuals who want to sponsor the establishment of a narcotic treatment program. After reviewing some of the history of the involvement of Federal and State regulatory agencies in the treatment of opioid addicts, the guide offers a step-by-step overview. It covers the basics of what to expect from Federal and State agencies during the process of program approval and monitoring.

The term "narcotic treatment," which is uniformly used throughout this guide, is intended to refer to the use of a narcotic drug as the primary element of treatment. While methadone treatment is only one intervention in a spectrum of services available to persons with opioid addiction, it is currently the most frequently used substitution therapy. Thus the approval and monitoring procedures reviewed in this guide are applicable to methadone treatment; however, the same procedures are expected to be used by Federal and State regulatory agencies to approve programs using other opioid medication therapies, as they are approved by the Food and Drug Administration (FDA).

Use of the following features of the guide will help clarify the details of each topic reviewed:

- The side bars contain references from Federal regulations that are included as appendices. You can use the references to locate and review the standards for each topic.
- The exhibits amplify details and help clarify interpretations of the regulations. These are intended to assist you in developing solutions to problems; they are not mandated strategies.
- Copies of relevant portions of the Federal regulations are provided as appendices. They combine, in a single source, the most critical information necessary.
- Sample forms required for application are included to help you complete the actual application forms.

# Part I—History of Federal and State Involvement in Narcotic Treatment

## How Did Federal and State Agencies Become Involved in Narcotic Treatment Programs?

Treatment modalities for opioid addiction have changed over time with shifts in social and political images of opioid addicts. Opioid addiction emerged as a serious problem in the United States after the Civil War, when narcotic drugs were widely prescribed to alleviate acute and chronic discomfort and stress. During that period, the majority of opioid-addicted persons were middle- and upper-class women and war veterans who became addicted through the use of prescribed medication. Such iatrogenic addiction was regarded as an unfortunate medical condition, and sanatoria were established to house and treat addicted people. The chronic nature of opioid addiction was evident, however, as many of the people who entered sanatoria for a cure relapsed to addictive use after discharge.

By the end of the 19th century, the prevalence of opioid addiction in Civil War veterans and women decreased as these people died and doctors became more cautious in prescribing narcotics to their patients. At that time, opium smoking was popular among small groups of Americans but most community leaders regarded the use of opium to be socially irresponsible and immoral.

In the early 20th century, the incidence of addiction in urban areas increased. Young, impoverished European immigrants, crowded into urban tenements, became susceptible to addiction. The use of opium, heroin, and cocaine and the increased crime in poor urban areas became important concerns to social, religious, and political leaders.

After World War II, opioid addiction continued in urban areas, but shifted from European immigrants to African-American and Hispanic people who moved into northern industrial cities as European immigrants moved into suburban areas. Attitudes toward the addict changed from compassion and support for women and veterans who had become iatrogenically addicted to disdain and stigmatization of poor and minority addicts in inner-city ghettos.

The first national response to the changing image of the addict occurred as a legal act of Congress. The Harrison Narcotic Act of 1914 was passed by Congress to fulfill the U.S. obligations to uphold the international agreement of the 1912 Hague Convention. The Harrison Act was not originally written as a prohibition law, but as a means to regulate the manufacture, distribution, and prescription of opiates, coca, and their derivatives and to decrease opium trade with southeast Asia and China. The Act made it illegal to possess any of these drugs unless licensed by the Internal Revenue Bureau of the Treasury Department. All manufacturers, pharmacists, and physicians had to be licensed and keep records regarding narcotics. The Act allowed physicians to prescribe narcotics for "legitimate medical purposes" in the course of their "professional practice only." It did not permit the prescribing of narcotics for maintenance, because the U.S. Treasury Department did not view addiction as a disease and addicts were not seen as legitimate patients.

The position of the Treasury Department was upheld in 1919 by a Supreme Court ruling, which in effect outlawed opioid addiction maintenance treatment. This interpretation of the Harrison Act led to an era of strong narcotics regulation.

In later years, the incidence of addiction and crimes related to addiction rose dramatically in urban areas. The Federal Government responded between 1936 and 1938 by opening two U.S. Public Health Service hospitals for the treatment of addiction. The hospitals, located in Lexington, Kentucky, and Fort Worth, Texas, were the principal resources for addiction treatment in the United States until the 1960s.

Both the legal and medical professions in the United States were upset by the rise in heroin addiction and its associated social, criminal, and medical consequences. In 1956, the Joint Committee of the American Bar Association and the American Medical Association was formed to review the problem. The committee issued a report in 1958 that recommended the establishment of an outpatient clinic to prescribe narcotics on a

controlled experimental basis. In 1963, President Kennedy's Advisory Commission on Narcotic and Drug Abuse also recommended that research be conducted to determine the effectiveness of dispensing narcotics in outpatient facilities.

The use of methadone for opioid maintenance treatment began in New York City in 1964 as part of research conducted by Drs. Vincent Dole and Marie Nyswander of The Rockefeller University. Because methadone presented distinct advantages over morphine as a drug for heroin detoxification (see "What is Methadone Treatment?"), Dole and Nyswander began using methadone in a controlled study. The study team proposed that heroin addiction may be a metabolic disease resulting from the repeated use of narcotics.

Successful patient outcomes from this study and many others in the following years led to the expansion of methadone treatment for heroin addiction as a major public health initiative. Legislative actions in the 1960s acknowledged the necessary role of a medical intervention toward solving the nation's narcotic addiction problem (see exhibit A). With program expansion came an array of administrative and programmatic problems, such as overcrowded program facilities and diversion of medication from patients to persons not enrolled in a program. Media attention to these problems fostered a negative public image of methadone treatment programs.

In the early 1970s White House staff under President Nixon commissioned the National Institute of Mental Health (NIMH), in collaboration with several other Federal offices, to provide policy and program recommendations for initiatives to respond to the increase in heroin addiction. At the same time White House staff invited comments from a nongovernmental advisory group of professionals in the field of substance abuse. The NIMH-led group recommended that methadone be further investigated and not approved as a treatment method. The non-Federal advisory group proposed a strategy to rapidly expand all forms of treatment including methadone treatment. In response to the policy recommendations, the President named Dr. Jerome Jaffe as the Director of the Special Action Office for Drug Abuse Prevention. One of the early goals of this office was to promulgate FDA regulations that would govern the use of methadone to treat opioid addiction.

In the late 1970s, the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA) jointly promulgated standards for methadone programs. These standards were developed to provide a means to regulate the safety and improve the effectiveness of methadone programs through a formal approval and monitoring process. The regulations created State Authorities (SAs) for the purpose of participating in the process of approving and evaluating programs. Yet, early regulations were criticized by practitioners as interfering in the practice of medicine, and both Federal and State regulations have been revised several times.

Exhibit A

## Major Federal Legislation and the Advent of Federal Regulation of Narcotic Treatment*

### The Narcotic Addict Rehabilitation Act

**1966**

This legislation stemmed from the perspective that narcotic addiction is an illness for which treatment services are necessary. Here, treatment included medical, educational, social, psychological, vocational, and rehabilitation services provided in an institution or through supervised aftercare. The law provided for the civil commitment of addicts not charged with a Federal offense to Public Health Service hospitals for treatment, if no comparable care was available in another appropriate facility. The Act authorized Federal courts to commit to the Public Health Service eligible narcotic addicts who were charged with a Federal offense and who desired treatment, in lieu of prosecution for the criminal charge. It allowed the commitment of addicts who had been convicted of a crime to receive treatment in a Bureau of Prisons facility.

(continued on next page)

*This summary of legislation reviews acts, laws, and proposals that are related to treatment issues or the roles of Federal agencies involved in the approval and monitoring processes. Many other laws were enacted between 1914 and 1970 that more specifically relate to the control of dangerous drugs.

Today, there are nearly 1,000 FDA-approved narcotic treatment programs in 43 States, 3 territories, and the District of Columbia. Each year since 1988, from 32 to 45 new methadone treatment programs and 14 to 16 hospital-based detoxification programs have been approved. Recent changes in patient characteristics present new challenges for narcotic treatment providers. The high incidence of HIV infection among injecting drug users, the changing demographics of the addicted population, the rapidly developing problem of multiple-drug-resistant tuberculosis, the epidemic of sexually transmitted diseases in parts of the country, and the increase in multiple drug abuse place additional pressure on programs to offer comprehensive primary care and public health services to opioid-dependent individuals.

# What Is Methadone Treatment?

Methadone treatment is one of the most widely used modes of treatment for opioid addiction. As designed by Drs. Dole and Nyswander, methadone is a medically safe and effective treatment. As a treatment for a chronic medical disorder, methadone treatment offers a long-term, sometimes permanent, replacement pharmacotherapy. Through use of this legally controlled medication, combined with counseling and other supportive services, many opioid addicts enrolled in methadone treatment programs are able to stop illegal opioid and other drug use and return to more stable, productive lives.

Methadone is a synthetic medication that was developed in Germany during World War II as a substitute painkiller when morphine was in short supply. Subsequent clinical research showed that the drug could be used effectively to treat opioid withdrawal syndrome by replacing morphine or heroin with methadone. Yet methadone differs from other narcotics; when properly prescribed it does not produce a euphoric or tranquilizing effect. Instead, it relieves the narcotic craving described by addicts. It is effective when administered orally, and because it is long-acting (24-36 hours), it can be taken once a day.

Methadone treatment has been used to treat opioid addiction in the United States since the mid-1960s. Despite extensive research documenting its effectiveness in reducing opioid use, decreasing criminal behavior, and improving health status, methadone treatment continues to be debated among medical and health care professionals, substance abuse providers, public officials, and policy makers. Some criticize methadone treatment as merely a substitution therapy that does not end opioid addiction, while others contend that methadone treatment provides a valuable mechanism for addressing important public health issues such as preventing the spread of HIV infection among injecting drug users. Other critics are leery about the potential risk of diversion of narcotic medications by patients who are allowed to take the medication home, but supporters of methadone programs believe that close monitoring of patient compliance with program rules prevents medication diversion.

Exhibit A continued

**1966** . . . (continued from page 4)

Public Law 89-793 made grant funds available to States for demonstration programs for treating narcotic addicts, the development of training and educational materials about treating narcotic addiction, the development of training programs, and surveys evaluating the adequacy of treatment programs. The Law authorized the Surgeon General to enter into jointly financed agreements with States to develop, construct, and staff addiction treatment programs, including aftercare programs.

## Reorganization of Federal Agency Tasks

**1968-1970** In 1968, responding to inconsistencies and fragmentation of laws related to drug abuse and control, President Johnson's administration developed a plan to reorganize the responsibilities of various agencies involved in control of dangerous narcotics and other drugs. Under this plan, functions of the Department of Health and Human Services (DHHS) (formerly the Department of Health, Education and Welfare) and the Treasury Department, with the exception of those involving customs, were merged and transferred to the Department of Justice as the Bureau of Narcotics and Dangerous Drugs (now the Drug

(continued on next page)

Exhibit A continued

**1968-1970** . . . (continued from page 5)

Enforcement Administration (DEA)). In 1969 recommendations were forwarded to Congress to reorganize existing laws under one statute that reflected the reorganization plan.

A variety of drug abuse treatment and control bills were introduced in the House of Representatives and the Senate. All these proposals were attempts to create a more comprehensive drug control and addiction treatment law.

## The Comprehensive Drug Abuse Prevention and Control Act (P.L. 91-513)

**1970** This law created a comprehensive statute for drug abuse issues by combining the intent of sections of existing laws and expanding on issues not previously addressed. It provided for increased research into drug abuse and drug dependence and their prevention; provided for treatment and rehabilitation of drug abusers and drug dependent persons; and strengthened existing law enforcement authority and criminal penalties involving illegal trafficking in controlled substances. The law established requirements for a special registration for physicians treating narcotic addiction. In addition, it established five schedules of controlled substances according to their potential for abuse. The law authorized the Attorney General (Department of Justice) to handle the control and diversion aspects of prescribing narcotics, and the Secretary of the Department of Health, Education and Welfare to handle the safety, effectiveness, and quality aspects.

One objective of this law was to improve the quality of treatment of narcotic addiction by encouraging private physicians to treat narcotic addicts. By clarifying the policy for acceptable standards of care for treating narcotic addicts, the law was intended to dispel the fears of prosecution for providing narcotic drugs that had previously kept physicians from treating addicted patients.

## Methadone Regulations (21 CFR Part 291)

**1972** The Food and Drug Administration (FDA), in consultation with the White House Special Action Office for Drug Abuse Prevention (SAODAP), the National Institute of Mental Health (NIMH), and the Department of Justice published regulations that placed methadone in a legal drug class between an investigational drug and an approved drug. The regulations allowed methadone to be used as an analgesic and as a treatment for narcotic addiction through a closed distribution system of approved pharmacies and methadone treatment programs. The regulations contained procedures for approval of treatment programs, mandated standards, and procedures for revoking approval for failure to comply with standards. The regulations required each State's appropriate official to designate a State Authority (SA) to be responsible for treatment of narcotic addiction with a narcotic drug within the State or territory.

## American Pharmaceutical Association (APhA) Challenge to FDA Regulations

**1972** The APhA challenged FDA regulations regarding the restriction of methadone distribution through approved pharmacies. This resulted in an amendment to FDA regulations that allowed methadone to be dispensed upon prescription through pharmacies for analgesic purposes only, but continued to restrict distribution for narcotic addiction treatment through approved methadone programs.

## Narcotic Addict Treatment Act (P.L. 93-281)

**1974** This law amended the Comprehensive Drug Abuse Prevention and Control Act of 1970. It recognized the use of a narcotic drug in the treatment of narcotic addiction as critical and, for the first time in Federal law, defined "maintenance treatment." In an effort to promote closer monitoring of programs using narcotics for maintenance treatment, the law required separate

(continued on next page)

Exhibit A continued

**1974** . . . (continued from page 6)

registration by DEA of medical practitioners who dispense narcotic drugs in the treatment of narcotic addiction. Prior to registration by DEA, DHHS must determine that the practitioner is qualified according to established standards of treatment. The law promoted increased coordination between DHHS and DEA.

Through P.L. 93-282, enacted in 1974, the National Institute on Drug Abuse (NIDA) was established as an institute independent from NIMH. The authority delegated by DHHS for the treatment of narcotic addiction was split between NIDA and FDA. NIDA became responsible for determining appropriate standards of treatment for medical, scientific, and public health aspects of drug abuse. FDA was delegated the authority to determine the safety and effectiveness of drugs and approve new drugs to be used in narcotic addiction treatment.

## Revisions to Methadone Regulations (21 CFR Part 291)

**1975-1989** Since 1975, the Commissioner of FDA and the Director of NIDA have worked to jointly publish methadone standards required by the Narcotic Addict Treatment Act. The standards were revised several times and revisions were published in the March 2, 1989 Federal Register. These regulations establish methadone as the only narcotic drug currently approved for narcotic addiction treatment, require methadone maintenance treatment programs to provide comprehensive services in addition to dispensing methadone, and establish a minimum standard of care that all programs must maintain.

## Proposed Revisions to Regulations

**1989-1990** In the *Federal Register* of March 2, 1989, FDA and NIDA jointly published a proposed regulation to revise the conditions for the use of methadone in narcotic treatment programs. This initiative was developed in response to the human immunodeficiency virus (HIV) epidemic in the injecting drug user population and evidence that methadone treatment is an effective method of limiting the transmission of HIV among this population. At the same time, many treatment programs were reporting waiting lists for treatment. The proposal allowed narcotic treatment programs to provide interim maintenance treatment to patients awaiting placement in comprehensive maintenance treatment and required such programs to provide counseling on avoidance and transmission of HIV disease. The proposal was intended to allow narcotic treatment programs greater flexibility in admitting narcotic addicts into treatment.

FDA and NIDA received over 80 comments on the proposed interim maintenance provisions, which revealed large differences of opinion both on the desirability of adopting the interim maintenance provisions and on a number of related issues. Several comments stressed the potential importance of interim maintenance in checking the spread of AIDS while others contended that the resources and funding that participating methadone treatment programs would have to provide to offer the proposed interim maintenance treatment would be at the expense of the current comprehensive maintenance treatment and would therefore diminish the role of comprehensive narcotic treatment programs in reducing injecting drug use.

Because of these differing views and in light of comments urging that an expert meeting be convened to address the complex issues posed by the proposal, the agencies concluded that it was necessary to solicit additional information before making a final decision. At a public hearing held February 28, 1990, 28 individuals representing 20 organizations provided testimony before representatives from FDA, NIDA, and other Public Health Service organizations.

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# Medication Under Study for Narcotic Treatment

Given that methadone is only effective for a 24-36 hour period, ongoing research is examining the effects of a longer acting medication with similar properties to methadone. Clinicians believe that longer acting medications could have practical therapeutic advantages because patients would receive medication less frequently, and would need fewer, if any, take-home medications. Recent studies indicate that levo-alpha-acetylmethadol (LAAM) has these qualities.

LAAM is a synthetic opioid that, when ingested orally, has been found to suppress opioid withdrawal symptoms for up to 72 hours with minimal side effects (Greenstein et al. 1992). Interim Federal regulations approving the use of LAAM as a substitution therapy for opioid addiction became effective July 20, 1993. (See appendix E.) A final regulation is currently under review by FDA. This approval applies to the Federal level only; availability of LAAM within a State will depend on State-level approvals as well.

# What Is Interim Maintenance Treatment?

Interim maintenance treatment services should be viewed as a bridge to the comprehensive methadone treatment system. The January 6, 1993 amendments to the methadone regulations established two types of methadone treatment: comprehensive maintenance treatment and interim maintenance treatment. Interim maintenance treatment was formulated to assist in reducing the transmission of HIV disease by enabling comprehensive maintenance treatment programs to admit an individual, otherwise eligible for treatment, to interim maintenance treatment when the comprehensive maintenance treatment program is unable to admit or readmit the individual in comprehensive treatment within 14 days of seeking admission.

CitatioN
21 CFR
291.505
(a)(2)*

Under interim maintenance treatment, patients must receive appropriate medical services, HIV counseling, and urine screens in addition to methadone medication. At a minimum, interim maintenance treatment services must include an initial urine screen and at least two other urine screens taken from interim patients during the maximum 120 days permitted for interim treatment. Interim maintenance treatment programs are also advised by Federal agencies to perform more frequent drug testing to assist in assessing patient needs and priorities for transfer to comprehensive maintenance programs. After 120 days, a patient enrolled in interim maintenance treatment must be transferred to a comprehensive maintenance program if he or she is still in need of treatment.

CitatioN
21 CFR
291.505
(d)(7)*

Exhibit A continued

## ADAMHA Reorganization Act (P.L. 102-321) and Interim Maintenance Final Regulations (21 CFR Part 291)

**1992-1993**

Effective October 1, 1992, section 501 of this act established the Substance Abuse and Mental Health Services Administration (SAMHSA) within the Public Health Service, consisting of a Center for Substance Abuse Treatment (CSAT), a Center for Substance Abuse Prevention (CSAP), and a Center for Mental Health Services (CMHS). SAMHSA was granted authority to coordinate Federal policy to provide substance abuse treatment services using anti-addiction medications including methadone. Among the responsibilities of CSAT, formerly the Office for Treatment Improvement, are administering the Substance Abuse Prevention and Treatment (SAPT) Block Grant, funding demonstration projects, conducting State and program evaluations, and providing technical assistance to States and block grant subrecipients.

The Act also authorized the Secretary of Health and Human Services, after consultation with the National Commission on AIDS, to issue regulations for the conditions under which a narcotic treatment program can provide interim maintenance treatment. On January 6, 1993, the Commissioner of FDA and the Acting Administrator of SAMHSA jointly issued regulations pertaining to interim maintenance. The regulations also require *all* narcotic treatment programs to provide counseling regarding exposure to and transmission of HIV disease for each patient admitted or readmitted to maintenance or detoxification treatment. ❖

*These citations refer to 21 CFR Part 291—Drugs Used for Treatment of Narcotic Addicts [Revisions]. (See appendix C.)

The interim maintenance treatment regulations are applicable only to a public or nonprofit private narcotic treatment program that is approved by the State and FDA as a comprehensive methadone treatment program. The interim maintenance regulations permit a comprehensive maintenance treatment program to provide interim maintenance only with the approval of the chief public health officer in the State. In the process of reviewing a request for interim maintenance, it is appropriate for the chief public health officer to consult with the SA.

CitatioN
21 CFR
291.505
(b)(2)(vi)*

Interim maintenance treatment must be provided in a manner consistent with all applicable Federal and State laws. In addition, all requirements for comprehensive maintenance treatment, as described in this guide, apply to interim maintenance treatment, with the following exceptions:

- The narcotic drug is required to be administered daily under observation.
- Take-home medication is not allowed for any reason.
- The initial treatment plan and periodic treatment plan evaluation are not required.
- A primary counselor is not required to be assigned to a patient.
- Vocational and educational rehabilitation services are not required.
- Interim maintenance cannot be provided for longer than 120 days in any 12-month period.

Each interim maintenance treatment program must establish and follow reasonable criteria for transferring patients from interim maintenance to comprehensive maintenance treatment. These transfer criteria should be in writing and available for inspection. The criteria must include a preference for pregnant women in admitting patients to interim maintenance and in transferring patients from interim maintenance to comprehensive maintenance treatment. The interim maintenance program must notify the chief public health officer of the State when a patient begins interim treatment, when a patient leaves interim maintenance, and before the date of mandatory transfer to a comprehensive maintenance program. The program should document such notifications.

CitatioN
21 CFR
291.505
(d)(7)*

The interim maintenance regulation does not require programs to maintain a specific counselor-to-patient ratio. However, programs are required to provide a number of services, including referrals for comprehensive medical services, prenatal care, and HIV testing. Programs should ensure that sufficient counseling staff are available to provide these services and respond to patient emergency situations.

Interim maintenance treatment programs, as well as comprehensive maintenance and detoxification programs, must provide patients with counseling on preventing exposure to, and transmission of, HIV disease. Although HIV testing is not required by this regulation, HIV testing is an important element in reducing the risk of HIV transmission and must be made accessible to patients who request it. If a program does not provide HIV testing on site, then the program must refer patients who request testing to facilities where testing is available. Programs must ensure access to HIV testing through agreements with HIV testing facilities.

CitatioN
21 CFR
291.505
(d)(4)(i)(C)*

# Part II—The Approval and Monitoring Process

## Who Does What? The Roles of the Various Federal and State Agencies

Given that there are many Federal and State agencies involved in regulating, monitoring, researching, funding, and providing assistance to narcotic treatment programs, "who does what" can appear very confusing. Yet understanding the roles of various agencies is the key to operating your program according to the established standards. The responsibilities for approving and disapproving, monitoring, and setting standards for narcotic treatment programs are shared between State and Federal agencies (see exhibit B).

### State Agencies

#### *State Authorities (SAs)*

Each State is responsible for approving narcotic treatment program applications and monitoring compliance with State regulations, licensing, and other requirements. State approval and monitoring regulations must be at least as restrictive as the Federal regulations, but States may have any other regulations that fall within the authority of State law, as long as there is no conflict between Federal and State laws that prevents the two from standing together consistently. Many States have developed more stringent standards, and in some States methadone treatment is not available. Since each State may regulate methadone

Exhibit B. **Roles of Federal and State Agencies**

| Roles | FDA | DEA | NIDA | CSAT | SA |
|---|---|---|---|---|---|
| Approval | • | • | | | • |
| Monitoring | • | • | • | | • |
| Research | | | • | | • |
| Planning | | | | | • |
| Technical Assistance | | | | • | • |
| Program Development | | | | • | • |
| Standard Setting | • | • | • | | • |
| Funding | | | | • | • |

treatment, you may find that the rules governing methadone in your State differ from the Federal rules, and that the rules vary from State to State. Should you want to establish a program in more than one State, you will need to work with each State individually.

Each State choosing to permit a narcotic treatment program to operate within its borders is required by FDA methadone regulations to designate an SA. The SA's major role is determining the need for approving and disapproving narcotic treatment programs within the State. In most States, the SA is the agency that has responsibility for planning and funding of substance abuse treatment services in that State; however, this agency does not always have licensing or regulatory authority. Your SA will review each program application for its proximity to other programs and the service need in the location of the proposed program. In many instances, CSAT can provide technical assistance to the State in determining the need for narcotic treatment services in a specific locality.

CitatioN
21 CFR 291.505 (a)(9);
21 CFR 291.505 (b)(2)(i)

Your SA collaborates with FDA and DEA to ensure that a proposed program meets minimum quality standards. SA representatives are allowed to inspect your program for compliance with regulatory standards and, if necessary, to recommend revocation of approval to FDA. Also, FDA and DEA cannot approve your application unless your SA concurs. Experience has shown that in many instances successful narcotic treatment program applicants begin the process by gathering State information first, determining if their proposed program will meet State requirements, and then moving on to Federal standards.

### *State Chief Public Health Officer*

CitatioN
21 CFR 291.505 (b)(2)(vi)*

The chief public health officer of each State is responsible for certifying comprehensive methadone treatment programs to provide interim maintenance treatment services to patients who will be offered comprehensive maintenance services within 120 days of seeking treatment. The chief public health officer should involve the SA in this approval process. State certification for interim maintenance treatment must occur before FDA will act on a request for program approval.

## Federal Agencies

### *Food and Drug Administration (FDA)*

In partial fulfillment of its responsibilities under the Federal Food, Drug, and Cosmetics Act, the FDA, which is situated within DHHS, must ensure the safety and effectiveness of narcotic drugs. Within the FDA, this responsibility is delegated to the Center for Drug Evaluation and Research. Day-to-day responsibilities are conducted by the Division of Scientific Investigations, Regulatory Management Branch.

The Regulatory Management Branch is responsible for confirming that all programs using narcotics are in compliance with Federal narcotic treatment regulations for maintenance and detoxification. It is this entity within the FDA that has the authority to approve or disapprove your application to establish a narcotic treatment program. Using procedures developed specifically for narcotic treatment programs, FDA field investigators monitor your services by conducting periodic inspection site visits.

Exhibit C

## Federal Initiatives

### *MTQAS:*

NIDA is currently funding a feasibility study for the development of a Methadone Treatment Quality Assurance System (MTQAS). The goal of the project is to examine the feasibility of implementing a performance-based reporting and feedback system in methadone treatment programs and whether such a system would be useful in measuring treatment effectiveness. Preliminary MTQAS data are expected to be available by the spring of 1994.

### *Linkages to Primary Health Care Services:*

Concern over the increase in HIV, TB, and STD infection rates among injecting drug users has prompted Federal policy makers to explore options for increasing the intensity of primary health services to methadone patients. CSAT is currently exploring models for using MMTPs to demonstrate the effectiveness of linking these public health issues, and NIDA is also funding a number of studies in this area.

### *Interagency Methadone Policy Review Board:*

The Interagency Methadone Policy Review Board provides a forum to discuss and review major policy issues related to methadone. The FDA, DEA, NIDA, and CSAT are represented on this board, in addition to the Veterans Administration and other Federal policy offices involved in substance abuse treatment. ❖

### *Drug Enforcement Administration (DEA)*

Regulation of the diversion of controlled substances is one of the responsibilities delegated to the DEA, which is situated within the Department of Justice. With the 1974 Narcotic Addict Treatment Act, DEA became responsible for registering narcotic treatment programs that use methadone (or other approved narcotic drugs) in the treatment of narcotic addiction and ensuring that programs are in compliance with controlled substance laws. In addition to the usual registration of physicians and pharmacies, DEA requires that you register your program to prescribe, compound, or dispense controlled substances. DEA will also conduct site visits of your program to monitor compliance with controlled substance laws. These tasks are completed by the headquarters and regional field offices of the Office of Diversion Control within DEA.

### *National Institute on Drug Abuse (NIDA)*

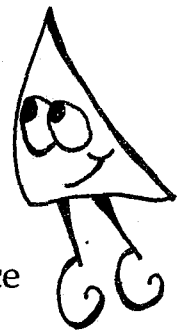
NIDA was established in 1974 as one of the institutes of the Alcohol, Drug Abuse and Mental Health Administration. Effective October 1, 1992, NIDA became a part of the National Institutes of Health (NIH). NIDA's role is to conduct research on the effectiveness of narcotic drugs used for maintenance and detoxification, in addition to quality-of-service issues. NIDA makes information available to the other Federal agencies on the results of research programs, including new information on treatment standards for methadone and other new medications to be used in the treatment of narcotic addiction. For example, the Narcotic Addict Treatment Act and regulations were revised to allow detoxification treatment to extend to 180 days. This revision was based on NIDA-supported research.

As a result of the 1974 Narcotic Addict Treatment Act, NIDA worked with FDA to develop medical standards for using narcotic medications to treat narcotic addiction. The two agencies jointly promulgated the methadone regulations that your program must follow.

### *Center for Substance Abuse Treatment (CSAT)*

CSAT, an agency of SAMHSA, has the principal function of improving treatment services for individuals who abuse drugs. CSAT provides financial support through the Substance Abuse Prevention and Treatment (SAPT) Block Grant; community demonstration grants; cooperative agreements; and technical assistance to States, communities, and treatment providers. These grant programs target resources to meet local or regional needs of targeted areas and special populations. CSAT also works with SAs and the other Federal agencies to identify programmatic and systemwide issues that require technical assistance or training interventions.

Through the Methadone Treatment Improvement Project (MTIP), CSAT provides technical assistance to the State alcohol and drug abuse agencies that are responsible for administering the SAPT block grant and narcotic treatment programs. In addition, CSAT is developing treatment guidelines and treatment improvement protocols for State program administrators and treatment providers. These initiatives are designed to assist you in developing and evaluating narcotic treatment services and in improving the quality of existing programs.



## So You Want to Start a Narcotic Treatment Program?

### Comprehensive Maintenance Treatment Program

Before you pick the perfect program name and open or break ground on your new facility, you absolutely must make three phone calls. First, use the list in appendix G of this guide to identify the contact person at your SA. Call to request an application form, instructions, and any applicable State regulations. The SA will be able to tell you if there are other State offices that you need to communicate with regarding licensure or other State permit or site approval procedures. It is suggested that you thoroughly review your program plans with the SA staff to ensure that your program will comply with State regulations before initiating the Federal process. As noted earlier in this guide, FDA and DEA cannot approve your program without State concurrence.

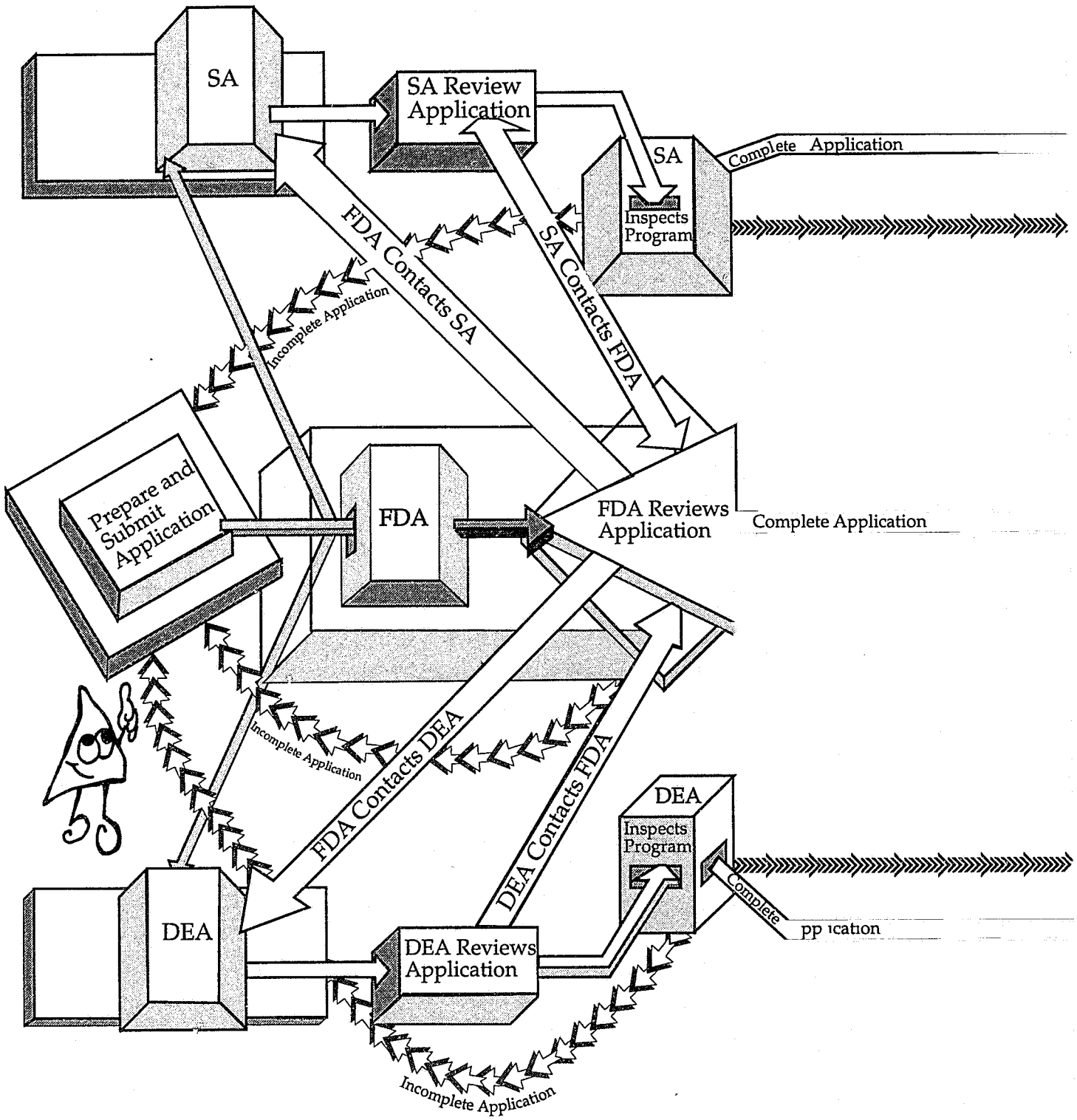
Next, contact the FDA's Division of Scientific Investigations, Regulatory Management Branch, and ask for an application package for a methadone treatment program. (See appendix A)

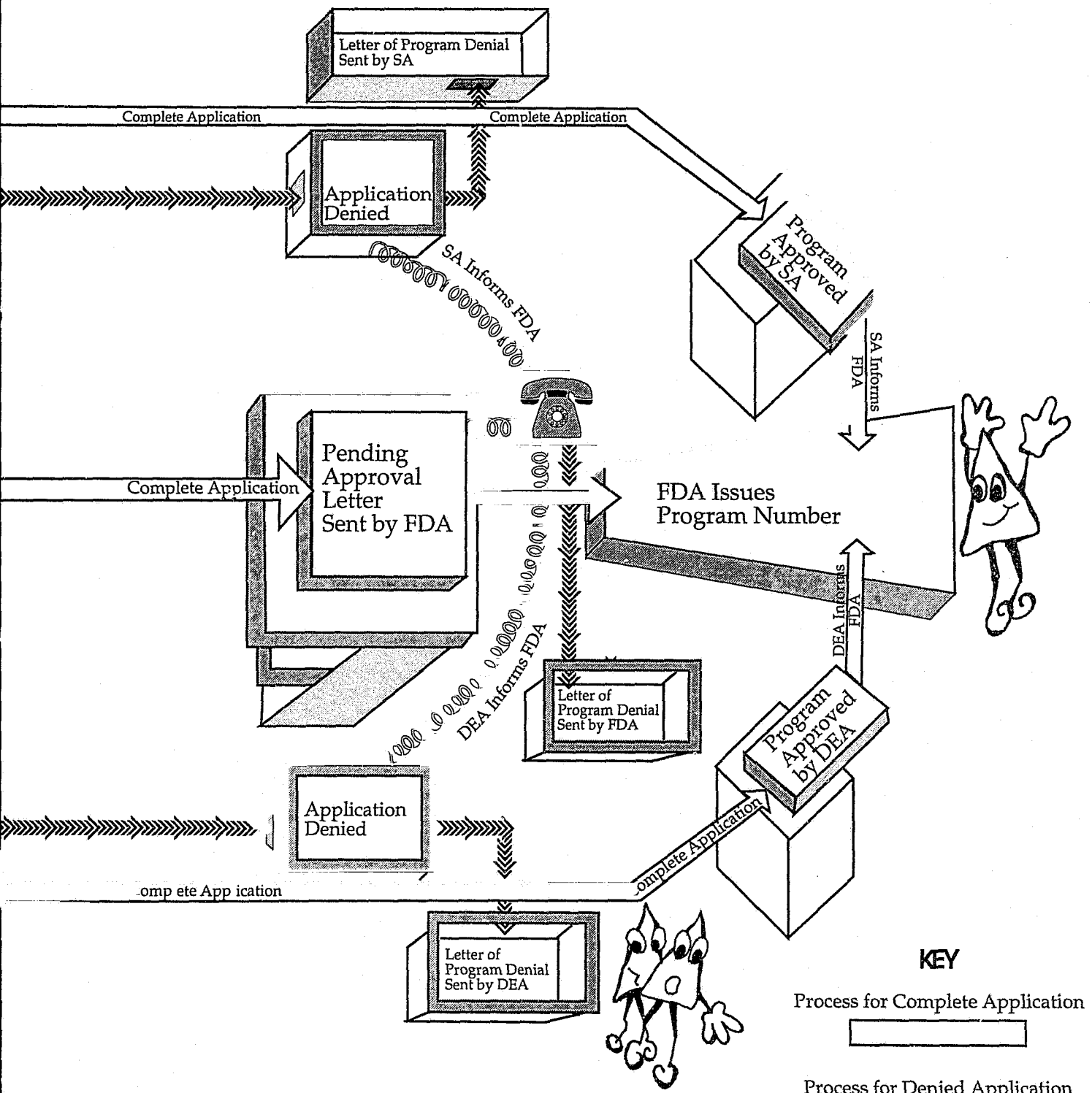
Third, locate the closest local DEA Field Office Diversion Unit from the list in appendix B and call to get an application. When you call DEA it is a good idea to have a discussion with a Diversion Investigator about the requirements for security that will be applicable to your site. Although they are minimal, DEA security requirements vary with the geographic location, the patient population of each program, and the potential security risks of a particular site. You may find it helpful to inquire about DEA recordkeeping requirements as well.

Be sure to read the application instructions **before** you begin!

Most likely, there will be differences between the State regulations and the Federal regulations. For example, some States place lower limits than the Federal regulations allow for the maximum dose of

Exhibit D. **Application Process Flow Chart**




Letter of Program Denial Sent by SA
Complete Application
Complete Application
Application Denied
SA Informs FDA
Program Approved by SA
SA Informs FDA
Pending Approval Letter Sent by FDA
Complete Application
FDA Issues Program Number
DEA Informs FDA
Letter of Program Denial Sent by FDA
DEA Informs FDA
Program Approved by DEA
Application Denied
omp ete App ication
omplete Application
Letter of Program Denial Sent by DEA
KEY
Process for Complete Application
Process for Denied Application
Intergency communication

methadone that may be prescribed without special approval. **Your program must be in compliance with both sets of regulations, and where one standard is more restrictive than another, you will be expected to follow the more restrictive requirement.**

Federal regulations allow you to request an exemption to specific Federal program standards provided that you submit a rationale for the request with your application. FDA does not often grant exemptions to the minimum program standards, so you will need to be sure that your program meets the minimum programmatic and treatment standards as fully explained in the regulations. The same is true for DEA. You are free to apply for an exemption, but the minimum standards must be met and exemptions are rarely granted. There are several situations that are exempted by DEA, however, because they do not require DEA registration. These exempted situations are as follows:

CitatioN
21 CFR 291.505 (d)(11)

- Methadone may be used to detoxify pregnant addicts in an inpatient hospital setting without separate registration of the hospital. Contact DEA for approval for this exemption.
- Patients of existing narcotic treatment programs may be dosed while incarcerated without registration of the jail. Contact DEA for approval for this exemption.
- Physicians who are not registered to conduct a narcotic treatment program may administer (not prescribe) narcotic drugs to patients for the relief of acute withdrawal symptoms while arrangements are being made to refer the patient for treatment. No more than a 1-day supply may be administered at a time. This treatment may last for a maximum of 3 days and may not be renewed or extended.
- A physician or authorized hospital may administer or dispense narcotic drugs in a hospital to maintain or detoxify a patient as an adjunct to medical or surgical treatment of conditions other than addiction, or for relief of pain when no relief or cure has been found after reasonable efforts to try other therapies.

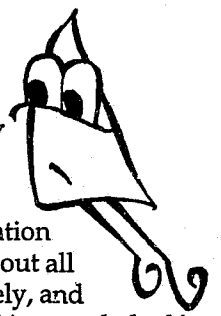
Remember, both State and Federal approvals must be obtained **before** you can operate your program! Also, you must **obtain approval for every different site from which you will dispense medication.** (See definition of a medication unit 21 CFR §291.505 (a) (4).) If you are a new provider, you may want to start with one site and expand to multiple sites at a later date.

CitatioN
21 CFR 291.505 (b)(3)
21 CFR 1301.22 (a)(6)
21 CFR 1301.23 (a)

## Interim Maintenance Treatment Program

Approved comprehensive methadone treatment programs may seek authorization to provide interim maintenance treatment. Again, contact your SA for application instructions. Keep in mind that you must obtain certification from the chief public health officer of your State as part of the approval process. The SA will be able to tell you the appropriate person to contact in your State public health office. As indicated below, you still need to follow the applicable Federal regulations.

# What Do I Have to Do to Complete My Application?



Each SA will have a different application process. Follow the instructions. Fill out all information completely and accurately, and if you have questions, contact your SA to get help. Your SA can tell you how many copies of the application are needed and where they should be sent. Typically, a State's package will include:

- An application plus application instructions
- Information about determining service needs in the area of the proposed program's service location
- Narcotic treatment program standards
- Licensure or other necessary program approval requirements

In addition, the State may send general information or application forms for Federal approvals or provide assistance by coordinating the Federal application process on your behalf.

## State Chief Public Health Officer Approval

Before FDA will grant approval for interim maintenance services, you must obtain approval from your State's chief public health officer and provide FDA with certification that:

- The chief public health officer does not object to interim maintenance treatment in the State.
- The establishment of an interim maintenance program will not adversely impact on the capacity or fiscal support of comprehensive maintenance treatment programs.
- The State ensures that patients enrolled in an interim maintenance program will be

CitatioN
21 CFR 291.505 (b)(2) (vi)(A-D)

transferred to a comprehensive maintenance treatment program within 120 days.

The Federal government expects States to give appropriate guidance to narcotic treatment programs in order to ensure that comprehensive maintenance treatment is not available within a reasonable geographic area before admitting an individual into interim maintenance treatment. Interim maintenance must be provided in a manner consistent with all applicable State and Federal laws and regulations. The chief public health officer may want to consider developing a procedure through which programs can fulfill their obligation to notify the State chief public health officer when a patient begins interim treatment, when a patient leaves interim treatment, and before the date of mandatory transfer to a comprehensive program.

## FDA Approval

### *Comprehensive Maintenance Treatment Program*

CitatioN
21 CFR 291.501**
(l)
21 CFR 291.505
(c)(4)(i-ii);
(d)(ii)**

You will receive a packet from FDA that contains all the necessary Federal forms. These Federal forms, which are subject to change, include the following:

**FDA Form 2632:** Application for Approval of Use of Narcotic Drugs in a Narcotic Addiction Treatment Program

**FDA Form 2633:** Medical Responsibility Statement for Use of Narcotic Drugs in a Treatment Program

**FDA Form 2635:** Consent to Treatment with an Approved Narcotic Drug

**FDA Form 2636:** Hospital Request for Methadone Detoxification Treatment

**DEA Form 363:** New Application for Registration Under Narcotic Addict Treatment Act of 1974

In addition to the forms, you will receive a checklist for completing the application. **Use this checklist** (see appendix A), because this is what the FDA reviewer will use to evaluate the completeness of your application!

CitatioN
21 CFR
291.505
(c)(4)(i)

**FDA Forms 2632** and **2636** are the application forms. If you are applying as a treatment program, use Form 2632; for hospital detoxification, use Form 2636. At first glance, the forms seem very short and quite simple to complete. This is because the form mainly asks for assurances of intent to uphold Federal program standards. However, as indicated on the checklist, there are several attachments that become the body of the application. These attachments include:

- **A description of the organizational structure** of the program that includes the name and complete address of the central administration or larger organizational structure responsible for the program, and a chart indicating the positions and titles of key personnel.
- **A tentative schedule of hours of operation** that shows dispensing hours, counseling hours, and hours to be worked by physicians, nurses, and counselors. This schedule should include any work performed away from the primary dispensing location.
- **A list of funding sources** that includes the name and address of each governmental agency providing funds.
- **A diagram and description of the facilities** to be used by the program. The description should demonstrate how the facilities are adequate for drug dispensing and for individual and group counseling.
- **A statement of the number of patients who will be treated** by the program when operating at full capacity.
- **A list of the names and State license numbers of all pharmacists, registered nurses, and practical nurses** licensed by law to dispense narcotic drugs who will be working with the program. If your program is in a hospital, you must also submit the names of all persons responsible for receiving and securing supplies of narcotic drugs.

CitatioN
21 CFR
291.505
(f)(2)(ii)

- **A statement of the name of the individual who will be responsible for providing rehabilitative guidance and employment placement services.** Should these services be provided through a contract with another agency, you must include a statement of the percentage of services contracted.
- **A list of the names and addresses of hospitals** providing medical services, laboratories providing drug testing or analyses, and any facility other than the primary dispensing site where methadone will be dispensed.

CitatioN
21 CFR
291.505
(d)(4)(i)(D)

- **A list of the name and address and a description of services for each public or private agency** that will be used as a part of the treatment program's plan to provide access to counseling and other social services.
- **An affirmative statement that the program will use containers having safety closures for take-home medication.**

**This citation refers to LAAM Regulation: Interim Rule. (See appendix C.)

- **A description of the manner in which methadone will be received, stored, prepared, and dispensed at the primary dispensing location.**

A copy of **FDA Form 2633** must be completed and signed by every physician licensed by law to administer or dispense narcotic drugs at the primary dispensing location of your program. If the physician is serving as medical director, he or she must indicate this on the form. If your medical director is also the medical director for another treatment program, enclose a written justification for this arrangement and a statement of how the medical director will fulfill his/her time commitment to your program.

**FDA Form 2635**, Consent to Treatment with an Approved Narcotic Drug, is used by patients after the program is in operation. When you sign the application for program approval (FDA-3632), you are assuring that your program will use this consent form.

The completed application must demonstrate that your program meets several required conditions.

- The staff responsible for administering or dispensing medications must be practitioners as defined by Section 102 (21) of the Controlled Substance Act.
- As the program sponsor, you must be responsible for all personnel and other individuals providing services in your facility.
- You must ensure that all regulations regarding the use of narcotic drugs are followed and that all persons serving patients of your program are informed of these regulations.
- You must show that you have access to physical facilities adequate for the provision of all services.
- The program must have access to a complete range of services, and when you sign the application (FDA-2632), you are assuring that you will provide "a comprehensive range of medical and rehabilitation services to patients."

When you have gathered all of this information and packaged it in the order suggested on the checklist, send two sets to FDA (the address is on the application form) and two sets to your SA. Both FDA and the SA must each receive at least one application with an original signature.

### *Interim Maintenance Treatment Programs*

Citation
21 CFR 291.505 (b)(2)(vi)
21 CFR 291.505 (d)(7)

FDA must authorize approved comprehensive programs to provide interim maintenance treatment services. If you are a public or private nonprofit methadone treatment program approved by FDA to provide comprehensive maintenance treatment and there is a need to provide interim treatment, you must submit a request to FDA that includes a written certification of approval of interim services from the chief public health officer of your State. The need for interim maintenance means that your program is unable to place the individual in comprehensive treatment within a reasonable geographic area within 14 days of the time the individual attempts to be admitted to the comprehensive program. The interim program must establish and follow appropriate and reasonable criteria for establishing priorities for transferring patients from interim maintenance to comprehensive maintenance treatment. These transfer criteria must be in writing and available for inspection by FDA. Criteria must include, at a minimum, a preference for pregnant women in admitting patients to interim maintenance and transferring patients from interim maintenance to comprehensive maintenance treatment. The program should also maintain documentation of notifications to the State chief public health officer of when a patient begins interim treatment, when a patient leaves interim treatment, and before the date of mandatory transfer to a comprehensive program.

Request for authorization as an interim maintenance treatment program should be submitted to FDA's Regulatory Management Branch, as is your original comprehensive maintenance application. (See appendix A.)

Should your State chief public health officer decertify interim maintenance treatment or should your program not maintain compliance with interim maintenance treatment standards, FDA will revoke your authorization for interim maintenance.

## DEA Approval

Citation
21 CFR 1301.11 (f)
21 CFR 1301.32 (a)(9); (b)(9)

The DEA application is only one page in length. It is included in the package sent to you by FDA or can be obtained from your local DEA office. It is very simple to complete and requires no attachments. An application fee must be submitted with the application. The FDA approval number (item 5) should be left blank because this number is assigned simultaneously with the DEA-approved program registration, which is renewed annually, You will be mailing your application to DEA headquarters (the address is on the form). Keep the last copy of the triplicate form for your files and send in the other two copies. One copy of the form will be forwarded to the local DEA Field Office for your region.

You will probably save some time and money if you clarify DEA security, safety, and recordkeeping requirements for your site before submitting your application. You can call DEA staff, or send proposed

Exhibit E

# Questions Often Asked About FDA Regulations

## *What are the minimum staffing requirements for program approval?*

Each program must designate a medical director who is responsible for administering medical services performed by the program. The medical director must be a physician licensed in your State. Other program staff are required based on the number of patients and the complexity of their problems. (Federal regulations require narcotic drugs to be administered and dispensed by practitioners licensed under State law, so be sure to check the State regulations related to program staffing.) 21 CFR 291.505(a)(3); (d)(4)(ii); (d)(5)(i); (d)(6)(c)(ii)

## *What are the most important recordkeeping requirements that I should know about?*

Each program is required to maintain a confidential and "adequate" patient record. Here, adequate means a comprehensive record that includes documentation of appropriateness for admission to the program and documentation of the services provided to the patient in the form of a treatment plan, progress notes, history, and medical information. In addition, the program must completely document medication dispensing, drug testing, and urinalysis results, and the patient record must contain FDA's patient consent form. Various signatures are required for the physician and counselors, as well as documentation of the review of the treatment plan, and lab results. 21 CFR 291.505 (d)(3)(ii); (d)(6)(v)(A)(3); (d)(13)(i)

## *Does FDA have requirements for a patient to be admitted to a program?*

Yes. FDA methadone regulations establish minimum standards for admission that state that a patient may be admitted only if the program's physician determines that the person is physiologically dependent on a narcotic drug and has been dependent for at least 1 year. This 1 year of dependence may be continual or episodic. If it is impossible to determine the date that dependence started, the program physician may use reasonable clinical judgment to determine that there was a 1-year physiologic dependence and may approve admission of the patient. There are exemptions to these standards for incarcerated persons and pregnant women. 21 CFR 291.505 (d)(1)(i)

## *Are there limitations on the dosage of narcotics that can be given to patients?*

Yes. A patient may not receive more than 30 mg of methadone as an initial dose, and the total dose for the first day may not exceed 40 mg unless the medical director documents that 40 mg did not suppress opiate abstinence symptoms. Any dose greater than 100 mg must be justified by the program's physician, and ingestion must be observed at least 6 days per week. If a patient is to receive take-home medication greater than 100 mg for more than 1 day, approval must be obtained from FDA and the State. (Some States have more stringent dosage requirements so be sure to review the State regulations.) 21 CFR 291.505 (d)(6)(i)(A); (d)(6)(i)(C); (d)(6)(v)(D)

## *Are there requirements for maintaining a treatment plan for each patient?*

Yes. An initial treatment plan that outlines short-term goals and behavioral tasks a patient must perform to complete the goals must be completed within 4 weeks of admission to the program. This treatment plan must be reviewed and evaluated at least once each 90 days during the first year of treatment and twice a year thereafter. 21 CFR 291.505 (d)(3)(iv)(A)(1); (d)(3)(v)(A) ❖

Exhibit F

# Questions Often Asked About DEA Regulations

## *Do I really have to have my complete security system installed before my program is approved by DEA?*

Yes. DEA will not approve your application until your security system is fully installed and functional. If you submit your application, DEA is willing to advise about the type of system that would pass an inspection; and your application will be held until your system is installed. It is a good idea to discuss security concerns with DEA before submitting your application. 21 CFR 1301.72-1301.74

## *What business activity should be checked on my application?*

To complete the business activity section of your application you need to review DEA's definitions of compounder, detoxification treatment, and maintenance treatment to determine which service or combination of services you will provide at each site. DEA defines detoxification as the dispensing of medication by decreasing dosages for a "short-term" period of less than 30 days or a "long-term" period of 30-180 days. Maintenance means dispensing a narcotic drug for the treatment of narcotic dependence for a period of 21 or more days. A compounder is any program engaging in maintenance or detoxification that also mixes, prepares, packages, or changes the dosage form of a narcotic drug for use in maintenance or detoxification by another narcotic treatment program. So if you prepare medications in one site for dispensing at another site, your first site is a compounder. In cases where a conflict might arise between definitions of detoxification and maintenance, the narcotic treatment program must be registered with DEA in the business activity as maintenance and detoxification program. If a similar classification does not exist on your State application, the final determination whether the activity is detoxification or maintenance would be made by the SMA. 21 CFR 1301.2(d); (e); (h)

## *Who qualifies for the exemption from payment of qualifying fees?*

Members of the U.S. military, Department of Veterans Affairs, or Public Health Service are exempt from payment of fees for registration. Also exempt are any official, employee, or other civil officer or agency of the United States, a State, or municipality who is authorized to purchase, dispense, administer, or conduct research or instructional activities in the course of that person's official capacity. 21 CFR 1301.13 (a)

## *Does DEA have recordkeeping requirements?*

Yes. DEA has very strict requirements for records and inventories related to the control of diversion of narcotic drugs. Before submitting your application, it is a good idea to review your forms and proposed recordkeeping procedures with a DEA investigator to be sure you will be in compliance. 21 CFR 1304

## *Does my medical director have to be registered with DEA?*

A separate registration is not required for the medical director as long as the physician is solely engaged in the usual course of business for the program and is licensed in the State of the program, and no other controlled substance activities are conducted. However, if the program conducts any controlled substance activity other than narcotic maintenance or detoxification, a separate registration is needed for those other activities. 21 CFR 1301.22 (a)(3); (6)

## *Why is the regular review of urinalysis results so important to DEA?*

The regular review of urinalysis results can serve as a first indication of a patient's involvement in drug diversion. A patient who tests negative for methadone and positive for other illicit drugs may be involved in drug diversion. DEA considers adherence to medical standards an essential part of diversion control efforts of a program, and the review and follow-up of urinalysis results are considered critical. ❖

Citation

21 CFR
1301.71-74

blueprints or other documentation, but it is better to arrange an appointment with a DEA field investigator to review the needs of your specific site. As mentioned earlier, the specific requirements for security and safety at your facility are based on the location and the expected patient population. When your application reaches the DEA Field Office, your program will be scheduled for a preregistration investigation site visit. If your site is fully functional, with all security systems and diversion control procedures operational when your application is submitted, the DEA approval process can be expedited.

It is also important to clarify your plans for preparing and dispensing methadone. If you plan to compound methadone on site for use at the site or transporting to another site, you will need to apply as both a treatment program and a compounder.

## For Programs That Plan to Perform Research

If you plan to conduct research involving patients served by your program, you will need to comply with Federal Protection of Human Research Subjects regulations (45 CFR 46). Should your research involve the use of an unapproved drug, you will need to submit a separate application to FDA for approval to use the drug. **Do not use the Investigational New Drug (IND) process to request exemptions from the minimum program standards!**

Citation

21 CFR 291.505
(d)(12)

21 CFR 312

21 CFR 1301.32
(a)(4)-(6)

DEA also has a separate registration process for programs that will conduct research. This separate registration does not exempt a program from meeting the basic standards required for all programs. If you plan to do any research that involves the use of medications, you will need to submit a separate application for registration. Obtaining approval for using medications in a research protocol can be a very complicated process depending on the specifications of your project, so be sure to clarify your plans with DEA before you begin.

# What Happens to My Application?

Be prepared for the fact that parts of your application will be reviewed separately by the three regulatory sources—the SA, FDA, and DEA. Each will concentrate on different aspects of the program. The SA will review your application for compliance with State regulations and usually will examine your program's geographic proximity to other programs as a means of assessing the need for the service in your area. FDA will review your program for compliance with Federal Health and Human Service regulations 21 CFR 291.505 and Federal Public Health Service confidentiality regulations 42 CFR Part 2, focusing on treatment and programmatic aspects. DEA checks compliance with the Federal Department of Justice regulations, 21 CFR 1300. DEA staff will look at drug security and drug control issues and ensure that your program meets the requirements of the Controlled Substances Act. **Each application review is separate, but as stated earlier, program approval is dependent on the applicant's receiving the approval of all three agencies. If you are not in compliance with the requirements of any one set of standards, your total application will be denied.**

## The SA Review

As with the application, each SA has its own process for reviewing applications. You should ask your SA contact for specifics of your State's review process, but you can at least expect that your application will be assigned to an SA staff person and reviewed for completeness, accuracy, and available service need in the area of your program. The reviewer will ensure that your application documents your intention to comply with all applicable State regulations for narcotic treatment programs.

## FDA Review

Your application can make it through the FDA review process in as little as 2 weeks, assuming that all information submitted is complete and meets the minimum requirements. When your application arrives at the FDA Regulatory Management Branch it will be assigned to a reviewer. Your application reviewer will log your application onto the FDA computer tracking

system. In addition, FDA will notify the SA and DEA that your application has been received. The reviewer then looks at your material to be sure that you have included everything on the checklist and that the items submitted meet the standards of the Federal Government. If you are missing items from the application or if you need to make corrections to meet regulations, the reviewer will contact you by letter. The letter will specify which items are missing or deficient and the corrective actions needed to solve any problems. You will not be given a stringent time line to resubmit missing or corrected items, but the faster things get in, the faster the application moves through the FDA process.

Exhibit G

## What Should I Ask My SA Contact?

- How does the State determine the need for narcotic treatment programs?
- Is there available capacity in the neighborhood where I want to open my program?
- Are there any special regulations for the State such as patient rights, restrictions on methadone doses, or restrictions on the length of time a patient can be maintained on methadone?
- How are the State regulations different from the Federal regulations?
- How long will it take to review my application?
- Can I have the name of the person assigned to my application so that I may contact that person if I have questions?
- How will I learn about the status of my application? Will I receive a letter?
- Will I have an opportunity to send follow-up information should you find problems with what I have submitted? ❖

If you have questions about the application, you should call FDA for clarification, and the reviewer will assist you over the telephone in completing the form or send out samples of the types of information required.

Once your application is complete, the FDA reviewer will send you a letter indicating that you have met the requirements of FDA and that full approval of the program can be granted **only after** approval is granted by DEA and the SA. FDA then waits to hear from your SA and DEA regarding approval or denial of your application. If your application is approved by all three reviewing agencies, FDA assigns a program number and issues an official program approval letter. Also, FDA provides manufacturers and the public with the names and locations of approved programs. Once approved, your program will be added to the FDA Narcotic Treatment Program Directory.

CitatioN
21 CFR 291.505
(b)(2)(i)
(j)(2)

When you receive your approval letter with your FDA program number from FDA, you are cleared to open your program. **However, you should confirm your State approval directly with your SA before you begin operating your program!**

### DEA Review

If your application is complete when it arrives at DEA headquarters, it is accepted for filing. If there are minor problems, the application will be accepted with a request for more information. If the application is considered defective and is not accepted for filing, it will be returned to you with a statement of the reasons why it has not been accepted. You are free to make corrections and resubmit the application at any time.

CitatioN
21 CFR
1301.41

The bulk of the DEA review is conducted at the preregistration investigation site visit. Prior to the investigation, however, DEA staff will review all existing information about your program, sponsor, and medical director. DEA staff will check to see if anyone associated with the program has had a history of violations related to drug issues. The investigator will also check with FDA and the SA to learn of any problems related to FDA or State regulations. Once the investigator is satisfied that there are no outstanding problems, a site visit will be conducted (see "The Inspectors Are Here!").

Generally, the registration process can be completed in 4 to 6 weeks, depending on how well you have prepared your site. If you need to make improvements

on security, safety, or recordkeeping procedures to meet DEA requirements, the investigator will provide technical assistance as necessary and will schedule another time to come to conduct the preregistration investigation. The DEA registration is the last approval you will receive for your program because FDA and SA approvals are prerequisites to DEA registration.

## What Do You Mean My Program Application Was Denied?

Any one of the application reviewers—FDA, DEA, or the SA—can deny approval of your application for a variety of reasons. If your application is denied, your FDA letter will indicate which agency denied the application and why your program was denied. If you have any questions, contact that agency directly to request clarification.

### Application Denial by the SA

Given that each SA has its own application denial process, contact your SA directly should problems with the SA review be the cause of denial of your application. SAs can deny your application if the program does not comply with State regulations, but they can also deny your program if there is no documented need for the program in the area of its location. If you are applying to open a second program, the SA may deny this application if you have had a history of problems with your first program. This includes any problems reported to the SA by FDA or DEA. In most cases, your SA will offer technical assistance.

### Application Denial by FDA

It is rare that a new application is denied by FDA. This is because FDA allows each applicant as many opportunities as necessary to submit the correct application materials. However, should your application be denied, your letter from FDA will indicate the reasons for denial of approval and will offer you an opportunity to explain any issues through an informal conference or in writing. If the reasons for denial can be corrected, the denial of approval can be reversed.

CitatioN

21 CFR 291.505 (h)(1)-(5)

Exhibit H

## Most Common Reasons Programs Are Denied DEA Registration

- Material falsification of your application information
- Owner, operator, officer, or major stockholder has been convicted of a drug-related felony
- Your State license, registration, or certification is suspended, revoked, or denied and you are not authorized by State law to handle controlled substances
- Lack of adequate controls against theft and diversion
- Your registration is inconsistent with public interest based upon criteria established in 21 U.S.C. 823(f) ❖

### Application Denial by DEA

The DEA registration process focuses on security and control issues, but DEA has the authority to deny registration based on failure to comply with all regulations including FDA and State requirements. Should DEA conduct a preregistration investigation and find your program in violation of FDA or State regulations, DEA is authorized to cite these issues as part of the DEA investigation report.

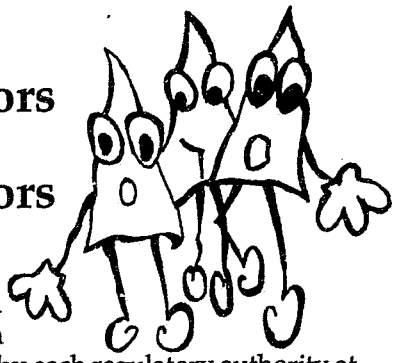
CitatioN

21 CFR 1301.48

21 CFR 1301.55

Should your application be denied, DEA will issue an order to show cause as to why the application should not be denied. The order to show cause will document the reasons for denial of the application and will ask you to present further information at a hearing. During this hearing, you will have the "burden of proof" to demonstrate that you are qualified to operate the program. DEA will expect you to address all issues, including any problems cited by the SA or FDA.

# The Inspectors Are Here! The Inspectors Are Here!



Once you have opened your program, you can expect to be inspected by each regulatory authority at some point in time. The best thing to do is to be prepared at all times because these inspections can, and usually will, occur unannounced. As many experienced providers know, one of the hardest things to do is to maintain compliance with every standard all of the time, but this should be your goal!

## Inspections by the SA

Most SAs have some form of on-site visit before the program begins or within a short time after the program opens its doors. Since each SA inspection process is specific to the State, contact your SA to get details about how to prepare for its visit. Typically, SA staff will review your physical facility, medication storage and administration policies and procedures, recordkeeping practices, medical procedures, and treatment program. Most likely the SA inspector will look at a sample of client records and interview staff and patients. In addition, the inspector may observe medication administration, urine collection, counseling or case conference sessions, and staff meetings.

The SA inspector will conduct an exit interview with clinical and management staff to discuss the findings of the visit. Usually, the SA will follow up with written communication that identifies any problem areas.

Exhibit I

### Preparing for an Inspection

- The inspectors look for documentation of service provision, so if it is not in the record it did not happen. Be sure to keep records up to date and document attempts to gather missing information.
- When the inspector asks to see records, try to get them in a timely fashion. Be sure to give complete information. For example, if urine records or other information are kept in a different location from the patient record, do not forget to give them to the inspector.
- If your program has a programwide exemption, keep a copy of the exemption letter on site so the investigator will know the exemption has been approved.
- If you have had deficiencies in the past, make sure to have corrected these problems according to your corrective action plan. The investigator will look at the old problems. ❖

## Inspections by FDA

Through the network of local district FDA offices, FDA will assign a field investigator to your program. Within the constraints of staffing at each local office, FDA will try to inspect your program within 1 year of program approval, and biannually thereafter. In addition, FDA is mandated to inspect programs that have had a history of problems to ensure that promised corrections have been made. It is the policy of FDA to make unannounced inspections.

CitatioN
21 CFR 291.505 (d)(10)

The job of the investigator is to examine the program's operations and compare them with the regulations. It is important to remember that the Federal regulations are considered *minimal* standards.

CitatioN
21 CFR 291.505 (g)
42 CFR 2

When the investigator arrives, she or he will present FDA credentials. The investigator will then ask to see the most responsible person on site; ideally this would be the program sponsor or the medical director. At this time, the investigator will issue two FDA forms, a "Notice of Inspection" and a "Routine Notice" form. These documents formally introduce the inspection process and assure the confidentiality of any patient information that the investigator will see. The investigator will look at your physical facility and examine patient records.

The investigator has the right to review all records pertaining to patients. He or she will select a sample of patient records that represent a variety of patients, such as pregnant patients, patients on exemption, patients with reduction in pick-up schedules, and so forth. The investigator will

CitatioN
21 CFR 291.505 (d)(10)
21 CFR 291.505 (d)(13)(i)

review confidentiality issues. He or she will want to see that your patient records are properly stored. Should the inspector find problems, he or she will make copies of sections of records that document deficiencies.

During the review of the physical facility, the investigator will go into the medication station and talk to the nurses about the program's procedures for administering and recording medication. He or she will check to be sure that take-home doses are properly labeled and in the right kind of containers. The investigator will check for tracking of lot numbers of methadone. Although he or she will look at drug security issues, FDA generally leaves the major review of this matter to DEA inspectors. The FDA investigator will look at how returned bottles are handled and disposed of. He or she will review your procedures for drug screening and testing to be sure that you have ways of minimizing the possibility of falsification. Investigators will also look at general life safety code and health issues, such as operational smoke detectors and the availability of toilet paper in the bathrooms.

CitatioN

21 CFR 291.505 (d)(14)

Some investigators will discuss issues with program staff as they conduct the inspection; others may wait until the conclusion of the visit to release any information. This is really a matter of style for each investigator. In either case, the findings of the site visit will be issued on FDA Form 483. FDA-483 lists the results of the investigator's inspection with regard to any problems with the program. In addition, the investigator will write a narrative that states any deviations from the regulations. These issues must be documented, however, so that anyone reviewing the information will have references to the deficiencies. When FDA-483 is issued, the investigator will request a conference with the most responsible person on site. At this time, you will be given an opportunity to respond to the findings by producing additional records that provide explanations for the findings or address the issues raised. The conclusions of this discussion are also included in the investigator's narrative Establishment Inspection Report (EIR), which discusses the contents of FDA-483 in greater detail. In addition, you will have an opportunity to respond to the findings in writing. Should any problems arise during the inspection that seem serious enough, FDA may ask you to attend an informal meeting with the local district office. In this case, you will be sent a letter requesting your attendance at such a meeting. At the meeting you will be asked to justify the findings of the inspections and offer corrective action plans.

If regulatory action may be taken against your program, it is a good idea to obtain a copy of the EIR, which is available from FDA through the Freedom of Information Act.

## Inspections by DEA

CitatioN

21 CFR 1316.03

DEA uses regional field office staff to conduct investigations. These visits are always unannounced. You can expect to be inspected by DEA during the registration application process and periodically thereafter. DEA will inspect your program more often if there are problems that need to be reviewed or if there have been allegations of impropriety filed about your program. DEA requires that the program comply with all security and recordkeeping regulations. Security includes the review of adherence to FDA standards of effective medical and counseling interventions established to minimize diversion by individual patients. DEA considers violations of these FDA standards in determining the appropriate action required to bring the program into compliance.

It is important to note that DEA considers the control of your drug supply and the potential for diversion to be a serious programmatic issue. DEA feels that the program is responsible for monitoring and controlling diversion. Not only does this mean that security measures must be effective, it also means that you must have effective medical and counseling interventions that minimize diversion by individual patients. In addition, security and control issues do not stop at the front door of your program. DEA will expect you to employ all possible means to control the actions of patients and staff in your program to prevent diversion.

In preparation for your site visit, the investigator will examine all past reports and available information about your program. He or she will monitor your progress on correcting old deficiencies. DEA staff will also check with FDA and SA staff to discuss any issues that FDA or the SA have identified during their inspections.

The DEA review is based on the following physical security and handling requirements that will vary with the specifications of your site:

- The type of activity conducted
- The type and form of controlled substances used
- The quantity of controlled substances handled
- The location of the premises and the relationship of this location to the need for security
- The type of building construction

CitatioN

21 CFR 1316.71-74

- The type of vault, safe, and secure enclosures or other storage system
- The type of closures on vaults, safes, and secure enclosures
- The adequacy of key control systems and/or combination lock control systems
- The adequacy of electric detection and alarm systems, including supervised transmittal lines and emergency power systems
- The extent of unsupervised public access to the facility, including the presence of exterior fencing
- The adequacy of supervision over employees having access to storage areas
- The procedures for handling business guests, visitors, methadone treatment personnel, and nonemployee service personnel
- The availability of local police or security personnel
- The adequacy of the program's system for monitoring the receipt, distribution, and disposition of controlled substances in its operations.

CitatioN

21 CFR
1316.06

When the investigator arrives, he or she will present agency credentials and a written Notice of Inspection, DEA Form 82. While on site, the investigator will examine security, safety, and recordkeeping practices and procedures. Specifically, the investigator will review inventory records, make a physical count of all the methadone on hand and verify this with inventory records, review narcotic order forms, and review dispensing records. The investigator will review the storage capacity and security system for the storage of narcotics and will test all alarm systems. The investigator will also review your procedures for delivery and receipt of methadone and the list of persons authorized to receive deliveries.

Following the site visit, the investigator will meet with management staff from the program to review results of the site visit. The investigator will help identify possible solutions to any identified problem areas. At this meeting, the program director will have a chance to provide any missing information, answer remaining questions from the investigator, and discuss corrective action plans. Following the site visit, the investigator will contact your narcotic suppliers to verify your purchase of medications. If your program is a compounder for other sites, the investigator will also verify delivery to other locations.

**Be sure to take notes during the site visit summary session because you will not receive a copy of the summary report on the investigation.** The DEA Report of Investigation is maintained at the field office and a copy forwarded to headquarters in Washington, D.C. for review or action.

## They Found Problems During My Inspection! Now What Do I Do?

All regulatory authorities offer opportunities to correct problems they have identified during an inspection. They are trained to be sensitive to the fact that, at times, compliance problems may be the result of larger issues, such as staffing shortages. The regulatory authorities, however, are there to monitor compliance with program standards. If problems are apparent, they are authorized to take action against your program.

### Adverse Finding Procedures of the SA

Again, each SA will have its own set of procedures that are specific to your State. Should you receive notification of an action against your program by your SA, get in touch with your SA contact. Usually, an SA

Exhibit J

### Typical Problems That Can Lead to Adverse Action by FDA

- Missing physician signatures on medication changes and laboratory results
- Missing toxicology reports for various patients
- Missing required physical exams
- Incomplete treatment plans
- Inadequate documentation for take-home medication or authorization given without FDA approval for take-home medications in amounts greater than the limits required based on the amount of time the patient has successfully been in treatment (e.g., 2 days after 3 months, 3 days after 2 years, 6 days after 3 years). Failure to reduce clinic attendance when indicated by urinalysis test results.
- Missing or incomplete psychosocial histories. ❖

will give progressively more stringent warnings before taking action against your program. Most SAs specify a formal grievance process in their State regulations. Typically, an SA will give you an opportunity to respond to written warnings within a given time period. SA staff will normally reinspect your program to ensure that changes have been made. If investigations reveal significant problems, the SA is authorized to take action against your program, such as issuing a moratorium on admissions or removing your State program approval.

Please note that your SA is authorized to recommend revocation of your program approval to FDA and DEA. Both FDA and DEA give these recommendations serious consideration in determining their courses of action with regard to your program!

## Adverse Finding Procedures of FDA

The FDA Regulatory Management Branch (the organization that originally approved your application) has the power to approve or deny regulatory action against your program. If problems are grave enough, they have the authority to administratively or judicially enforce sanctions against you, including seizure of medication supplies, injunctions, approval revocation, recommendation of revocation of your DEA registration, civil fines, and even criminal prosecution. The Regulatory Management Branch can initiate this without notice! However, notice is usually provided through several means.

CitatioN
21 CFR 291.505 (i)

Notice of violations is first given verbally by the investigator at the conclusion of the inspection. Written notification is then provided on FDA-483. Should the identified problems seem great enough to involve the Regulatory Management Branch, you could be issued a "warning letter." This letter will specify the sections of the regulations that have been violated, describe the facts establishing these violations, and state a period of time for you to submit a corrective action statement as a response. FDA will most likely conduct a second inspection visit to ensure that corrective actions have been implemented. If your corrective action statement is not submitted in a timely fashion or is unacceptable, you can be sure that a second site visit will ensue.

It is an indication of a good faith attempt to correct violations cited in the warning letter if your response to the letter is comprehensive, specific, and presented point by point. If you disagree with a charge, it should be stated clearly and respectfully with supportive documentation. Be careful not to make any commitment in your response letter that you do not intend to fully implement, because the follow-up inspection will look closely at how you implemented your proposed corrections.

If the problems with your program are even worse, or if they are found to be intentional, flagrant, part of a history of similar violations, or indicative of a callous disregard for the health and safety of your patients, FDA may conclude that administrative or judicial action should be taken immediately. If this should happen, you will be notified in writing of the action to be taken and offered an opportunity for an informal conference. You will be required to justify approval of your program, or revocation action may be immediately initiated. If your approval is revoked, this decision can be reversed if you can justify your application to the Commissioner of FDA's Center for Evaluation and Research. If your program is a multisite program, you should be aware that if approval is revoked at the primary site, approval will also be revoked at all medication unit locations.

CitatioN
21 CFR 291.505 (c)(5)(ii) (h)(1)-(5)

## Adverse Finding Procedures by DEA

Just as with FDA, DEA has authority to take action against your program should investigators find violations of regulatory standards. The DEA action may include an Investigative Warning or Letter of Admonition for less serious violations; and an Administrative Hearing, Order to Show Cause, and civil or criminal actions against the program sponsor, stockholders, or key staff for serious violations or those reflecting a continuing disregard for the regulations. In all cases, DEA will document evidence of noncompliance with various regulations.

DEA has the authority to proceed civilly or criminally against violators of law. If problems indicate a threat to the health and safety of patients or document significant breaks of security or diversion of narcotics, DEA can take immediate action against your program. This means the agency can issue an Immediate Suspension Order and revoke your registration, close the program, seize supplies of medications, and recommend that FDA and the SA revoke their approvals of your program. If registration is revoked, DEA will issue an order for this action that specifies the reasons for revocation, the facts documenting this action, and the date that revocation is to take effect. Following this action, however, you are entitled to an Order to Show Cause hearing, at which time you may appeal the Immediate Suspension Order.

As indicated earlier, following each inspection, the investigator will meet with program management staff to review the results of the inspection. DEA expects that corrective actions will be implemented within a

Exhibit K

## Typical Problems That Can Lead to Loss of DEA Registration

- Failure to maintain security within the program and in the area immediately surrounding the program
- Urinalysis results not regularly reviewed, which may indicate diversion of medication by patients
- Failure to report theft or loss of narcotics from the program
- Evidence of unauthorized access to narcotic drugs maintained at the facility
- Incomplete recordkeeping and medication inventories ❖

reasonable amount of time. Should follow-up site visits show that no changes have been made, or that new violations are discovered, DEA will proceed with additional administrative action as deemed necessary to bring you into compliance.

For violations not warranting serious action, DEA gives notice and you are allowed to take corrective action. If you have serious repeat and/or multiple violations, you will receive either a Letter of Admonition or DEA may request a hearing. The Letter of Admonition is written to advise you of any violations that are alleged to have occurred and documents them in written form. You must respond to this letter with a written corrective action plan.

CitatioN

21 CFR 1316.31-1316.34

The hearing provides an opportunity for you and DEA to discuss the necessary corrective action(s). DEA is authorized to indicate violations of FDA or State standards as evidence of noncompliance. DEA may ask you to sign a memorandum of understanding that documents the corrective actions required and the potential for registration suspension, civil or criminal action, or revocation of registration that could result if you do not make changes.

## Now That My Program Is Up and Running, What Do I Do If I Need to Make Changes?

After your program is operating, you may find it necessary to make changes in the original program design, or, over time, you will have changes in staffing, vendors, or suppliers with whom you work. Some of these changes will need to be communicated to the regulatory authorities, and some will need their approval before you implement the change.

### Amending Program Requirements of the SA

SAs have different processes for approving program changes that vary by State. Be sure to check with your SA contact before you make any changes. You can expect that the SA will at least require notification of changes in key staff or program location. In most States, a change in location will warrant a new application for approval, and a site visit. In addition, SAs require notification of temporary and permanent changes in your program's protocols, such as the hours of operation. With changes that impact on patients, the SA usually requires a written statement that documents how they will be affected by the change and how their needs will be met. The SA customarily responds with a written acknowledgment and a review of the change at the next site visit.

### Amending Program Requirements of FDA

You must notify FDA when you make certain changes to your program, but you may make them without FDA approval. These changes include the following:

CitatioN

21 CFR 291.505 (b)(2)(i)

21 CFR 291.505 (c)(2)(ii)

21 CFR 291.505 (d)(4)(i)(D)

- Notifying FDA within 3 weeks if you close a facility that was a part of the program or add a program that will not be a site for methadone dispensing. (If you add a site that will dispense methadone, you need to submit a new program approval application.)
- Notifying FDA within 3 weeks if you change the program sponsor or medical director.

- Notifying FDA immediately if you add, modify, or eliminate any off-site services.

FDA can be notified by telephone, but be sure to follow up with a letter.

A variety of other situations also require notification and approval by FDA. These situations include the following:

- Changing the laboratory used for testing or analysis.
- Placing a patient on a daily dose of methadone that is greater than 100 mg with less than 6 days per week of observed ingestion.
- Exempting an individual patient from usual participation in the methadone administration schedule because of job conflicts, distance traveled to the program, vacation, and so forth.
- Temporarily changing program hours of operation because of holidays, and so forth.
- Hospital programs acting as temporary narcotic addict treatment programs when another appropriate facility is not available for the patient.

CitatioN

21 CFR 291.505 (d)(2)(i)

21 CFR 291.505 (d)(6)(v)(D)

21 CFR 291.505 (d)(6)(vi-vii)

CitatioN

21 CFR 291.505 (f)(2)(i)

Requests for approval of these exemptions to the regulations can usually be processed over the telephone by calling the Regulatory Management Branch. In such instances, FDA will follow up its approval by sending you a letter as soon as possible. FDA logs all program approvals that it grants. This process serves as the official documentation of the granting of an approval for an exemption. Any program changes that are not properly communicated or approved will be cited as deficiencies on your next inspectional visit.

## Amending Program Requirements of DEA

CitatioN

21 CFR 1301.61

After you are registered with DEA, any modifications to your registration must be made via a written request to the DEA field office prior to implementation. Your registration is specific to the approved location and is void if you move. If you plan to move your program, contact the DEA field office well in advance to ensure that you fully understand the safety and security requirements specific to the new location.

## My Program Is Closing! What Happens Now?

Generally, programs close for one of two reasons: either they want to, or they have to. Programs that want to close should work with the SA to develop plans that will ensure an orderly transfer of patients, records, and assets. Programs that are required to close should expect to receive instructions from the SA.

Contacts with Federal agencies in regard to program closures are straightforward. Programs that decide voluntarily to discontinue business should contact the local DEA office prior to taking such action. The DEA registration certificate and any unused Narcotic Order Forms (DEA Form 222) will need to be returned to DEA, and arrangements will have to be made to dispose of the controlled substances properly.

CitatioN

21 CFR 1307.14 (a) 1307.21

In regard to programs that are closed involuntarily, the FDA regulations are silent on the procedures that need to be followed after program approval has been revoked; DEA regulations in these situations speak only to that program's responsibility for securing and disposing of controlled substances. It is the State AOD agency that is likely to have policies, guidelines, or regulations to govern this type of program closure, and it is usually this entity that oversees and monitors the event.

The role and responsibility of the SA relative to program closure varies from State to State. For example, in some States, the SA may assume all the responsibility for handling the closure; while in others, it may be a shared responsibility with a local or regional office of the State agency. In some States, county officials may also be involved.

Although the circumstances surrounding program closures may vary, the foremost concern should be to ensure continuity of care for patients. They will need to be referred to other programs for treatment; with signed consent, their records will have to be transferred to these programs as well. State agency personnel may facilitate and assist in this process. In localities where other methadone treatment programs are not readily available, the State agency should attempt to make alternative arrangements.

Records of patients who are no longer in treatment will need to be secured and maintained for a specified period of time. Policies governing the location and ownership of these records vary from State to State; you

should contact your SA to determine the procedures you will need to follow.

Finally, publicly funded programs are likely to have assets, for example furniture and equipment, that were purchased with Federal and State dollars. These assets may be confiscated by the State and redistributed throughout the treatment system.

# Appendix A—FDA Forms and Information

**For copies of the attached forms or more information about the FDA approval and monitoring process, contact:**

Food and Drug Administration
Division of Scientific Investigations
Regulatory Management Branch
7520 Standish Place, Room 115
Rockville, MD 20855
(301) 594-1029

*FDA Forms:*

| | | |
|---|---|---|
| a. | Form FDA 2632 (4/93) | Application for Approval for Use of Narcotic Drugs in a Narcotic Addiction Treatment Program |
| b. | Form FDA 2633 (6/93) | Medical Responsibility Statement for Use of Narcotic Drugs in a Treatment Program |
| c. | Form FDA 2635 (7/93) | Consent to Treatment with an Approved Narcotic Drug |
| d. | Form FDA 2636 (8/92) | Hospital Request for Methadone Detoxification Treatment |
| e. | Form FDA 482 (5/85) | Notice of Inspection (sample) |
| f. | Form FDA 2438b (5/84) | Routine Notice to Observe Patient Identifying Information |
| g. | Form FDA 483 (5/85) | Inspectional Observations |

i. Checklist Guide for Completing Form FDA–2632, Application for Approval of Use of Narcotic Drugs in a Narcotic Addiction Treatment Program

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
Food and Drug Administration

**APPLICATION FOR APPROVAL FOR USE OF NARCOTIC DRUGS IN A NARCOTIC ADDICTION TREATMENT PROGRAM**

FORM APPROVED: OMB NUMBER 0910-0140
EXPIRATION DATE: July 31, 1995.
See OMB Statement on Reverse.

DATE OF SUBMISSION

**NOTE:** This form is required by 21 CFR 291.505 pursuant to Sec. 303, Controlled Substances Act (21 USC 823) and the Drug Abuse Prevention and Control Act of 1970 (42 USC 275(a)). Failure to report can result in a recommendation for the suspension or revocation of the Narcotic Treatment Program registration.

NAME OF PROGRAM *(Name of primary dispensing location)*

ADDRESS OF PRIMARY DISPENSING LOCATION *(Include Zip Code)*

TELEPHONE NUMBER. *(Include Area Code)*

NAME AND ADDRESS OF PROGRAM SPONSOR *(Include Zip Code)*

TELEPHONE NUMBER *(Include Area Code)*

APPROXIMATE NUMBER OF PATIENTS TO BE TREATED AT ANY GIVEN TIME:
_____ METHADONE _____ LEVO-ALPHA-ACETYL-METHADOL (LAAM) OTHER *(Specify)* _____

PROGRAM FUNDING SOURCES *(Check each appropriate agency and attach the address of each)*

| | | |
|---|---|---|
| ☐ NIDA | ☐ LEAA | ☐ CETA |
| ☐ NIMH | ☐ CLIENT FEE | ☐ BUREAU OF PRISONS |
| ☐ U.S. COURTS | ☐ STATE GOVERNMENT | ☐ VETERANS ADMINISTRATION |
| ☐ INDIAN HEALTH SERVICE | ☐ PRIVATE INSURANCE | ☐ PUBLIC HEALTH SERVICE |
| ☐ PRIVATE CHARITIES | ☐ CITY & COUNTY GOVERNMENT | ☐ OTHER *(Specify)* _____ |

Commissioner
Food and Drug Administration
Division of Scientific Investigations (HFD-342)
7520 Standish Place
Rockville, MD 20855

Dear Sir/Madam:

As the person responsible for this program, I submit this application in duplicate for approval to use approved narcotic drugs in a program for detoxification and/or maintenance treatment for narcotic addicts in accordance with 21 CFR 291.505, standards for Drugs Used for Treatment of Narcotic Addicts. A copy of this application has been sent to the State Authority within which State the program is located. I understand that FDA and State approvals are necessary to obtain a registration from the Drug Enforcement Administration (DEA).

I. I have a copy of, or access to 21 CFR 291.505, Drugs Used for Treatment of Narcotic Addicts. I have read, understand and will comply with the standards established under that regulation which governs the treatment of narcotic addiction with approved narcotic drugs.

II. I have a copy of, or access to 42 CFR Part 2, Confidentiality of Alcohol and Drug Abuse Patient Records, published June 9, 1987. I have read and understand the requirements to maintain the confidiality of alcohol and drug abuse treatment patient records. I agree to protect the identity of all patients in accordance with the regulations.

III. I shall comply with the security standards for the distribution of controlled substances, as required by 21 CFR 1301, Registration of Manufacturers, Distributors, and Dispensers of Controlled Substances.

IV. A patient records system will be established to document and monitor patient care in this program. It shall be maintained so as to comply with the Federal and State reporting requirements relevant to narcotic treatment. A drug dispensing record will be maintained to show dates, quantity, and batch or code marks of the drug administered or dispensed, traceable to specific patients. This drug dispensing record must be retained for a period of three years from the date of dispensing.

A patient treatment record will be maintained for each patient. It will contain a signed Form FDA 2635, "Consent to Treatment with an Approved Narcotic Drug," the date of each visit, the result of each urinalysis, a description of any significant physical or psychological disability, the type of rehabilitative and counseling efforts employed, an account of the patient's progress, and other relevant aspects of the patient's treatment.

*(Continued on Back)*

**FORM FDA 2632 (4/93)** PREVIOUS EDITION OBSOLETE. *(Submit in Duplicate)*

V. Attached is a description of the organizational structure of this program which includes the name and complete address of any central administration or larger organizational structure to which this program is responsible.

VI. The Form FDA 2633, "Medical Responsibility Statement for Use of Narcotic Drugs in a Treatment Program," is completed and submitted in duplicate to the Food and Drug Administration and the State authority by each physician authorized to administer or dispense narcotic drugs. Attached is a list of other persons employed by the program who are licensed by law to administer narcotic drugs, even if they are not presently responsible for administering the drug.

VII. A medical director will be designated to assume responsibility for administering all medical services performed by the program. If a medical director is responsible for more than one program, the feasiblity of such an arrangement will be documented and submitted to the Food and Drug Administration. Within three weeks of any replacement of the medical director, notification will be sent to the Food and Drug Administration and the State authority.

VIII. This program shall provide a comprehensive range of medical and rehabilitative services to its patients. The addition, modification or deletion of any program services will be reported to the Food and Drug Administration.

IX. Attached is a diagram and a description of the program's facilities which demonstrate that such facilities are sufficiently spacious and well maintained to provide all necessary program services.

X. Attached are the names, addresses, and a description of each hospital, institution, clinical laboratory, or other facility used by this program to provide necessary medical and rehabilitative services. The Food and Drug Administration and State authority will be advised within three weeks of the addition or deletion of any facility which provide service other than administration or dispensing of medication.

XI. Any new dispensing site for this program, including medication units shall be approved by the Food and Drug Administration and the State authority prior to its use. The Food and Drug Administration and the State authority shall be notified within three weeks of the deletion of any facility used to dispense narcotic drugs.

XII. I agree to adhere to all rules, directives, and procedures, set forth in 21 CFR 291.505, and any regulation regarding the use of a narcotic drug for the treatment of narcotic addiction which may be promulgated in the future. I shall inform other individuals who work in this treatment program of the provisions of this regulation, and monitor their activities to assure compliance with the provisions. If I am the replaced, the Food and Drug Administration and the State authority will be notified within three weeks.

XIII. I understand that failure to abide by the rules, directives, and procedures described above may cause a suspension or revocation of approval of my registration by the Drug Enforcement Administration.

| PROGRAM SPONSOR *(Signature)* | DATE |
|---|---|
| | |

PRINT OR TYPE NAME

***Please send two copies of this form to:***

Commissioner
Food and Drug Administration
Division of Scientific Investigations (HFD-342)
7520 Standish Place
Rockville, MD 20855

***and two copies to the appropriate State methadone authority.***



**FORM FDA 2632 (4/93)**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: 0910-0140
Expiration Date: July 31,1995

DATE

## MEDICAL RESPONSIBILITY STATEMENT FOR USE OF NARCOTIC DRUGS IN A TREATMENT PROGRAM

*(Completed by each physician licensed to dispense / administer a narcotic drug under an approved program)*

**Note:** This form is required by 21 CFR 291.505 pursuant to Sec. 303, Controlled Substances Act (21 USC 823) a Drug Abuse Prevention and Control Act of 1970 (42 USC 275(a)). Failure to report can result in a recommendation for the suspension or revocation of the Narcotic Treatment Program registration.

NAME OF PROGRAM *(Name of primary dispensing location)*

ADDRESS OF PRIMARY LOCATION *(Include City, State, Zip Code)*

TELEPHONE NO. *(Include Area Code)*

I. The undersigned agrees to assume responsibility for the administration and dispensing of narcotic drugs under the above identified program and to abide by the required standards for detoxification and maintenance treatment described in 21 CFR 291.505, Standards for Drugs Used for Treatment of Narcotic Addicts; Conditions for Use of Narcotic Drugs. I have read and understand the treatment standards established by the regulations.

II. I have read and understand 42 CFR Part 2, Confidentiality of Alcohol and Drug Abuse Patient Records, published June 9, 1987. I agree to protect the identity of all patients in accordance with this regulation.

III. If I am, or should become medical director, I will assume responsibility for administering all medical services performed by the program and ensure that the program is in compliance with all Federal, State, and local laws and regulations regarding medical treatment of narcotic addiction.

**PHYSICIAN FURNISHING MEDICAL SERVICES AT THIS LOCATION**

IS THE PHYSICIAN ALSO A MEDICAL DIRECTOR? ☐ YES ☐ NO

STATE MEDICAL LICENSE NUMBER

DEA CONTROLLED SUBSTANCES REGISTRATION NUMBER

TYPED OR PRINTED NAME

SIGNATURE

***Please send two copies of this completed form to the appropriate State methadone authority and two copies to:***

Commissioner
Food and Drug Administration
Division of Scientific Investigations (HFD-342)
7520 Standish Place
Rockville, Maryland 20855

**Public reporting burden for this collection of information** is estimated to average 15 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Reports Clearance Officer, PHS
Hubert H. Humphrey Building, Room 721-B
200 Independence Avenue, S.W.
Washington, DC 20201
Attn: PRA

and to

Office of Management and Budget
Paperwork Reduction Project (0910-0140)
Washington, DC 20503

Please **DO NOT** return this report to either of these addresses.



**FORM FDA 2633 (6/93)** PREVIOUS EDITION IS OBSOLETE.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

FOOD AND DRUG ADMINISTRATION

# CONSENT TO TREATMENT WITH AN APPROVED NARCOTIC DRUG

(Provisions of this form may be modified to conform to any applicable State law)

| NAME OF PATIENT | DATE |
|---|---|
| | |

NAME OF PRACTITIONER EXPLAINING PROCEDURES

NAME OF MEDICAL DIRECTOR

I hereby authorize and give voluntary consent to the above named Program Medical Director and/or any appropriately authorized assistants he/she may select, to administer or prescribe the drug(s) methadone and/or Levo-Alpha-Acetyl-Methadol (LAAM) as an element in the treatment for my dependence on heroin or other narcotic drugs.

The procedures to treat my condition have been explained to me, and I understand that it will involve my taking the prescribed narcotic drug at the schedule determined by the Program Medical Director, or his/her designee, which will help control my dependence on heroin or other narcotic drugs.

It has been explained to me that methadone and LAAM are narcotic drugs which can be harmful if taken without medical supervision. I further understand that methadone and LAAM are addictive medications and may, like other drugs used in medical practice, produce adverse results. The alternative method of treatment, the possible risks involved, and the possibilities of complications have been explained to me, but I still desire to receive methadone and/or LAAM due to the risk of my return to heroin or other narcotic drugs.

The goal of narcotic treatment is total rehabilitation of the patient. Eventual withdrawal from the use of all drugs is an appropriate treatment goal. I realize that for some patients narcotic treatment may continue for relatively long periods of time, but that periodic consideration shall be given concerning my complete withdrawal from the use of all narcotic drugs.

I understand that I may withdraw from this treatment program and discontinue the use of the drug at any time, and I shall be afforded detoxification under medical supervision.

I agree that I shall inform any doctor who may treat me for any medical problem that I am enrolled in a narcotic treatment program, since the use of other drugs in conjunction with narcotic drugs prescribed by the treatment program may cause me harm.

I also understand that during the course of treatment, certain conditions may make it necessary to use addional or different procedures than those explained to me. I understand that these alternate procedures shall be used when in the Program Medical Director's professional judgement, it is considered advisable.

(See reverse of this form for additional consent elements)

**FORM FDA 2635 (7/93) (FRONT)** PREVIOUS EDITION IS OBSOLETE.

| FEMALE PATIENTS OF CHILD - BEARING AGE | PATIENTS UNDER 18 YEARS OF AGE |
|---|---|
| **METHADONE PATIENTS ONLY**<br><br>To the best of my knowledge, I ☐ am ☐ am not pregnant at this time.<br><br>Besides the possible risks involved with the long-term use of methadone, I further understand that, like heroin and other narcotic drugs, information on its effects on pregnant women and on their unborn children is at present inadequate to guarantee that it may not produce significant or serious side effects.<br><br>It has been explained to me, and I understand that methadone is transmitted to the unborn child and will cause physical dependence. Thus, if I am pregnant and suddenly stop taking methadone, I or the unborn child may show signs of withdrawal which may adversely affect my pregnancy or the child. I shall use no other drugs without approval of the Medical Director or his authorized assistant, since these drugs, particularly as they might interact with methadone, may harm me or my unborn child. I shall inform any other physcian who sees me during my present or any future pregnancy or who sees the child, after birth, of my current or past participation in a narcotic treatment program in order that he / she may properly care for my child and me.<br><br>It has been explained to me that after the birth of my child I should not nurse the baby because methadone is transmitted through the milk to the baby, and this may cause physical dependence on methadone in the child. I understand that for a brief period following the birth, the child may show temporary irritability or other ill effects due to my use of methadone. It is essential for the child's physician to know of my participation in a narcotic treatment program so that he / she may provide appropriate medical treatment for the child.<br><br>All the above possible effects of methadone have been explained to me, and I understand that at present there have not been enough studies conducted on the long term use of the drug to assure complete safety to my child. With full knowledge of this, I consent to its use and promise to inform the Medical Director or one of his / her assistants immediately if I become pregnant. | **LAAM MAY NOT BE PRESCRIBED FOR THESE PATIENTS— ONLY METHADONE**<br><br>The patient is a minor, _____ years of age,<br><br>born ___ ___ /___ ___ /___ ___ .<br><br>The risks of the use of methadone have been explained to (me/us) and (I/we) understand that methadone is a drug on which long term studies are still being conducted and that information on its effects in adolescents is incomplete. It has been explained to (me/us) that methadone is being used in the minor's treatment only because the risk of (his/her) return to the use of heroin is sufficiently great to justify this treatment.<br><br>(I/we) declare that participation in the narcotic treatment program is wholly voluntary on the part of both the parent(s)/guardians(s) and the patient and that methadone treatment may be stopped at any time on (my/our) request or that of the patient. With full knowedge of the potential benefits and possible risks involved with the use of methadone in the treatment of an adolesent, (I/we) consent to its use upon the minor, since (I/we) realize that otherwise (he/she) shall continue to be dependent upon heroin or other narcotic drugs.<br><br>**LAAM PATIENTS ONLY**<br><br>Female patients treated with LAAM maintenance must have an initial and monthly pregnancy test. There is insufficient evidence to recommend an appropriate dosage regimen in pregnant patients. Therefore, LAAM patients who are or become pregnant shall not be started or continued on LAAM, except by the written order of a physician. |

I certify that no guarantee or assurance has been made as to the results that may be obtained from narcotic addiction treatment. With full knowledge of the potential benefits and possible risks involved, I consent to narcotic treatment, since I realize that I would otherwise continue to be dependent on herion or other narcotic drugs.

| SIGNATURE OF PATIENT | DATE OF BIRTH<br>___ ___ /___ ___ /___ ___ | DATE |
|---|---|---|
| SIGNATURE OF PARENT(S) OR GUARDIAN(S) | RELATIONSHIP | DATE |
| SIGNATURE OF WITNESS | | DATE |

**FORM FDA 2635 (7/93) (BACK)**

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION<br>**HOSPITAL REQUEST FOR METHADONE DETOXIFICATION TREATMENT** | *Form Approval: OMB No. 0910-0140*<br>*Expiration Date: July 31, 1995.*<br>*See Reverse for OMB Statement.*<br>FOR FDA USE ONLY<br>HOSPITAL NUMBER<br>DATE |
|---|---|

**NOTE:** *This form is required by 21 CFR 291.505 pursuant to Sec. 303, Controlled Substances Act (21 USC 823) and Section 4, Comprehensive Drug Abuse Prevention and Control Act of 1970 (42 USC 275(a)). Failure to report can result in a recommendation for the suspension or revocation of the Narcotic Treatment Program registration.*

| NAME OF HOSPITAL | |
|---|---|
| ADDRESS *(Include City, State, Zip Code)* | TELEPHONE NUMBER *(Include Area Code)* |
| NAME OF PHARMACIST RESPONSIBLE FOR RECEIVING AND SECURING SUPPLIES OF METHADONE | |

| NUMBER OF BEDS IN HOSPITAL | NUMBER OF BEDS COMMITTED TO METHADONE TREATMENT *(May be expressed in parts, such as tenths)* | ANTICIPATED NUMBER OF GRAMS OF METHADONE FOR NARCOTIC ADDICT TREATMENT NEEDED ANNUALLY |
|---|---|---|
| | | |

Commissioner
Food and Drug Administration
Division of Scientific Investigations (HFD-342)
5600 Fishers Lane
Rockville, Maryland 20857

Dear Sir:

As hospital administrator, I submit this request for approval to receive supplies of methadone to be used for detoxification treatment in accordance with 21 CFR 291.505. I understand that the failure to abide by the requirements described below may result in suspension or revocation of registration to receive shipments of methadone pursuant to the Controlled Substances Act of 1970, as amended by the Narcotic Addict Treatment Act of 1974.

I. A general description of the hospital including specialized treatment facilities and nature of patient care to be undertaken is attached.

II. Methadone or narcotic addict treatment will be administered or dispensed only for detoxification treatment of hospitalized patients. I understand that the approval of this application is not necessary to permit the hospital to maintain or detoxify a person as an adjunct to medical or surgical treatment of conditions other than addiction.

III. Accurate records shall be maintained showing dates, quantity, and batch or code marks of the drugs used for inpatient detoxification treatment. The records shall be retained for a period of three years.

IV. The Food and Drug Administration, the National Institute on Drug Abuse, and the State authority may inspect supplies of the drug and evaluate compliance with applicable parts of 21 CFR 291.505. The identity of the patient will be kept confidential *(except when it is necessary to make follow-up investigations on adverse effect information related to the drug, when the medical welfare of the patient would be threatened by a failure to reveal such information, or when it is necessary to verify records relating to approval of the hospital or any portion thereof).* The confidentiality requirements or 42 CFR Part 2 shall be followed.

| TYPED OR PRINTED NAME OF HOSPITAL ADMINISTRATOR | SIGNATURE OF HOSPITAL ADMINISTRATOR | DATE |
|---|---|---|
| | | |

**FORM FDA 2636 (8/92)** PREVIOUS EDITION IS OBSOLETE

***Please send two copies of this form to:***

Commissioner
Food and Drug Administration
Division of Scientific Investigations (HFD-342)
5600 Fishers Lane
Rockville, Maryland 20857

***and two copies to the appropriate State methadone authority.***

**Public reporting burden for this collection of information** is estimated to average 10 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Reports Clearance Officer, PHS
Hubert H. Humphrey Building, Room 721-B
200 Independence Avenue, S.W.
Washington, DC 20201
Attn: PRA

and to:

Office of Management and Budget
Paperwork Reduction Project (0910-0140)
Washington, DC 20503

Please **DO NOT** return this form to either of these addresses.

**FORM FDA 2636 (8/92)**

Page 2

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

1. DISTRICT ADDRESS & PHONE NO.

TO

2. NAME AND TITLE OF INDIVIDUAL

3. DATE

4. FIRM NAME

5. HOUR a.m. p.m.

6. NUMBER AND STREET

7. CITY AND STATE & ZIP CODE

8. PHONE # & AREA CODE

**Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374(a)][1] and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264][2]**

9. SIGNATURE *(Food and Drug Administration Employee(s))*

10. TYPE OR PRINT NAME AND TITLE *(FDA Employee(s))*



**Applicable portions of Section 704 and other Sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:**

**[1]Sec. 704. (a)(1) For purposes of enforcement of this Chapter, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs or restricted devices are manufactured, processed, packed, or held, the inspection shall extend to all things therein *(including records, files, papers, processes, controls, and facilities)* bearing on whether prescription drugs or restricted devices which are adulterated or misbranded within the meaning of this Chapter, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Chapter, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Chapter. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data *(other than data as to qualifications of technical and professional personnel performing functions subject to this Act)*, and research data *(other than data, relating to new drugs, antibiotic drugs and devices and, subject to reporting and inspection under regulations lawfully issued pursuant to section 505(i) or (k), section 507(d) or (g), section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(k) of the title.* A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.**

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify, such records.

Section 512 (l)(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

**[2]Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:**

Part F - Licensing — Biological Products and Clinical Laboratories and******

Sec. 351(c) "Any officer, agent, or employee of the Department of Health & Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or other product aforesaid for sale, barter, or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession."

Part F — ******Control of Radiation.

Sec. 360 A(a) "If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safety in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times any area in such factory, warehouse, or establishment in which the manufacturer's tests *(or testing programs)* required by section 358 (h) are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this subpart and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 359(a)(2) or 359(e)."

(b) "Every manufacturer of electronic products shall establish and maintain such records *(including testing records)*, make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this subpart and standards prescribed pursuant to this subpart and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to section 359(a)."

******

(f) "The Secretary may by regulation (1) require dealers and distributors of electronic products, to which there are applicable standards prescribed under this subpart and the retail prices of which is not less than $50, to furnish manufacturers of such products such information as may be necessary to identify and locate, for purposes of section 359, the first purchasers of such products for purposes other than resale, and (2) require manufacturers to preserve such information.

FORM FDA 482 (5/85) PREVIOUS EDITION IS OBSOLETE NOTICE OF INSPECTION

(Continued On Reverse)

Any regulation establishing a requirement pursuant to clause (1) of the preceding sentence shall (A) authorize such dealers and distributors to elect, in lieu of immediately furnishing such information to the manufacturer to hold and preserve such information until advised by the manufacturer or Secretary that such information is needed by the manufacturer for purposes of section 359, and (B) provide that the dealer or distributor shall, upon making such election, give prompt notice of such election *(together with information identifying the notifier and the product)* to the manufacturer and shall, when advised by the manufacturer or Secretary, of the need therefor for the purposes of Section 359, immediately furnish the manufacturer with the required information. If a dealer or distributor discontinues the dealing in or distribution of electronic products, he shall turn the information over to the manufacturer. Any manufacturer receiving information pursuant to this subsection concerning first purchasers of products for purposes other than resale shall treat it as confidential and may use it only if necessary for the purpose of notifying persons pursuant to section 359(a)."

Sec. 360 B.(a) It shall be unlawful—
(1) ***
(2) ***
(3) "for any person to fail or to refuse to establish or maintain records required by this subpart or to permit access by the Secretary or any of his duly authorized representatives to, or the copying of, such records, or to permit entry or inspection, as required or pursuant to section 360A."
***

Part G — Quarantine and Inspection

Sec. 361(a) "The Surgeon General, with the approval of the Secretary is authorized to make and enforce such regulations as in his judgement are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgement may be necessary."

PROGRAM 7348.002 ATTACHMENT D(1)

ROUTINE NOTICE TO OBSERVE
PATIENT IDENTIFYING INFORMATION

Confidentiality of Alcohol and Drug Abuse Patient Records



_____
(Approval Number)

_____
(CF Number)

TO: _____
(Sponsor, Medical Director or Agency in Charge)

The following written statement is given pursuant to 42 CFR 2.53(a). In connection with the inspection of:

_____

_____

_____

_____
(Name and Address of Program)

initiated on _____. I agree to comply with the limitations on re-disclosure and use of patient identifying information in accordance with 42 CFR 2.53(d).

_____ _____
(Date) (Investigator)

_____
(Name of Agency)

Distribution:
Original-to individual in charge of narcotic treatment program
2 copies-to be attached to District and HFD-342 copies of EIR

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."

| PROGRAM | | ATTACHMENT |
|---|---|---|

| TRANSMITTAL NO | PAGE |
|---|---|
| FORM FDA 2438b (2/89) | COMPLIANCE PROGRAM |

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION | DISTRICT ADDRESS AND PHONE NUMBER | |
|---|---|---|
| NAME OF INDIVIDUAL TO WHOM REPORT ISSUED<br>TO: | PERIOD OF INSPECTION | C. F. NUMBER |
| TITLE OF INDIVIDUAL | TYPE ESTABLISHMENT INSPECTED | |
| FIRM NAME | NAME OF FIRM, BRANCH OR UNIT INSPECTED | |
| STREET ADDRESS | STREET ADDRESS OF PREMISES INSPECTED | |
| CITY AND STATE *(Zip Code)* | CITY AND STATE *(Zip Code)* | |

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE *(Print or Type)* | DATE ISSUED |
|---|---|---|---|

FORM FDA 483 (5/85) PREVIOUS EDITION MAY BE USED. INSPECTIONAL OBSERVATIONS PAGE OF PAGES

# CHECKLIST GUIDE

## FOR COMPLETING FORM FDA-2632

## APPLICATION FOR APPROVAL OF USE OF NARCOTIC DRUGS IN A NARCOTIC ADDICTION TREATMENT PROGRAM

1. Form FDA-2632 completed and signed by the program sponsor. The sponsor is the individual, or agent of an organization, who bears responsibility for assuring compliance with the requirements of the Methadone Regulation (21 CFR 291.505).

2. Form FDA-2633, Medical Responsibility Statement, completed and signed by each physician licensed by law to administer or dispense narcotic drugs at the primary dispensing location of this program. The physician must indicate whether he/she will be the medical director of the program. The medical director is the physician ultimately responsible for the policies and practices of the program related to ordering, prescribing, and dispensing of drugs at the primary dispensing location. Sponsors, medical directors, and physicians may be one-and-the same, or different individuals.

3. If the medical director of this facility is also the medical director for another treatment program, enclose a written justification for the feasibility of such an arrangement. This feasibility statement shall address the portion of the medical director's time spent in the treatment of unrelated medical patients, memberships on boards and committees that compete for time allocated to the treatment program.

4. List the names and State license numbers of individuals (other than physicians) licensed by law to dispense narcotic drugs even if they are not at present responsible for administering or dispensing methadone. These would include pharmacists, registered nurses, and licensed practical nurses.

5. Enclose a tentative schedule which shows (1) dispensing hours, (2) counseling hours, and (3) hours to be worked by physicians, nurses, and counselors. Any work to be performed away from the primary dispensing site, should also be stated. The program must be open for dispensing at least six days per week.

6. A description of the organizational structure of the program. A chart indicating the position and title of key personnel.

7. A list of the sources of funding, including the name and address of each governmental agency providing funds.

**Page 2 - Checklist Guide**

8. A diagram and description of the facilities to be used by this program. Demonstrate how the facilities are adequate for drug dispensing and for individual and group counseling.

9. Describe the number of patients who will treated by the program when it is operating at capacity.

10. Specify the name of the individual who will be responsible for providing rehabilitative guidance and employment placement to the patients. If any of these services are provided off site, describe the percentage contracted. The use of State or local employment agencies will not substitute for services required to be provided by the treatment program.

11. Provide the name and address of the hospital or hospitals providing medical services to the patients.

12. Provide a list containing the name, address, and a description of each public and private agency, organization, or institution that will be used as part of the treatment program's plan to provide access to counseling, rehabilitative and other social services (e.g. vocational and educational guidance, employment placement). The program sponsor must be able to document that medical and rehabilitative services are fully available to patients.

13. Provide the name and address of the laboratory providing the required drug testing or analyses. The laboratory must affirm its compliance with all applicable Federal and State proficiency testing and licensing standards.

14. Provide the name and address of any facility other than the primary dispensing site where methadone will be dispensed either on a regular basis or on weekends, and a service to the treatment program.

15. Provide an affirmative statement that the treatment program will use containers having safety closures for all take-home medication dispensed to outpatients.

16. Describe clearly and concisely the manner in which methadone will be received, stored, prepared and dispensed at the primary dispensing location.

# Appendix B—DEA Forms and Information

**For copies of the attached forms or more information about the DEA approval and monitoring process, contact:**

Drug Enforcement Administration
Registration Unit
P.O. Box 28083
Central Station
Washington, D.C. 20005
(202) 307-7250

*DEA Forms:*

a. Form DEA–363 (Apr. 1984) — New Application for Registration Under Narcotic Addict Treatment Act of 1974

b. Form DEA–363a (April 1984) — Renewal Application for Registration Under Narcotic Addict Treatment Act of 1974

c. Diversion Field Offices in Alphabetical Order by Office (July 7, 1992)

Form DEA (Apr. 1984) – 363 OMB No. 1117-0015

# NEW APPLICATION FOR REGISTRATION UNDER NARCOTIC ADDICT TREATMENT ACT of 1974

PLEASE Print OR Type ALL ENTRIES

No registration may be issued unless a completed application form has been received (1301.21 CFR 21).

PROGRAM NAME

BUSINESS ADDRESS *(Do not use P.O. Box)*

CITY STATE ZIP CODE

UNITED STATES DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION
P.O. Box 28083
CENTRAL STATION
WASHINGTON, D.C. 20005

*For INFORMATION, Call:* 202 254-8255

See "Privacy Act" Information on Reverse

THIS BLOCK FOR DEA USE ONLY

**REGISTRATION CLASSIFICATION:** Submit Check or Money Order Payable to THE DRUG ENFORCEMENT ADMINISTRATION in Amount of: $20.00. *DO NOT send CASH or STAMPS.*

1. BUSINESS ACTIVITY: *(Check ☑ one only. See Definitions on Reverse Side)*

N ☐ MAINTENANCE P ☐ DETOXIFICATION R ☐ MAINTENANCE & DETOXIFICATION S ☐ COMPOUNDER/MAINTENANCE
T ☐ COMPOUNDER/DETOXIFICATION U ☐ COMPOUNDER/MAINTENANCE & DETOXIFICATION

2. DRUG SCHEDULES *(Check Appropriate Schedule(s))* AND DRUG CODES *(Must indicate below the Narcotic Drug Code Number(s))* FOR SCHEDULES CHECKED

2 ☐ II 3 ☐ III 5 ☐ IV 6 ☐ V

3. ☐(E) CHECK THIS BLOCK IF INDIVIDUAL NAMED HEREON IS A FEDERAL, STATE, OR LOCAL OFFICIAL, IF CHECKED, *also complete Item 8.*

4. ☐(Y) CHECK HERE IF YOU REQUIRE ORDER FORMS.

5. FDA APPROVAL NUMBER

6. ALL APPLICANTS MUST ANSWER THE FOLLOWING:

(a) Are you currently authorized to prescribe, distribute, dispense, conduct research, or otherwise handle the controlled substances in the schedules for which you are applying, under the laws of the state or jurisdiction in which you are operating or propose to operate? ☐ YES ☐ NO

Current State License Number for the State in which you are applying for Registration

ATTACH CHECK HERE

(b) Has the applicant been convicted of a felony in connection with controlled substances under state or federal law? ☐ YES ☐ NO

(c) Has the applicant ever surrendered a previous CSA registration or had a CSA registration revoked, suspended, or denied? ☐ YES ☐ NO

(d) If the applicant is a corporation, association, or partnership; has any officer, partner, or stockholder been convicted of a felony in connection with controlled substances under state or federal law? ☐ YES ☐ NO

(e) If the applicant is a corporation, association, or partnership, has any officer, partner, or stockholder surrendered a previous CSA registration or had a CSA registration revoked, suspended or denied? ☐ YES ☐ NO

IF ANSWER TO QUESTIONS (b), (c), (d) or (e) is YES, *attach a letter setting forth the circumstances.*

SIGN HERE ▶ *Signature of applicant or authorized individual* *Date*

*Title (If the applicant is a corporation, institution, or other entity, enter the TITLE of the person signing on behalf of the applicant ((e.g. President, Dean, Procurement Officer, etc...))*

*Applicants Business Phone Number (Optional)*

7. SUPPLY ANY OTHER CURRENT DEA REGISTRATION NUMBERS

8. CERTIFICATION OF EXEMPT OFFICIAL *(Complete only if Item 3 is checked)*

ONLY OFFICERS, EMPLOYEES AND AGENCIES OF FEDERAL, STATE, OR LOCAL GOVERNMENTS ARE EXEMPT FROM PAYMENT OF REGISTRATION FEES.

(a) Name of governmental unit by whom applicant is employed or of which agency is a part *(e.g., U.S. Public Health Service, Iowa Department of Mental Health, Ohio State University King's County Hospital, Dallas City Health Clinic, etc...)*

(b) Is the official whose signature appears in Item 6 authorized to obtain from official stock, dispense, administer, conduct research, instructional activities or chemical analyses with controlled substances? ☐ YES ☐ NO

(c) Is he authorized to purchase controlled substances? ☐ YES ☐ NO

*Signature of applicant's certifying superior* *Date*

*Official Title of Applicant's certifying superior*

**WARNING: SECTION 843 (a)(4) OF TITLE 21, UNITED STATES CODE, STATES THAT ANY PERSON WHO KNOWINGLY OR INTENTIONALLY FURNISHES FALSE OR FRAUDULENT INFORMATION IN THIS APPLICATION IS SUBJECT TO IMPRISONMENT FOR NOT MORE THAN FOUR YEARS, A FINE OF NOT MORE THAN $30,000.00 OR BOTH**

MAIL the Original and 1 Copy with FEE to the above address. Retain 3rd copy for your records.

## DEFINITIONS

Maintenance Treatment
The dispensing for a period in excess of twenty-one days, of a narcotic drug in the treatment of an individual for dependence upon heroin or other morphine-like drugs.

Detoxification Treatment
The dispensing for a period not in excess of twenty-one days, of a narcotic drug in decreasing doses to an individual in order to alleviate adverse physiological or psychological effects incident to withdrawal from the continuous or sustained use of a narcotic drug, as a method of bringing the individual to a narcotic drug-free state within such period.

Compounder
An entity engaging in maintenance treatment or detoxification treatment which also changes the dosage form of a narcotic drug for use in maintenance treatment or detoxification treatment at other locations. Order forms are required for all transfers by a compounder for off-site use.

## PRIVACY ACT INFORMATION

Authority: Section 302 and 303 of the Controlled Substances Act of 1970 (PL 91-513)

Purpose: To obtain information required to register applicants pursuant to the Controlled Substances Act of 1970 (PL 91-513)

Routine Uses: The Controlled Substances Act Registration Records produces special reports as required for statistical analytical purposes. Disclosures of information from this system are made to the following categories of users for the purposes stated:

A. Other Federal law enforcement and regulatory agencies for law enforcement and regulatory purposes

B. State and local law enforcement and regulatory agencies for law enforcement and regulatory purposes

C. Persons registered under the Controlled Substances Act (Public Law 91-513) for the purpose of verifying the registration of customers and practitioners

Effect: Failure to complete form will preclude processing of the application.

Form DEA - 363a
(April 1984)

# RENEWAL APPLICATION FOR REGISTRATION UNDER NARCOTIC ADDICT TREATMENT ACT OF 1974

*Please PRINT or TYPE all Entries*

No registration may be issued unless a completed application form has been received (1301.21 CFR 21).

PROGRAM NAME AND ADDRESS

OMB No. 1117-0015

DEA REGISTRATION NUMBER

YOUR CURRENT REGISTRATION EXPIRES ON

NOTE: FEE CHANGE
Retain Copy 2. Mail First Copy with Fee to:

UNITED STATES DEPARTMENT OF JUSTICE
**DRUG ENFORCEMENT ADMINISTRATION**
P.O. Box 28083
CENTRAL STATION
WASHINGTON, D.C. 20005

*For INFORMATION, Call: (202) 254-8255*

**See "Privacy Act" Information on Reverse**

**REGISTRATION CLASSIFICATION:** Submit Check or Money Order Payable to *THE DRUG ENFORCEMENT ADMINISTRATION* in the Amount of **$20.00.**

1. BUSINESS ACTIVITY: *(Check ☑ one only.)*

N ☐ MAINTENANCE  P ☐ DETOXIFICATION  R ☐ MAINTENANCE & DETOXIFICATION  S ☐ COMPOUNDER/MAINTENANCE
T ☐ COMPOUNDER/DETOXIFICATION  U ☐ COMPOUNDER/MAINTENANCE & DETOXIFICATION

2. DRUG SCHEDULES *(Check Appropriate Schedule(s))*

2 ☐ II  3 ☐ III  5 ☐ IV  6 ☐ V

AND DRUG CODES *(Must indicate below the Narcotic Drug Code Number(s))*

3. ☐ (E) CHECK THIS BLOCK IF INDIVIDUAL NAMED HEREON IS A FEDERAL, STATE, OR LOCAL OFFICIAL. IF CHECKED, *ALSO COMPLETE ITEM 7.*

4. FDA APPROVAL NUMBER

5. **ALL APPLICANTS MUST ANSWER THE FOLLOWING:**

(a) Are you currently authorized to prescribe, distribute, dispense, conduct research, or otherwise handle the controlled substances in the schedules for which you are applying, under the laws of the state or jurisdiction in which you are operating or propose to operate? ☐ YES ☐ NO

Indicate current State License Number(s) _____
If State authorization is not required, indicate N/A on line above.

(b) Has the applicant been convicted of a felony in connection with controlled substances under state or federal law? ☐ YES ☐ NO

(c) Has the applicant ever surrendered a previous CSA registration or had a CSA registration revoked, suspended, or denied? ☐ YES ☐ NO

(d) If the applicant is a corporation, association, or partnership, has any officer, partner or stockholder been convicted of a felony in connection with controlled substances under state or federal law? ☐ YES ☐ NO

(e) If the applicant is a corporation, association, or partnership, has any officer, partner or stockholder surrendered a previous CSA registration or had a CSA registration revoked, suspended, or denied? ☐ YES ☐ NO

*ATTACH CHECK HERE*

IF ANSWER TO QUESTIONS (b) (c) (d) or (e) *is YES, attach a letter setting forth the circumstances.*

**SIGN HERE** ▶ _____ _____
*Signature of applicant or authorized individual* *Date*

*Title (If the applicant is a corporation, institution, or other entity, enter the TITLE of the person signing on behalf of the applicant ((e.g. President, Dean, Procurement Officer, etc...))*

*Applicants Business Phone Number (Optional)*

6. SUPPLY ANY OTHER CURRENT DEA REGISTRATION NUMBERS

7. CERTIFICATION OF EXEMPT OFFICIAL *(Complete only if Item 3 is checked)*

ONLY OFFICERS, EMPLOYEES AND AGENCIES OF FEDERAL, STATE, OR LOCAL GOVERNMENTS ARE EXEMPT FROM PAYMENT OF REGISTRATION FEES. ADDRESS ABOVE MUST REFLECT THAT OF THE GOVERNMENTAL OR STATE UNIT BY WHOM APPLICANT IS EMPLOYED.

(a) Name of governmental unit by whom applicant is employed or of which agency is a part *(e.g., Iowa Department of Mental Health, Ohio State University, King's County Hospital, Dallas City Health Clinic, etc...)*

(b) Is the official whose signature appears in Item 5 authorized to:

1) obtain from official stock, dispense, administer, conduct research, instructional activities or chemical analyses with controlled substances? ☐ YES ☐ NO

2) purchase controlled substances? ☐ YES ☐ NO

_____ _____
*Signature of applicant's certifying superior* *Date*

*Official Title of Applicant's certifying superior*

**WARNING: SECTION 843 (a) (4) OF TITLE 21, UNITED STATES CODE, STATES THAT ANY PERSON WHO KNOWINGLY OR INTENTIONALLY FURNISHES FALSE OR FRAUDULENT INFORMATION IN THIS APPLICATION IS SUBJECT TO IMPRISONMENT FOR NOT MORE THAN FOUR YEARS, A FINE OF NOT MORE THAN $30,000.00 OR BOTH.**

MAIL the First Copy with **FEE** to the above address. Retain copy for your records.

**PRIVACY ACT INFORMATION**

AUTHORITY: Section 302 and 303 of the Controlled Substances Act of 1970 (PL 91-513)

PURPOSE: To obtain information required to register applicants pursuant to the Controlled Substances Act of 1970 (PL 91-513)

ROUTINE USES: The Controlled Substances Act Registration Records produces special reports as required for statistical analytical purposes. Disclosures of information from this system are made to the following categories of users for the purposes stated:

A. Other Federal law enforcement and regulatory agencies for law enforcement and regulatory purposes.

B. State and local law enforcement and regulatory agencies for law enforcement and regulatory purposes.

C. Persons registered under the Controlled Substances Act (Public Law 91-513) for the purpose of verifying the registration of customers and practitioners.

EFFECT: Failure to complete form will preclude processing of the application.

## DIVERSION FIELD OFFICES
## IN ALPHABETICAL ORDER BY OFFICE
## JULY 7, 1992

| | | |
|---|---|---|
| ALBUQUERQUE RESIDENT OFFICE<br>4775 Indian School Road, N.E.<br>Suite 100<br>Albuquerque, NM 87110 | S/I Barry Halsey<br>& Chris Widaski<br>(505) 262-6283<br>(505) 262-6186 (fax) | Jurisdiction<br>New Mexico |
| ATLANTA DIVISION<br>75 Spring Street, SW<br>Room 740<br>Atlanta, GA 30303 | G/S Robert Williamson<br>(404) 331-7328<br>(404) 331-7340 (fax) | Jurisdiction<br>Georgia & South Carolina |
| BALTIMORE DISTRICT OFFICE<br>955 Federal Building<br>31 Hopkins Plaza<br>Baltimore, MD 21201 | G/S Robert Bickel<br>(410) 962-7580<br>(410) 962-3470 (fax) | Jurisdiction<br>Maryland (Except<br>Washington, D.C. suburbs) |
| BOSTON DIVISION<br>50 Staniford Street<br>Suite 200<br>Boston, MA 02114 | G/S Nancy M. Traub<br>(617) 557-2192<br>(617) 557-2135 (fax) | Jurisdiction<br>Maine, Massachusetts,<br>Vermont, Rhode Island,<br>New Hampshire |
| BUFFALO RESIDENT OFFICE<br>28 Church Street, Suite 300<br>Buffalo, NY 14202 | G/S Sean Mahoney<br>(716) 846-5241<br>(716) 846-5160 (fax) | Jurisdiction<br>Western & Central<br>New York |
| CAMDEN RESIDENT OFFICE<br>1000 Crawford Place Ste. 200<br>Mt. Laurel, NJ 08054 | S/I Maureen O'Keefe<br>(609) 757-5407<br>(609) 757-5006 (fax) | Jurisdiction<br>Southern New Jersey |
| CHARLESTON RESIDENT OFFICE<br>2 Monongalia Street, Suite 202<br>Charleston, WV 25302 | S/I Randy Rine<br>(304) 347-5209<br>(304) 347-5212 (fax) | Jurisdiction<br>West Virginia |
| CHICAGO DIVISION<br>500 Dirkson Federal Bldg.<br>219 S. Dearborn St., Ste. 500<br>Chicago, IL 60604 | G/S Joseph L. Rhodes<br>(312) 353-5839<br>G/S Thomas Crow<br>(312) 353-9161<br>(312) 886-8439 (fax) | Jurisdiction<br>Central& Northern<br>Illinois |

| | | |
|---|---|---|
| CLEVELAND RESIDENT OFFICE<br>Courthouse Square<br>310 Lakeside Ave., Ste. 395<br>Cleveland, OH 44113 | G/S James Crawford<br>(216) 522-3705 X349<br>(216) 522-3704 (fax) | Jurisdiction<br>Northern Ohio |
| COLUMBUS RESIDENT OFFICE<br>78 East Chestnut<br>Room 409<br>Columbus, OH 43215 | G/S Gerald R. Kopp<br>(614) 469-2595<br>(614) 469-5788 | Jurisdiction<br>Central & Southern Ohio |
| DALLAS DIVISION<br>1880 Regal Row<br>Dallas, TX 75235 | G/S Robert Wimberly<br>(214) 767-7250<br>(214) 767-7139 (fax) | Jurisdiction<br>Northern Texas |
| DENVER DIVISION<br>115 Inverness Drive East<br>Englewood, CO 80112 | G/S Michael Mapes<br>(303) 784-6381<br>(303) 784-6414 (fax) | Jurisdiction<br>Colorado & Wyoming |
| DES MOINES RESIDENT OFFICE<br>Federal Building, Rm. 937<br>210 Walnut Street<br>Des Moines, IA 50309 | S/I David Law<br>(515) 284-4700<br>(515) 284-4920 (fax) | Jurisdiction<br>Iowa |
| DETROIT DIVISION<br>357 Federal Building<br>231 W. Lafayette<br>Detroit, MI 48226 | G/S James Geldhof<br>(313) 226-2972<br>G/S James Tillman<br>(313) 226-6235<br>(313) 226-6145 (fax) | Jurisdiction<br>Michigan |
| FRESNO RESIDENT OFFICE<br>1260 M. Street, Rm. 200<br>Fresno, CA 93721 | S/I Kenneth Lott<br>(209) 487-5402<br>(209) 487-5287 (fax) | Jurisdiction<br>Central California |
| FT. LAUDERDALE RESIDENT OFFICE<br>1475 W. Cypress Creek Road<br>Suite 301<br>Ft. Lauderale, FL 33309 | G/S Louis Fisher<br>(305) 356-7740<br>(305) 365-7703 (fax) | Jurisdiction<br>South Central Florida |
| GREENSBORO RESIDENT OFFICE<br>2370 W. Meadowview Road<br>Suite 224<br>Greensboro, NC 27407 | G/S Judett R. Black<br>(919) 333-5052<br>(919) 333-5414 (fax) | Jurisdiction<br>North Carolina |

| | | |
|---|---|---|
| HARRISBURG RESIDENT OFFICE<br>P.O. Box 557<br>Harrisburg, PA 17108 | S/I Joseph Connolly<br>(717) 782-2270<br>(717) 782-4851 | Jurisdiction<br>Central<br>Pennsylvania |
| HARTFORD RESIDENT OFFICE<br>450 Main Street<br>Room 628<br>Hartford, CT 06103 | G/S Richard Seidel<br>(203) 240-3770/3231<br>(203) 240-3703 (fax) | Jurisdiction<br>Connecticut |
| HONOLULU RESIDENT OFFICE<br>300 Ala Moana Blvd., Rm 3129<br>P.O. Box 50163<br>Honolulu, HI 96850 | S/I Leila Bush<br>(808) 541-2821<br>(808) 541-3048 (fax) | Jurisdiction<br>Hawaii |
| HOUSTON DIVISION<br>333 West Loop North<br>Suite 300<br>Houston, TX 77024 | G/S John Moseman<br>(718) 681-9361 X300<br>(718) 681-9213 (fax) | Jurisdiction<br>Eastern &<br>Southern Texas |
| INDIANAPOLIS RESIDENT OFFICE<br>575 N. Pennsylvania, Rm 290<br>Indianapolis, IN 46204 | G/S Paul Hugentober<br>(317) 226-7977<br>(317) 226-7703 (fax) | Jurisdiction<br>Indiana |
| KANSAS CITY RESIDENT OFFICE<br>8600 Farley, Ste. 200<br>Overland Park, KS 66212 | G/S Terrence Boyle<br>(913) 236-3176<br>(913) 236-3186 (fax) | Jurisdiction<br>Kansas &<br>Western Missouri |
| LITTLE ROCK RESIDENT OFFICE<br>10825 Financial Parkway<br>Suite 317<br>Little Rock, AR 72211 | S/I Nancy Brusenhan<br>(501) 324-5981<br>(501) 324-6900 (fax) | Jurisdiction<br>Arkansas |
| LONG ISLAND DISTRICT OFFICE<br>1 Huntington Quadrangle<br>Suite 1C-02<br>Melville, NY 11747 | G/S Robert Brown<br>(516) 420-4532<br>(516) 420-6944 (fax) | Jurisdiction<br>Long Island, NY |
| LOS ANGELES DIVISION<br>Edward Roybal Federal Bldg.<br>255 East Temple St., 20th fl.<br>Los Angeles, CA 90012 | G/S Valencia Abrams<br>(213) 894-4016<br>(213) 894-4244 (fax) | Jurisdiction<br>South Central<br>California & Nevada |

| | | |
|---|---|---|
| LOUISVILLE RESIDENT OFFICE<br>1006 Federal Building<br>600 Martin Luther King, Jr. Pl.<br>Louisville, KY 40202 | G/S Marsha Jones<br>(502) 582-5908<br>(502) 582-5535 (fax) | Jurisdiction<br>Kentucky |
| MIAMI DIVISION<br>8400 N.W. 53rd Street<br>Miami, FL 33166 | G/S Harold Dieter<br>(305) 590-4980<br>(305) 590-4500 (fax) | Jurisdiction<br>Southeastern Florida |
| MILWAUKEE RESIDENT OFFICE<br>228 FB-USCH<br>517 E. Wisconsin<br>Milwaukee, WI 53202 | S/I Marilyn Sumner<br>(414) 297-3395<br>(414) 297-1169 (fax) | Jurisdiction<br>Wisconsin |
| MINNEAPOLIS RESIDENT OFFICE<br>402 Federal Building<br>110 S. 4th Street<br>Minneapolis, MN 55401 | G/S Carl Dahl<br>(612) 348-1723<br>(612) 348-1708 (fax) | Jurisdiction<br>Minnesota &<br>North Dakota |
| MOBILE RESIDENT OFFICE<br>1110 Mountlimar Suite 270<br>Mobile, AL 36609 | S/I Linda Traub<br>(205) 690-3368<br>(205) 690-4289 (fax) | Jurisdiction<br>Alabama |
| NASHVILLE RESIDENT OFFICE<br>801 Broadway, Room A929<br>Nashville, TN 37203 | G/S Michael Arpaio<br>(615) 736-5988<br>(615) 736-2221 (fax) | Jurisdiction<br>Tennessee |
| NEWARK DIVISION<br>Federal Office Building<br>970 Broad Street<br>Newark, NJ 07102 | G/S John Anthony<br>(201) 645-4719<br>G/S Joanne Chiavarc<br>(201) 645-5940<br>(201) 645-3724 (fax) | Jurisdiction<br>Northern & Central<br>New Jersey |
| NEW ORLEANS DIVISION<br>3838 North Couseway Blvd.<br>Suite 1800<br>Three Lake Center<br>Metairie, LA 70002 | G/S Wayne Michaels<br>(504) 840-1100<br>(504) 840-1103 (fax) | Jurisdiction<br>Louisiana &<br>Mississippi |
| NEW YORK DIVISION<br>99 Tenth Avenue<br>New York, NY 1001 | G/S John Mulvey<br>(212) 337-1575<br>G/S John Murphy<br>(212) 337-1584<br>(212) 337-2799 (fax) | Jurisdiction<br>New York (minus<br>Buffalo & Long<br>Island areas) |

| | | |
|---|---|---|
| OKLAHOMA CITY RESIDENT OFFICE<br>Federal Building<br>200 N.W. 5th St., Ste. 960<br>Oklahoma City, OK 73102 | G/S Sharon Partlo<br>(405) 231-5757<br>(405) 231-4888 (fax) | Jurisdiction<br>Oklahoma |
| OMAHA RESIDENT OFFICE<br>106 South 15th Street, Rm 1003<br>Omaha, NB 68103 | S/I Gary Anderson<br>(402) 221-4222<br>(402) 221-4225 | Jurisdiction<br>Nebraska &<br>South Dakota |
| PHILADELPHIA DIVISION<br>William J. Green Federal Bldg.<br>600 Arch Street, Rm. 10224<br>Philadelphia, PA 19106 | G/S Peaches Larro<br>(215) 597-9540<br>(215) 597-6063 (fax) | Jurisdiction<br>Delaware & Eastern<br>Pennsylvania |
| PHOENIX DIVISION<br>3010 N. 2nd Street, Set. 301<br>Phoenix, AZ 85012 | G/S Thomas Babicke<br>(602) 640-5735 x701<br>(602) 640-5741 (fax) | Jurisdiction<br>Arizona |
| PITTSBURGH RESIDENT OFFICE<br>Federal Building<br>1000 Liberty Ave., Rm 2306<br>Pittsburgh, PA 15222 | G/S Dennis M. Johnson<br>(412) 644-3388<br>(412) 644-4745 (fax) | Jurisdiction<br>Western<br>Pennsylvania |
| PORTLAND RESIDENT OFFICE<br>1220 S.W. 3rd Avenue, Rm. 1525<br>Portland, OR 97204 | G/S Gary Wyler<br>(503) 326-2466<br>(503) 326-2341 (fax) | Jurisdiction<br>Oregon |
| RICHMOND RESIDENT OFFICE<br>8600 Staples Mill Road, Ste. B<br>Richmond, VA 23228 | G/S Raymond Conner<br>(804) 771-8163<br>(804) 771-8167 (fax) | Jurisdiction<br>Central & Southern<br>Virginia |
| RIVERSIDE RESIDENT OFFICE<br>6377A Riverside Avenue, Ste. 200<br>Riverside, CA 92516-2946 | G/S Thomas A. Cox<br>(714) 276-6642<br>(714) 276-6269 (fax) | |
| SACRAMENTO RESIDENT OFFICE<br>1860 Howe Avenue, Ste. 250<br>Sacramento, CA 95821 | S/I William Davis<br>(916) 978-4225<br>(916) 978-4316 (fax) | Jurisdiction<br>Northern California |

| | | |
|---|---|---|
| SALT LAKE CITY RESIDENT OFFICE<br>American Towers III<br>47 West 200 South, Rm 401<br>Salt Lake City, UT 84101 | S/I Richard Maughan<br>(801) 524-4156<br>(801) 524-5364 (fax) | Jurisdiction<br>Utah |
| SAN ANTONIO RESIDENT OFFICE<br>10127 Morocco, STe. 200<br>San Antonio, TX 78216 | G/S Wilbur Morris<br>(512) 525-2900 x3022<br>(512) 525-2930 (fax) | Jurisdiction<br>Central & Western Texas |
| SAN DIEGO DIVISION<br>402 W. 35th Street<br>National City, CA 90250 | G/S William Paieda<br>(619) 585-4236<br>(619) 585-4224 (fax) | Jurisdiction<br>Southern California |
| SAN FRANCISCO DIVISION<br>450 Golden Gate Ave., Rm 12215<br>P.O. Box 36035<br>San Francisco, CA 94102 | G/S Carolyn Jones<br>(415) 556-3325<br>(415) 556-2042 (fax) | Jurisdiction<br>Central California Coast |
| SAN JUAN DISTRICT OFFICE<br>Casa Lee Building<br>2432 Loiza Street<br>Santurce, PR 00913 | G/S Piertro Morgess<br>(809) 253-4234<br>(809) 253-4254 (fax) | Jurisdiction<br>Puerto Rico &<br>U.S. Vergin Islands |
| SEATTLE DIVISION<br>220 W. Mercer Street, Ste. 104<br>Seattle, WA 98119 | G/S John Uncapher<br>(206) 553-5990<br>(206) 553-1576 | Jurisdiction<br>Alaska, Idoho, Montana, Washington |
| ST. LOUIS DIVISION<br>United Missouri Bank Bldg.<br>7911 Forsyrthe Blvd., Suite 500<br>St. Louis, MO 63105 | G/S Michael Peroutka<br>(314) 425-3241<br>(314) 425- 3245 (fax) | Jurisdiction<br>Eastern Missouri & Southern Illinois |
| TAMPA RESIDENT OFFICE<br>5436 Bay Center Drive<br>Tampa, FL 33609 | G/S Sherry C. Miller<br>(813) 228-2486<br>(813) 228-2298 (fax) | Jurisdiction<br>West Central Florida |
| WASHINGTON DIVISION<br>400 Sixth Street, S.W., Ste. 2558<br>Washington, D.C. 20024 | G/S Kathryn Daniels<br>(202) 401-7647<br>(202) 401-7037 (group)<br>(202) 401-7061 (fax) | Jurisdiction<br>Washington, D.C., Maryland, Northern Virginia |

# Appendix C—FDA Regulations

a. 21 CFR Part 291—Drugs Used for Treatment of Narcotic Addicts

b. 21 CFR Part 291—Drugs Used for Treatment of Narcotic Addicts [Revisions]

c. 21 CFR Part 291—Drugs Used for Treatment of Narcotic Addicts [Interim Rule]

# Part 291

# DRUGS USED FOR TREATMENT OF NARCOTIC ADDICTS

Secs.

291.501

Methadone in the maintenance treatment of narcotic addicts.

291.505

Conditions for the use of narcotic drugs; appropriate methods of professional practice for medical treatment of the narcotic addiction of various classes of narcotic addicts under Section 4 of the Comprehensive Drug Abuse Prevention and Control Act of 1970.

Authority: Secs. 505, 701 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355, 371); 21 U.S.C. 823; Secs. 301(d), 548 of the Public Health Service Act (42 U.S.C. 241(d), 290ee-3); 42 U.S.C. 257a.

## §291.501 Methadone in the maintenance treatment of narcotic addicts

(a) The Food and Drug Administration and the Drug Enforcement Administration recognize that the investigational use of methadone requiring the prolonged maintenance of narcotic dependence as part of a total treatment effort has shown promise in the management and rehabilitation of selected narcotic addicts. It is also recognized that a number of dangers and possible abuses may arise from such efforts if professional services and controls are inadequately applied. It is further felt that additional research is urgently needed so that data may be accumulated which will permit sound determinations of safety, efficacy, and necessary procedural safeguards.

(b) Therefore, the commissioner of Food and Drugs and the Director of the Drug Enforcement Administration Department of Justice, agree that interested professionals, municipalities, and organizations should be allowed to conduct further research in this area within a framework of adequate controls designed to protect the individual patients and the community. To facilitate this purpose, the Food and Drug Administration and the Drug Enforcement Administration, Department of Justice, have jointly agreed upon acceptable criteria and guidelines which are set forth in §291.505. In addition, such other provisions of the Federal narcotic laws and regulations as are applicable must also be observed.

[42 FR 46698, Sept. 16, 1977]

## §291.505 Conditions for the use of narcotic drugs; appropriate methods of professional practice for medical treatment of the narcotic addiction of various classes of narcotic addicts under Section 4 of the Comprehensive Drug Abuse Prevention and Control Act of 1970.

(a) Definitions. As used in this part:

(1) "Detoxification treatment" means the dispensing of a narcotic drug in decreasing doses to an individual to alleviate adverse physiological or psychological effects incident to withdrawal from the continuous or sustained use of a narcotic drug and as a method of bringing the individual to a narcotic drug-free state within such period. There are two types of detoxification treatment: short-term detoxification treatment and long-term detoxification treatment.

(i) "Short-term detoxification treatment" is for a period not in excess of 30 days.

(ii) "Long-term detoxification treatment" is for a period more than 30 days, but not in excess of 180 days.

(2) "Maintenance treatment" means the dispensing of a narcotic drug in the treatment of an individual for dependence on heroin or other morphine-like drug.

(3) A "medical director" is a physician, licensed to practice medicine in the jurisdiction in which the program is located, who assumes responsibility for the administration of all medical services performed by the narcotic treatment program, including ensuring that the program is in compliance with all Federal, State, and local laws and regulations regarding the medical treatment of narcotic addiction with a narcotic drug.

(4) A "medication unit" is a facility established as part of, but geographically dispersed, i.e., separate from a narcotic treatment program from which licensed private practitioners and community pharmacists-

(i) Are permitted to administer and dispense a narcotic drug, and

(ii) Are authorized to collect samples for drug testing or analysis for narcotic drugs.

(5) "Narcotic dependent" means an individual who physiologically needs heroin or a morphine-like drug to prevent the onset of signs of withdrawal.

(6) A "narcotic treatment program" is an organization (or a person, including a private physician) that administers or dispenses a narcotic drug to a narcotic addict for maintenance or detoxification treatment, provides, when appropriate or necessary, a comprehensive range of medical and rehabilitative services, is approved by the State authority and the Food and Drug Administration, and that is registered with the Drug Enforcement Administration to use a narcotic drug for the treatment of narcotic addiction.

(7) A "program sponsor" is a person (or representative of an organization) who is responsible for the operation of a narcotic treatment program and who assumes responsibility for all its employees, including any practitioners, agents, or other persons providing services at the program (including its medication units).

(8) The term "services," as used in this part, includes medical evaluations, counseling, rehabilitative and other social programs (e.g., vocational and educational guidance, employment placement, which will help the patient become a productive member of society.

(9) A "State authority" is the agency designated by the Governor or other appropriate official to exercise the responsibility and authority within the State or Territory for governing the treatment of narcotic addiction with a narcotic drug.

(b) Organizational structure and approval requirements-

(1) Organizational structure

(i) A narcotic treatment program may be an independent organization or part of a centralized organization. For example, if a centralized organizational structure consists of a primary facility and other outpatient facilities, all of which conduct initial evaluation of patients and administer or dispense medication, the primary facility and each outpatient facility are separate programs, even though some services (e.g., the same hospital or rehabilitative services) are shared.

(ii) The program sponsor shall submit to the Food and Drug Administration and the State authority a description of the organizational structure of the program, the name of the persons responsible for the program, the address of the program, and the responsibilities of each facility or medication unit. The sources of funding for each program shall be listed and the name and address of each governmental agency providing funding shall be stated.

(iii) Where two or more programs share a central administration (e.g., a city or State-wide organization), the person responsible for the organization (administrator or program sponsor) is required to be listed as the program sponsor for each separate participating program. An individual program shall indicate its participation in the central organization at the time of its application. The administrator or sponsor may fulfill all recordkeeping and reporting requirements for these programs, but each program must continue to receive separate approval.

(iv) One physician may assume primary medical responsibility for more than one program and be listed as medical director. If a physician assumes medical responsibility for more than one program, a statement documenting the feasibility of the arrangement is required to be attached to the application.

(v) [Reserved]

(2) Program approval

(i) Before a narcotic treatment program may be lawfully operated, the program, whether an outpatient facility or a private practitioner, shall submit the applications specified in this section simultaneously to the Food and Drug Administration and the State authority and must receive the approval of both, except as provided for in Paragraph (h)(5) of this section. Before granting approval, the Food and Drug Administration will consult with the Drug Enforcement Administration, Department of Justice, to ascertain if the program is in compliance with Federal controlled substances laws. Each physical location within any program is required to be identified and listed in the approval application. At the time of application for approval, the program sponsor shall indicate whether medication will be administered or dispensed at the facility. Before medication may be administered or dispensed at a location not previously approved for this purpose, the program is required to obtain approval from FDA and the State agency.

However, no approval is necessary, but notification is required when a facility in which medication is administered or dispensed is deleted by a program. In that event, the program shall notify the Food and Drug Administration and the State authority within three weeks of the deletion. Similarly, addition or deletion of facilities which provide services other than administering or dispensing medication is also permitted without approval, but notification must be made within 3 weeks to the Food and Drug Administration and the State authority about the addition and/or deletion.

(ii) Exemption of Federal programs. The provisions of this section requiring approval (or permitting disapproval or revocation of approval) by the State authority, compliance with requirements imposed by State law, or the submission of applications or reports required by the State authority do not apply to programs operated directly by the Veterans' Administration or any other department or agency of the United States. Federal agencies operating narcotic treatment programs have agreed to cooperate voluntarily with State agencies by granting permission on an informal basis for designated State representatives to visit Federal narcotic treatment programs and by furnishing a copy of Federal reports to the State authority, including the reports required under this section.

(iii) Services. Each narcotic treatment program shall provide medical and rehabilitative services and programs. (See Paragraph (d)(4) of this section.) These services should normally be made available at the primary facility, but the program sponsor may enter into a formal documented agreement with private or public agencies, organizations, or institutions for these services if they are available elsewhere. The program sponsor, in any event, must be able to document that medical and rehabilitative services are fully available to patients.

(iv) Prohibition against unapproved use of narcotic drugs. No prescribing, administering, or dispensing of a narcotic drug for the treatment of narcotic addiction may occur without prior approval by the Food and Drug Administration and the State authority, except as provided for in Paragraph (h)(5) of this section, unless specifically exempted by this section.

(v) Approved narcotic drugs for use in treatment programs. The following narcotic drug has been approved for use in the treatment of narcotic addiction: Methadone.

(3) Medication unit.

(i) A program may establish a medication unit to facilitate the needs of patients who are stabilized on an optimal dosage level. To lawfully operate a medication unit, the program shall, for each separate unit, obtain approval from the Food and Drug Administration, the Drug Enforcement Administration, and the State authority, except as provided for in Paragraph (h)(5) of this section. The Food and Drug Administration, in determining whether to approve a medication unit, will consider the distribution of units within a particular geographic area. Any new medication unit is required to receive approval before it may lawfully commence operation.

(ii) Revocation of approval. If the Food and Drug Administration revokes the primary program's approval, the approval for any medication unit associated with the program is deemed to be automatically revoked. The Food and Drug Administration's revocation of the approval of a particular medication unit, will not, in and of itself, affect the approval of the primary program.

(iii) Narcotic drug supply. A medication unit must receive its supply of the narcotic drug directly from the stocks of the primary facility. Only persons permitted to administer or dispense the drug or security personnel licensed or otherwise authorized by State law to do so may deliver the drug to a medication unit.

(iv) Referral.

(A) The patient shall be stabilized at his or her optimal dosage level before he or she may be referred to a medication unit.

(B) Since the medication unit does not provide a range of services, the program sponsor shall determine that the patient to be referred is not in need of frequent counseling, rehabilitative, and other services which are only available at the primary program facility.

(v) Services. A medication unit is limited to administering or dispensing a narcotic drug and collecting samples for drug testing or analysis for narcotic drugs in accordance with Paragraph (d)(2) of this section. If a private practitioner wishes to provide other services besides administering or dispensing a narcotic drug and collecting samples for drug testing or analysis for narcotic drugs, he or she must submit an application for separate approval.

(vi) Responsibility for patient. After a patient is referred to a medication unit, the program sponsor retains continuing responsibility for the patient's care. The program sponsor shall ensure that the patient receives needed medical and rehabilitative services at the primary facility.

(c) Conditions for approval of the use of a narcotic drug in a treatment program-

(1) Applicants. An individual listed as program sponsor for a treatment program using a narcotic drug need not personally be a licensed practitioner, but shall employ a licensed physician for the position of medical director. Persons responsible for administering or dispensing the narcotic drug shall be practitioners as defined by Section 102(21) of the Controlled Substances Act (21 U.S.C. 802(21)) and licensed to practice by the State in which the program is to be established.

(2) Assent to regulation.

(i) A person who sponsors a narcotic treatment program, and any persons responsible for a particular program, shall agree to adhere to all the rules, directives, and procedures, set forth in this section, and any regulation regarding the use of narcotic drugs in the treatment of narcotic addiction which may be promulgated in the future. The program sponsor has responsibility for all personnel and individuals providing services, who work in the program at the primary facility or at other facilities or medication units. The program sponsors shall agree to inform all personnel and individuals providing services of the provisions of this section and to monitor their activities to assure compliance with the provisions.

(ii) The Food and Drug Administration and the State authority are required to be notified within 3 weeks of any replacement of the program sponsor or medical director. Activities in violation of this regulation may give rise to the sanctions set forth in paragraph (i) of this section.

(3) Description of facilities. Only program site(s) approved by Federal, State, and local authorities may treat narcotic addicts with a narcotic drug. To obtain program approval, the applicant shall demonstrate that he or she will have access to adequate physical facilities to provide all necessary services. A program must have ready access to a comprehensive range of medical and rehabilitative services so that the services may be provided when necessary. The name, address and description of each hospital, institution, clinical laboratory, or other facility available to provide the necessary services are required to be included in the application submitted to the Food and Drug Administration and the State authority. The application is also required to include the name and address of each medication unit.

(4) Submission of proper applications. The following applications shall be filed simultaneously with both the Food and Drug Administration and the State authority.

(i) Form FDA-2632 "Application for Approval of Use of Methadone in a Treatment Program." This form, required by Paragraph (k) of this section, shall be completed and signed by the program sponsor and submitted in duplicate to the Food and Drug Administration and the State authority.

(ii) Form FDA-2633 "Medical Responsibility Statement for Use of Methadone in a Treatment Program." This form required by Paragraph (k) of this section, shall be completed and signed by each licensed physician authorized to administer or dispense narcotic drugs and submitted in duplicate to the Food and Drug Administration and the State authority. The names of any other persons licensed by law to administer or dispense narcotic drugs working in the program shall be listed even if they are not responsible for administering or dispensing the drug at the time the application is submitted.

(5) State and Federal approval, denial, and revocation of approval of narcotic treatment programs.

(i) The Food and Drug Administration may grant approval to a program only after FDA has received notification from both the State authority and the Drug Enforcement Administration that the program conforms to all pertinent State and Federal requirements.

(ii) The Food and Drug Administration will revoke the approval of a narcotic treatment program if so requested by the State authority or the Drug Enforcement Administration. If approval of a program is denied or revoked, the program shall have a right to appeal to the Commissioner, as provided for in Paragraph (h)(5) of this section.

(iii) No shipment of a narcotic drug may lawfully be made to any program which does not have current approval from the Food and Drug Administration. Within 60 days after receipt of the application from the

program sponsor for approval, the Food and Drug Administration will notify the sponsor whether the application is approved or denied.

(d)(1) Minimum standards for admission-

(i) History of addiction and current physiologic dependence.

(A) A person may be admitted as a patient for a maintenance program only if a program physician determines that the person is currently physiologically dependent upon a narcotic drug and became physiologically dependent at least 1 year before admission for maintenance treatment. A 1-year history of addiction means that an applicant for admission to a maintenance program was physiologically addicted to a narcotic at a time at least 1 year before admission to a program and was addicted, continuously or episodically, for most of the year immediately before admission to a program. In the case of a person for whom the exact date on which physiological addiction began cannot be ascertained, the admitting program physician may, in his or her reasonable clinical judgment, admit the person to maintenance treatment, if from the evidence presented, observed, and recorded in the patient's record, it is reasonable to conclude that there was physiologic dependence at a time approximately 1 year before admission.

(B) Although daily use of a narcotic for an entire year could satisfy the regulatory definition of a 1-year history of addiction, operationally one might be physiologically dependent without daily use during the entire 1-year period and still satisfy the definition. The following, although not exhaustive, are examples of applicants who would meet the minimum standard of a 1-year history of addiction and who, if currently physiologically dependent on the date of application for admission, would be eligible for admission to a maintenance program:

(*1*) Physiologic addiction began in August 1987 and continued to the date of application for admission in August 1988.

(2) Physiologic addiction began in January 1988 and continued until April 1988. Physiologic addiction began again in July 1988 and continued until the application for admission in January 1989.

(*3*) Physiologic addiction began in January 1987 and continued until October 1987. The date of application for admission was January 1988, at which time the patient had been readdicted for 1 month preceding his or her admission.

(*4*) Physiologic addiction consisted of four episodes in the last year, each episode lasting 2½ months.

(C) The program physician or an appropriately trained staff member designated and supervised by the physician shall record in the patient's record the criteria used to determine the patient's current physiologic dependence and history of addiction. In the latter circumstances, the program physician shall review, date, and countersign the supervised staff member's evaluation to demonstrate his or her agreement with the evaluation. The program physician shall make the final determination concerning a patient's physiologic dependence and history of addiction. The program physician shall sign, date, and record a statement that he or she has reviewed all the documented evidence to support a 1-year history of addiction and the current physiologic dependence and that in his or her reasonable clinical judgment the patient fulfills the requirements for admission to maintenance treatment. The program physician shall complete and record the statement before the program administers any methadone to the patient.

(ii) Voluntary participation, informed consent. The person responsible for the program shall ensure that: A patient voluntarily chooses to participate in a program; all relevant facts concerning the use of the narcotic drug used by the program are clearly and adequately explained to the patient; all patients, with full knowledge and understanding of its contents, sign the "Consent to Methadone Treatment" Form FDA-2635 (see Paragraph (k) of this section); a parent, legal guardian, or responsible adult designated by the State authority (e.g., "emancipated minor" laws) sign for patients under the age of 18 the second part of Form FDA-2635 "Consent to Methadone Treatment."

(iii) Exceptions to minimum admission criteria-

(A) Penal or chronic care. A person who has resided in a penal or chronic care institution for 1 month or longer may be admitted to maintenance treatment within 14 days before release or discharge, or within 6 months after release from such an institution without documented evidence to support findings of physiological dependence, provided the person would have been eligible for admission before he or she was incarcerated or institutionalized and, in the reasonable clinical judgment of a program physician, treatment is medically justified. Documented evidence of the prior residence in a penal or chronic care institution and evidence of all other findings and the criteria used to determine the findings are required to be recorded in the patient's record by the admitting program physician, or by

program personnel supervised by the admitting program physician. The admitting program physician shall date and sign these recordings or review the health-care professional's recordings before the initial dose is administered to the patient. In the latter case, the admitting program physician shall date and sign the recordings in the patient's record made by the health-care professional within 72 hours of administration of the initial dose to the patient.

(B) Pregnant patients.

(*1*) Pregnant patients, regardless of age, who have had a documented narcotic dependency in the past and who may return to narcotic dependency, with all its attendant dangers during pregnancy, may be placed on a maintenance regimen. For such patients, evidence of current physiological dependence on narcotic drugs is not needed if a program physician certifies the pregnancy and, in his or her reasonable clinical judgment, finds treatment to be medically justified. Evidence of all findings and the criteria used to determine the findings are required to be recorded in the patient's record by the admitting program physician, or by program personnel supervised by the admitting program physician. The admitting program physician shall date and sign these recordings or review the health-care professional's recordings before the initial methadone dose is administered to the patient. In the latter case, the admitting program physician shall date and sign the recordings in the patient's record made by the health-care professional within 72 hours of administration of the initial methadone dose to the patient. Pregnant patients are required to be given the opportunity for prenatal care either by the program or by referral to appropriate health-care providers.

(*2*) If a program cannot provide direct prenatal care for pregnant patients in treatment, the program shall establish a system for informing the patients of the publicly or privately funded prenatal care opportunities available. If there are no publicly funded prenatal referral opportunities and the program cannot provide such services or the patient cannot afford them or refuses them, then the treatment program shall, at a minimum, offer her basic prenatal instruction on maternal, physical, and dietary care as part of its counseling service.

(*3*) Counseling records and/or other appropriate patient records are required to reflect the nature of prenatal support provided by the program. If the patient is referred for prenatal services, the physician to whom she is referred is required to be notified that she is in maintenance treatment, provided that notification is in accordance with the Department of Health and Human Services' confidentiality regulations (42 CFR Part 2). If a pregnant patient refuses direct treatment or appropriate referral for treatment, the treating program physician should consider using informed consent procedures; e.g., to have the patient acknowledge in writing that she had the opportunity for this treatment but refuses it. The program physician, consistent with the confidentiality regulations, shall request the physician or the hospital to which a patient is referred to provide, following birth, a summary of the delivery and treatment outcome for the patient and offspring. If the program physician does not receive a response to the request, he or she shall document in the record that such a request was made.

(*4*) Within 3 months after termination of pregnancy, the program physician shall enter an evaluation of the patient's treatment state into her record and state whether she should remain in the maintenance program or be detoxified.

(*5*) Caution should be taken in the maintenance treatment of pregnant patients. Dosage levels should be maintained at the lowest effective dose if treatment is deemed necessary. The program sponsor shall ensure that each female patient is fully informed of the possible risks to her or to her unborn child from continued use of illicit drugs and from the use of or withdrawal from, a narcotic drug administered or dispensed by the program in maintenance or detoxification treatment.

(C) Previously treated patients. Under certain circumstances, a patient who has been treated and later voluntarily detoxified from maintenance treatment may be readmitted to maintenance treatment, without evidence to support findings of current physiologic dependence, up to 2 years after discharge, if the program attended is able to document prior narcotic drug maintenance treatment of 6 months or more, and the admitting program physician, in his or her reasonable clinical judgment, finds readmission to maintenance treatment to be medically justified. For patients meeting these criteria, the quantity of take-home medication will be determined in the reasonable clinical judgment of the program physician, but in no case may the quantity of take-home medication be greater than would have been allowed at the time the patient voluntarily terminated previous treatment. The admitting program physician or a program employee under supervision of the admitting program physician must enter in the patient's record documented evidence of the patient's prior treatment and evidence of all decisions and criteria used relating to the admission of the patient and the quantity of take-home medication permitted. The admitting program physician shall date and sign these entries in the patient's record or review the health-care professional's entries therein before the

program administers any medication to the patient. In the latter case, the admitting program physician shall date and sign the entries in the patient's record made by the health-care professional within 72 hours of administration of the initial dose to the patient.

(iv) Special limitation; treatment of patients under 18 years of age. A person under 18 is required to have had two documented attempts at short-term detoxification or drug-free treatment to be eligible for maintenance treatment. A 1-week waiting period is required after such a detoxification attempt, however, before an attempt is repeated. The program physician shall document in the patient's record that the patient continues to be or is again physiologically dependent on narcotic drugs. No person under 18 years of age may be admitted to a maintenance treatment program unless a parent, legal guardian or responsible adult designated by the State authority (e.g., "emancipated minor" laws) completes and signs consent form, Form FDA-2635 "Consent to Methadone Treatment."

(v) Denial of admission. If in the reasonable clinical judgment of the medical director a particular patient would not benefit from treatment with a narcotic drug, the patient may be refused such treatment even if the patient meets the admission standards.

(2) Minimum testing or analysis for drugs: Uses and frequency.

(i) The person(s) responsible for a program shall ensure that: An initial drug-screening test or analysis is completed for each prospective patient; at least eight additional random tests or analyses are performed on each patient during the first year in maintenance treatment; and at least quarterly random tests or analyses are performed on each patient in maintenance treatment for each subsequent year, except that a random test or analysis is performed monthly on each patient who receives a 6-day supply of take-home medication. When a sample is collected from each patient for such test or analysis, it must be done in a manner that minimizes opportunity for falsification. Each test or analysis must be analyzed for opiates, methadone, amphetamines, cocaine, and barbiturates. In addition, if any other drug or drugs have been determined by a program to be abused in that program's locality, or as otherwise indicated, each test or analysis must be analyzed for any of those drugs as well. Any laboratory that performs the testing required under this regulation shall be in compliance with all applicable Federal proficiency testing and licensing standards and all applicable State standards. If a program proposes to change a laboratory used for such testing or analysis, the program shall have the change approved by the Food and Drug Administration.

(ii) The person responsible for a program shall ensure that test results are not used as the sole criterion to force a patient out of treatment but are used as a guide to change treatment approaches. The person responsible for a program shall also ensure that when test results are used, presumptive laboratory results are distinguished from results that are definitive.

(3) Patient evaluation; minimum admission and periodic requirements-

(i) Minimum contents of medical evaluation. Each patient is required to have a medical evaluation by a program physician or an authorized health-care professional under the supervision of a program physician on admission to a program. At a minimum, this evaluation is required to consist of a medical history which includes the required history of narcotic dependence, evidence of current physiologic dependence unless excepted by the regulations, and a physical examination, and includes the following laboratory examinations: serological test for syphilis, a tuberculin skin test, and a test or analysis for drug determination. If in the reasonable clinical judgment of the program physician, a patient's subcutaneous veins are severely damaged to the extent that a blood specimen cannot be obtained, the serological test for syphilis may be omitted. The physical examination is required to consist of an investigation of the organ systems for possibilities of infectious disease, pulmonary, liver, and cardiac abnormalities, and dermatologic sequelae of addiction. In addition, the physical examination is required to include a determination of the patient's vital signs (temperature, pulse, and blood pressure and respiratory rate); an examination of the patient's general appearance, head, ears, eyes, nose, throat (thyroid), chest (including heart, lungs, and breasts), abdomen, extremities, skin, and neurological assessment; and the program physician's overall impression of the patient.

(ii) Recordings of findings. The admitting program physician or an appropriately trained health care professional supervised by the admitting program physician shall record in the patient's record all findings from the admission medical evaluation. In each case, the admitting program physician shall date and sign these entries, or date, review, and countersign these recordings in the patient's record to signify his or her review of and concurrence with the history and physical findings.

(iii) Admission evaluation.

(A) Each patient seeking admission or readmission for treatment services is required to be interviewed by a well-trained program counselor, qualified by virtue of education, training, or experience to assess the psychological and sociological background of drug abusers, to determine the appropriate treatment plan for the patient. To determine the most appropriate treatment plan for a patient, the interviewer shall obtain and document in the patient's record the patient's history.

(B) A patient's history includes information relating to his or her educational and vocational achievements. If a patient has no such history; i.e., he or she has no formal education or has never had an occupation, this requirement is met by writing this information in the patient's history.

(iv) Initial treatment plan.

(A)(1) The initial treatment plan is required to contain a statement that outlines realistic short-term treatment goals which are mutually acceptable to the patient and the program. The initial treatment plan is also required to spell out the behavioral tasks a patient must perform to complete each short-term goal; the patient's requirements for education, vocational rehabilitation, and employment; and the medical, psychosocial, economic, legal, or other supportive services that a patient needs. The plan is also required to identify the frequency with which these services are likely to be provided. Prior to developing a treatment plan, the patient's needs for medical, social, and psychological services; education; vocational rehabilitation; and employment must be assessed, and the needs reflected, when clinically appropriate, in the treatment plan.

(2) A primary counselor is one who is assigned by the program to develop, implement, and evaluate the patient's initial and periodic treatment plan and to monitor a patient's progress in treatment. The primary counselor shall enter in the patient's record the counselor's name, the contents of a patient's initial assessment, and the initial treatment plan. The primary counselor shall make these entries immediately after the patient is stabilized on a dose or within 4 weeks after admission, whichever is sooner.

(B) It is recognized that patients need varying degrees of treatment and rehabilitative services which are often dependent on or limited by a number of variables; e.g., patient resources, available program, and community services. It is not the intent of this regulation to prescribe a particular treatment and rehabilitative service or the frequency at which a service should be offered.

(C) The program supervisory counselor or other appropriate program personnel so designated by the program physician shall review and countersign all the information and findings required to be recorded in each patient's record under Paragraph (d)(3)(iv) of this section.

(v) Periodic treatment plan evaluation.

(A) The program physician or the primary counselor shall review, reevaluate, and alter where necessary each patient's treatment plan at least once each 90 days during the first year of treatment, and then at least twice a year after the first year of continuous treatment.

(B) The program physician shall ensure that the periodic treatment plan becomes part of each patient's record and that it is signed and dated in the patient's record by the primary counselor and is countersigned and dated by the supervisory counselor.

(C) At least once a year, the program physician shall date, review, and countersign the treatment plan recorded in each patient's record and ensure that each patient's progress or lack of progress in achieving the treatment goals is entered in the patient's record by the primary counselor. When appropriate, the treatment plan and progress notes should deal with the patient's mental and physical problems, apart from drug abuse. The treatment plan is required to include the name of and the reasons for prescribing any medication for emotional or physical problems.

(D) The requirement for annual physician review and signature by the program physician in Paragraph (d)(3)(v)(C) of this section is discretionary, however, as it applies to a patient, who has satisfactorily adhered to program rules for at least 3 consecutive years from his or her entrance into the maintenance treatment program and who has made substantial progress in rehabilitation.

(4) Minimum program services-

(i)(A) Access to a range of services. A treatment program shall provide a comprehensive range of medical and rehabilitative services to its patients, especially during the first 3 years of treatment.

(B) Pregnant patients

(1) For pregnant patients in a treatment program who were not admitted under Paragraph (d)(1)(iii)(B) of this section, a treatment program shall give them the opportunity for prenatal care either by the narcotic treatment program or by referral to appropriate health care providers. If a program cannot provide direct prenatal care for pregnant patients in treatment, it shall establish a system of referring them for prenatal care which may be either publicly or privately funded. If there is no publicly funded prenatal care available to which a patient may be referred, and the program cannot provide such services, or the patient cannot afford or refuses prenatal care services, then the treatment program shall, at a minimum, offer her basic prenatal instruction on maternal, physical, and dietary care as a part of its counseling service.

(2) Counseling records and other appropriate patient records are required to reflect the nature of prenatal support provided by the program. If the program refers a patient for prenatal services, it shall inform the physician to whom she is referred that the patient is in maintenance treatment, provided such notification is in accordance with the Department of Health and Human Services' confidentiality regulations (42 CFR Part 2). If a pregnant patient refuses direct prenatal services or appropriate referral for prenatal services, the treating program physician should consider using informed consent procedures; i.e., to have the patient acknowledge in writing that she has the opportunity for this treatment but refuses it. The program physician shall request the physician or the hospital to which a patient is referred to provide, following birth, a summary of the delivery and treatment outcome for the patient and offspring. The information should be obtained in accordance with the Department of Health and Human Services' confidentiality regulations (42 CFR Part 2). If no response is received, the program physician shall document in the record that such a request was made and no response was received.

(3) Caution should be taken in the maintenance treatment of pregnant patients. Dosage levels should be maintained at the lowest effective dose if continued treatment is deemed necessary. It is the responsibility of the program sponsor to ensure that each female patient is fully informed of the possible risks to a pregnant woman and her unborn child from continued use of illicit drugs and from the use of, or withdrawal from, a narcotic drug administered or dispensed by the program in maintenance or detoxification treatment.

(C) [Reserved]

(D) Off-site services. Any service not furnished at the primary facility is required to be listed in any application for approval submitted to the Food and Drug Administration or to the State authority. The addition, modification, or deletion of any program service is required to be reported immediately to the Food and Drug Administration.

(ii) Minimum medical services; designation of medical director and responsibilities. Each program shall have a designated medical director who assumes responsibility for administering all medical services performed by the program. The medical director and other authorized program physicians are required to be licensed to practice medicine in the jurisdiction in which the program is located. The medical director is responsible for ensuring that the program is in compliance with all Federal, State, and local laws and regulations regarding medical treatment of narcotic addiction. In addition, the medical director or other authorized physicians shall:

(A) Ensure that evidence of current physiologic dependence, length of history of addiction, or exceptions to criteria for admission are documented in the patient's record before the patient receives the initial dose.

(B) Ensure that a medical evaluation, including a medical history has been taken, and physical examination has been done before the patient receives the initial dose (except that in an emergency situation, the initial dose may be given before the physical examination).

(C) Ensure that appropriate laboratory studies have been performed and reviewed.

(D) Sign or countersign all medical orders as required by Federal or State law. (Such medical orders include but are not limited to the initial medication orders and all subsequent medication order changes, all changes in the frequency of take-home medication and prescribing additional take-home medication for an emergency situation.)

(E) Review and countersign treatment plans at least annually as qualified by Paragraph (d)(3)(v)(D) of this section.

(F) Ensure that justification is recorded in the patient's record for reducing the frequency of clinic visits for observed drug ingesting, providing additional take-home medication under exceptional circumstances or when there is physical disability, or prescribing any medication for physical or emotional problems.

(iii) Use of health-care professionals. Although the final decision to accept a patient for treatment may be made only by the medical director or other designated program physician, it is recognized that physicians can train program personnel to detect and document narcotic abstinence symptoms and that some jurisdictions allow State-licensed or certified health-care professionals; e.g., physician's assistants, nurse practitioners, to perform certain functions — record medical histories, perform physical examinations, and prescribe, administer, or dispense certain medications — that are ordinarily performed by a licensed physician. These regulations do not prohibit licensed or certified health-care professionals from performing those functions in narcotic treatment programs if it is authorized by Federal, State, and local laws and regulations, and if those functions are delegated to them by the medical director, and records are properly countersigned by the medical director or a licensed physician.

(iv) Vocational rehabilitation, education, and employment. Each program shall provide opportunities directly, or through referral to community resources, for patients who either desire or have been deemed by the program staff to be ready to participate in educational job training programs or to obtain gainful employment as soon as possible.

(5) Staffing patterns-

(i) Program personnel. The person(s) responsible for a program shall determine program personnel requirements after considering the number of patients who are vocationally and educationally impaired; the number of patients with significant psychopathology; the number of patients who are also non-narcotic drug or alcohol abusers; the number of patients with behavioral problems in the program; and the number of patients with serious medical problems.

(ii) Supportive services. The person(s) responsible for the program shall take notice, when considering the staffing pattern, that maintenance treatment programs need to establish supportive services in accordance with the varying characteristics and needs of their patient populations. The person(s) responsible for a program shall also take notice of the availability of existing community resources which may complement or enhance the program's delivery of supportive services and then establish a staffing pattern based on a combination of patient needs and available, accessible community resources.

(6) Frequency of attendance; quantity of take-home medication; dosage of methadone; initial and stabilization-

(i) Dosage and responsibility for administration.

(A) The person(s) responsible for the program shall ensure that the initial dose of methadone does not exceed 30 milligrams and that the total dose for the first day does not exceed 40 milligrams, unless the program medical director documents in the patient's record that 40 milligrams did not suppress opiate abstinence symptoms.

(B) A licensed physician shall assume responsibility for the amount of the narcotic drug administered or dispensed and shall record, date, and sign in each patient's record each change in dosage schedule.

(C) The administering licensed physician shall ensure that a daily dose greater than 100 milligrams is justified in the patient's record.

(ii) Authorized dispensers of narcotic drugs; responsibility. A narcotic drug may be administered or dispensed only by a practitioner licensed under the appropriate State law and registered under the appropriate State and Federal laws to order narcotic drugs for patients, or by an agent of such a practitioner, supervised by and under the order of the practitioner. This agent is required to be a pharmacist, registered nurse, or licensed practical nurse, or any other health-care professional authorized by Federal and State law to administer or dispense narcotic drugs. The licensed practitioner assumes responsibility for the amounts of narcotic drugs administered or dispensed and shall record and countersign all changes in dosage schedule.

(iii) Form. Methadone may be administered or dispensed in oral form only when used in a treatment program. Hospitalized patients under care for a medical or surgical condition are permitted to receive methadone in parenteral form when the attending physician judges it advisable. Although tablet, syrup concentrate, or other formulations may be distributed to the program, all oral medication is required to be administered or dispensed in a liquid formulation. The oral dosage form is required to be formulated in such a way as to reduce its potential for parenteral abuse. Take-home medication is required to be labeled with the treatment center's name, address, and telephone number and must be packaged in special packaging as required by 16 CFR 1700.14 in accordance with the Poison Prevention Packaging Act (Pub. L. 91-601, 15 U.S.C. 1471 et seq.) to reduce the chances of accidental ingestion.

Exceptions may be granted when these provisions conflict with State law with regard to the administering or dispensing of drugs.

(iv) Take-home medication

(A) Take-home medication may be given only to a patient who, in the reasonable clinical judgment of the program physician, is responsible in handling narcotic drugs. Before the program physician reduces the frequency of a patient's clinical visits, she or he or a designated staff member shall record the rationale for the decision in the patient's clinical record. If this is done by a designated staff member, a program physician shall review, countersign, and date the patient's record where this information is recorded.

(B) The program physician shall consider the following in determining whether, in his or her reasonable clinical judgment, a patient is responsible in handling narcotic drugs:

(*1*) Absence of recent abuse of drugs (narcotic or non-narcotic), including alcohol;

(2) Regularity of clinic attendance;

(*3*) Absence of serious behavioral problems at the clinic;

(*4*) Absence of known recent criminal activity, e.g., drug dealing;

(*5*) Stability of the patient's home environment and social relationships;

(*6*) Length of time in maintenance treatment;

(*7*) Assurance that take-home medication can be safely stored within the patient's home; and

(*8*) Whether the rehabilitative benefit to the patient derived from decreasing the frequency of clinic attendance outweighs the potential risks of diversion.

(v) Take-home requirements. The requirement of time in treatment is a minimum reference point after which a patient may be eligible for take-home privileges. The time reference is not intended to mean that a patient in treatment for a particular time has a specific right to take-home medication. Thus, regardless of time in treatment, a program physician may, in his or her reasonable judgment, deny or rescind the take-home medication privileges of a patient.

(A)(*1*) In maintenance treatment, it is required that a patient come to the clinic for observation daily or at least 6 days a week. If, in the reasonable clinical judgment of the program physician, a patient demonstrates that he or she has satisfactorily adhered to program rules for at least 3 months, has made substantial progress in rehabilitation and responsibility in handling narcotic drugs (see Paragraphs (d)(6)(iv)(B) (1) through (8) of this section, and would improve his or her rehabilitative progress by decreasing the frequency of attendance at the clinic for observation, the patient may be permitted to reduce his or her attendance at the clinic for observation to three times weekly. The patient may receive no more than a 2-day take-home supply of medication.

(2) If, in the reasonable clinical judgment of the program physician, a patient demonstrates that he or she has satisfactorily adhered to program rules for at least 2 years from his or her entrance into the program, has made substantial progress in rehabilitation and responsibility in handling narcotic drugs (see Paragraphs (d)(6)(iv)(B) (1) through (8) of this section), and would improve his or her rehabilitative progress by decreasing the frequency of attendance at the clinic for observation, the patient may be permitted to reduce his or her clinic attendance at the clinic for observation to twice weekly. Such a patient may receive no more than a 3-day take-home supply of medication.

(*3*) If, in the reasonable clinical judgment of the program physician, a patient demonstrates that he or she has satisfactorily adhered to program rules for at least 3 consecutive years from his or her entrance into the maintenance treatment program, has made substantial progress in rehabilitation, has no major behavioral problems, is responsible in handling narcotic drugs (see Paragraphs (d)(6)(iv)(B) (1) through (8) of this section), and would improve his or her rehabilitative progress by decreasing the frequency of his or her clinic attendance for observation, the patient may be permitted to reduce clinic attendance for observation to once weekly, provided that the following additional criteria are met:

The program physician has written into the patient's record an evaluation that the patient is responsible in handling narcotic drugs (Paragraphs (d)(6)(iv)(B) (1) through (8) of this section); the patient is employed (or actively seeking employment), attends school, is a homemaker, or is considered unemployable for mental or physical reasons by a program physician; the patient is not known to have abused drugs, including alcohol in the last year; and the patient is not known to have engaged in criminal activity; e.g., drug dealing in the last year. A patient is permitted to reduce clinic attendance for observation to once weekly may receive no more than a 6-day take-home supply of medication.

(B)(*1*) If a patient, after receiving a supply of take-home medication, is inexcusably absent from or misses a scheduled appointment with a treatment program without authorization from the program staff, the program physician shall increase the frequency of the patient's clinic attendance for drug ingestion under observation. For such a patient, the program physician shall not reduce the frequency of the patient's clinic attendance for drug ingestion under observation until she or he has had at least three consecutive monthly tests or analyses that are neither positive for morphine-like drugs (except from the narcotic drug administered or dispensed by the program) or other drugs of abuse, nor negative for the narcotic drug administered or dispensed by the program, and until she or he is again determined by a program physician to be responsible in handling narcotic drugs (see Paragraphs (d)(6)(iv)(B) (1) through (8) of this section) and to meet criteria in Paragraph (d)(6)(v)(A) of this section.

(2) If a patient, after receiving a 6-day supply of take-home medication, has a test or analysis which is confirmed to be positive for morphine-like drugs (except for the narcotic drug administered or dispensed by the program) or other drugs of abuse, or negative for the narcotic drug administered or dispensed by the program, the program physician shall place the patient on probation for 3 months. If, during this probation, the patient has a test or analysis either positive for morphine-like drugs (except for the narcotic drug administered or dispensed by the program) or other drugs of abuse, or negative for the narcotic drug administered or dispensed by the program, the program physician shall increase the frequency of the patient's clinic attendance for observation to at least twice weekly. Such a patient may receive no more than a 3-day take-home supply of medication until she or he has had at least three consecutive monthly tests or analyses which are neither positive for morphine-like drugs (except for the narcotic drug administered or dispensed by the program) or other drugs of abuse, nor negative for the narcotic drug administered or dispensed by the program, and the program physician again determines that the patient is responsible in handling narcotic drugs (see Paragraphs (d)(6)(iv)(B) (1) through (8) of this section) and meets the criteria contained in Paragraph (d)(6)(v)(A) of this section.

(C) In calculating the number of years of maintenance treatment, the period is considered to begin on the first day the medication is administered, or on readmission if a patient has had a continuous absence of 90 days or more. Cumulative time spent by the patient in more than one program is counted toward the number of years of treatment, provided there has not been a continuous absence of 90 days or more.

(D) Each patient whose daily dose is above 100 milligrams is required to be under observation while ingesting the drug at least 6 days per week irrespective of the length of time in treatment, unless the program has received prior approval from the Food and Drug Administration with the concurrence of the State authority.

(vi) Exceptions to take-home requirements. If, in the reasonable clinical judgment of the program physician:

(A) A patient is found to have a physical disability which interferes with his or her ability to conform to the applicable mandatory schedule, she or he may be permitted a temporarily or permanently reduced schedule, provided she or he is also found to be responsible in handling narcotic drugs.

(B) A patient, because of exceptional circumstances such as illness, personal or family crises, travel, or other hardship, is unable to conform to the applicable mandatory schedule, she or he may be permitted a temporarily reduced schedule, provided she or he is also found to be responsible in handling narcotic drugs. The rationale for an exception to a mandatory schedule is to be based on the reasonable clinical judgment of the program physician and shall be recorded in the patient's record by the program physician or by program personnel supervised by the program physician. In the latter situation, the physician shall review, countersign, and date the patient's record where this rationale is recorded. In any event, a patient may not be given more than a 2 week supply of narcotic drugs at one time.

(vii) Official State holidays. If a treatment center program is not in operation due to the observance of an official State holiday, patients may be permitted one extra take-home dose per visit and one fewer clinic visit per week to allow patients not to have to attend the clinic on an official State holiday. An official State holiday is a holiday on which most State offices are usually closed and routine State government business is not conducted.

(7) [Reserved]

(8) Minimum standards for short-term detoxification treatment.

(i) For short-term detoxification from narcotic drugs, the narcotic drug is required to be administered by the program physician or by an authorized agent of the physician, supervised by and under the order of the physician. The narcotic drug is required to be administered daily, under close observation, in reducing dosages over a period not to exceed 30 days. All requirements for maintenance treatment apply to short-term detoxification treatment with the following exceptions:

(A) Take-home medication is not allowed during short-term detoxification.

(B) A history of 1 year physiologic dependence is not required for admission to short-term detoxification.

(C) Patients who have been determined by the program physician to be currently physiologically narcotic dependent may be placed in short-term detoxification treatment, regardless of age.

(D) No test or analysis is required except for the initial drug screening test or analysis.

(E) The initial treatment plan and periodic treatment plan evaluation required for maintenance patients are not necessary for short-term detoxification patients. However, a primary counselor must be assigned by the program to monitor a patient's progress toward the goal of short-term detoxification and possible drug-free treatment referral.

(F) The requirements of Paragraph (d)(4) of this section, except Paragraphs (d)(4)(ii) (A) through (D) and (d)(4)(iii) of this section, do not apply to short-term detoxification treatment.

(ii) A patient is required to wait at least 7 days between concluding a short-term detoxification treatment episode and beginning another. Before a short-term detoxification attempt is repeated, the program physician shall document in the patient's record that the patient continues to be, or is again, physiologically dependent on narcotic drugs. The provisions of these requirements, except as noted in Paragraph (d)(8)(i) of this section, apply to both inpatient and ambulatory short-term detoxification treatment.

(iii) Short-term detoxification treatment is not recommended for a pregnant patient.

(9) Minimum standards for long-term detoxification treatment.

(i) For long-term detoxification from narcotic drugs, the narcotic drug is required to be administered by the program physician or by an authorized agent of the physician, supervised by and under the order of the physician. The narcotic drug is required to be administered on a regimen designed to reach a drug-free state and to make progress in rehabilitation in 180 days or less. All requirements for maintenance treatment apply to long-term detoxification treatment with the following exception.

(A) In long-term detoxification treatment, it is required that the patient be under observation while ingesting the drug daily or at least 6 days a week, for the duration of the long-term detoxification treatment.

(B) A history of 1 year physiologic dependence is not required for admission to long-term detoxification.

(C) The program physician shall document in the patient's record that short-term detoxification is not a sufficiently long enough treatment course to provide the patient with the additional program services he or she deems necessary for the patient's rehabilitation. The program physician shall document this information in the patient's record before long-term detoxification may begin.

(D) Patients who have been determined by the program physician to be currently physiologically dependent on narcotics may be placed in long-term detoxification treatment, regardless of age.

(E) An initial drug screening test or analysis is required for each patient. And at least one additional random test or analysis must be performed monthly on each patient during long-term detoxification.

(F) The initial treatment plan and periodic treatment plan evaluation required for maintenance patients are also required for long-term detoxification patients, except that the required periodic treatment plan evaluation is required to occur monthly.

(ii) A patient is required to wait at least 7 days between concluding a long-term treatment episode and beginning another. Before a long-term detoxification attempt is repeated, the program physician shall document in the patient's record that the patient continues to be or is again physiologically dependent on narcotic drugs. The provisions of these requirements apply to both inpatient and ambulatory long-term detoxification treatment.

(iii) Long-term detoxification is not recommended for a pregnant patient.

(10) Inspections of programs; patient confidentiality. A program shall allow inspections by duly authorized employees of the State authority, and in accordance with Federal controlled substances law and Federal confidentiality laws, by duly authorized employees of the Food and Drug Administration, the Drug Enforcement Administration of the Department of Justice, and the National Institute on Drug Abuse.

(11) Exemptions from specific program standards.

(i) A program is permitted, at the time of application or any time thereafter, to request exemption from specific program standards. The rationale for an exemption shall be thoroughly documented in an appendix to be submitted with the application or at some later time. The Food and Drug Administration will approve such exemptions of program standards at the time of application, or any time thereafter, with the concurrence of the State authority. An example of a case in which an exemption might be granted would be for a private practitioner who wishes to treat a limited number of patients in a nonmetropolitan area with few physicians and no rehabilitative services geographically accessible and requests exemption from some of the staffing and service standards.

(ii) The Food and Drug Administration has the right to withhold the granting of an exemption requested at the time of application until a program is in actual operation in order to assess if the exemption is necessary. If periodic inspections of the program reveal that discrepancies or adverse conditions exist, the Food and Drug Administration shall reserve the right to revoke any or all exemptions previously granted.

(12) Research. When a program conducts research on human subjects or provides subjects for research, there must be written policies and written review to assure the rights of the patients involved. Appropriate informed consent forms are required to be signed by the patient and to be retained in his or her patient record at the program. All research, development, and related activities which involve human subjects and which are funded by grants from or contracts with the Department of Health and Human Services are required to comply with the Department of Health and Human Services' regulations on the protection of human subjects, 45 CFR Part 46, and confidentiality of information, 42 CFR Part 2. All investigational research involving human subjects conducted for submission to the Food and Drug Administration must be conducted in compliance with Part 312 of this chapter.

(13) Patient record system-

(i) Patient care. The person(s) responsible for a program shall establish a record system to document and monitor patient care. This system is required to comply with all Federal and State reporting requirements relevant to methadone. All records are required to be kept confidential and in accordance with all applicable Federal and State regulations regarding confidentiality.

(ii) Drug dispensing. The person(s) responsible for a program shall ensure that accurate records traceable to specific patients are maintained showing dates, quantity, and batch or code marks of the drug dispensed. These records must be retained for a period of 3 years from the date of dispensing.

(iii) Patient's record. An adequate record must be maintained for each patient. The record is required to contain a copy of the signed consent form(s), the date of each visit, the amount of drug administered or dispensed, the results of each test or analysis for drugs, any significant physical or psychological disability, the type of rehabilitative and counseling efforts employed, an account of the patient's progress, and other relevant aspects of the treatment program. For recordkeeping purposes, if a patient misses appointments for 2 weeks or more without notifying the program, the episode of care is considered terminated and is to be so noted in the patient's record. This does not mean that the patient cannot return for care. If the patient does return for care and is accepted into the program, this is considered a readmission and is to be so noted in the patient's record. This method of recordkeeping helps assure the easy detection of sporadic attendance and decreases the possibility of administering inappropriate doses of narcotic drugs (e.g., the patient who has received no medication for several days or more and upon return receives the usual stabilization dose). An annual evaluation of the patient's progress must be entered in the patient's record.

(14) Security of drug stocks. Adequate security is required to be maintained over drug stocks, over the manner in which it is administered or dispensed, over the manner in which it is distributed to medication units, and over the manner in which it is stored to guard against theft and diversion of the drug. The program is required to meet the security standards for the distribution and storage of controlled substances as required by the Drug Enforcement Administration, Department of Justice (21 CFR 1301.72-1301.76).

(e) Multiple enrollments-

(1) Administering or dispensing to patients enrolled in other programs. There is a danger of drug dependent persons attempting to enroll in more than one narcotic treatment program to obtain quantities of drugs for the purpose of self-administration or illicit marketing. Therefore, except in an emergency situation, drugs shall not be provided to a patient who is known to be currently receiving drugs from another treatment program.

(2) Patient attendance requirements. The patient shall always report to the same treatment facility unless prior approval is obtained from the program sponsor for treatment at another program. Permission to report for treatment at the facility of another program shall be granted only in exceptional circumstances and shall be noted on the patient's clinical record.

(f) Conditions for use of narcotic drugs in hospitals for detoxification treatment-

(1) Form. The drug may be administered or dispensed in either oral or parenteral form. (See Paragraph (d)(6)(iii) of this section.)

(2) Use of narcotic drugs in hospitals-

(1) [sic] Approved uses. For hospitalized patients, the use of a narcotic drug for narcotic addict treatment may be administered or dispensed only for detoxification treatment. If a narcotic drug is administered for treatment of narcotic dependence for more than 180 days, the procedure is no longer considered detoxification but is, rather, considered maintenance treatment. Only approved narcotic treatment programs may undertake maintenance treatment. This does not preclude the maintenance treatment of a patient who is hospitalized for treatment of medical conditions other than addiction and who requires temporary maintenance treatment during the critical period of his or her stay or whose enrollment in a program which has approval for maintenance treatment using narcotic drugs has been verified. (See 21 CFR 1306.07(c).) Any hospital which already has received approval under this paragraph (f) may serve as a temporary narcotic treatment program when an approved treatment program has been terminated, and there is no other facility immediately available in the area to provide narcotic drug treatment for the patients. The Food and Drug Administration may give this approval upon the request of the State authority or the hospital, when no State authority has been established.

(ii) Individuals responsible for supplies. Hospitals shall submit to the Food and Drug Administration and the State authority the name of the individual (e.g., pharmacist) responsible for receiving and securing supplies of narcotic drugs for the treatment of narcotic addicts. The individual responsible for supplies shall ensure that the only persons who receive supplies of narcotic drugs are those who are authorized to do so by Federal or State law.

(iii) General description. The hospital shall submit to the Food and Drug Administration and the State authority a general description of the hospital, including the number of beds, specialized treatment facilities for drug dependence, and nature of patient care undertaken.

(iv) Anticipated quantity of drug needed. The hospital shall submit to the Food and Drug Administration and the State authority the anticipated quantity of narcotic drugs for narcotic addict treatment needed per year.

(v) Records. The hospital shall maintain accurate records showing dates, quantity, and batch or code marks of the drug used for inpatient treatment. The hospital shall retain the records for at least a period of 3 years.

(vi) Inspection. The hospital shall permit the Food and Drug Administration and the State authority to inspect supplies of the drug at the hospital and evaluate the uses to which the drug is being put. The Food and Drug Administration and the State authority will keep the identity of the patients confidential in accordance with confidentiality requirements of 42 CFR Part 2. Records on the receipt, storage, and distribution of narcotic medication are subject to inspection under Federal controlled substances law; but use or disclosure of records identifying patients will, in any case, be limited to actions involving the program or its personnel.

(vii) Approval of hospital pharmacy. Application for a hospital pharmacy to provide narcotic drugs for detoxification treatment must be submitted to the Food and Drug Administration and the State authority and approval from both is required, except as provided for in Paragraph (h)(5) of this section. Within 60 days after the Food and Drug Administration receives the application, it will notify the applicant of approval or denial or will request additional information, when necessary.

(viii) Approval of shipments to hospital pharmacies. Before a hospital pharmacy may lawfully receive shipments of narcotic drugs for detoxification treatment, a responsible official shall complete, sign, and file in duplicate with the Food and Drug Administration and the State authority Form FDA-2636 "Hospital Request for Methadone Detoxification Treatment" (see Paragraph (k) of this section) and must have received from the Food and Drug Administration a notice that the request has been approved.

(ix) Sanctions. Failure to abide by the requirements described in this section may result in revocation of approval to receive shipments of narcotic drugs for narcotic addict treatment, seizure of the drug supply on hand, injunction, and criminal prosecution.

(g) Confidentiality of patient records.

(1) Except as provided in Paragraph (g)(2) of this section, disclosure of patient records maintained by any program is governed by the provisions of 42 CFR Part 2, and every program must comply with that part. Records on the receipt, storage, and distribution of narcotic medication are also subject to inspection under Federal controlled substances laws: But use or disclosure of records identifying patients will, in any case, be limited to actions involving the program or its personnel.

(2) A treatment program or medication unit or any part thereof, including any facility or any individual, shall permit a duly authorized employee of the Food and Drug Administration to have access to and to copy all records on the use of narcotic drugs in accordance with the provisions of 42 CFR Part 2. A treatment program may reveal such records only when necessary in a related administrative or court proceeding.

(h) Denial or revocation of approval.

(1) Complete or partial denial or revocation of approval of an application to receive shipments of narcotic drugs (Forms FDA-2632 "Application for Approval of Use of Methadone in a Treatment Program" and FDA-2636 "Hospital Request for Methadone Detoxification Treatment") may be proposed to the Commissioner of Food and Drugs by the Director of the Food and Drug Administration's Center for Drug Evaluation and Research, on his or her own initiative or at the request of representatives of the Drug Enforcement Administration, Department of Justice, National Institute of Drug Abuse, the State authority, or any other interested person.

(2) Before presenting such a proposal to the Commissioner, the Director of the Center for Drug Evaluation and Research, or his or her representative, will notify the applicant in writing of the proposed action and the reasons therefor and will offer the applicant an opportunity to explain the matters in question in an informal conference and/or in writing within 10 days after receipt of such notification. The applicant shall have the right to hear and to question the information on which the proposal to deny or revoke approval is based, and may present any oral or written information and views.

(3) If the explanation offered by the applicant is not accepted by the Center for Drug Evaluation and Research as sufficient to justify approval of the application, and denial or revocation of approval is therefore proposed, the Commissioner will evaluate information obtained in the informal conference and/or in writing before the Director of the Center for Drug Evaluation and Research. If the Commissioner finds that the applicant has failed to submit adequate assurance justifying approval of the application, the Commissioner shall issue a notice of opportunity for hearing with respect to the matter pursuant to §314.200 of this chapter and the matter shall thereafter be handled in accordance with established procedures for denial or revocation of approval of a new drug application. If the Secretary determines that there is an imminent hazard to health, revocation of approval will become effective immediately and any administrative procedure will be expedited. Upon revocation of approval of an application, the Commissioner will notify the applicant, the State authority, the Drug Enforcement Administration, Department of Justice, and all other appropriate persons that the applicant may no longer receive shipments of narcotic drugs, and will require the recall of all of the drugs from the applicant. Revocation of approval may also result in criminal prosecution.

(4) Denial or revocation of approval may be reversed when the Commissioner determines that the applicant has justified approval of the application.

(5) A treatment program or medication unit or any part thereof, including any facility or any individual, may appeal to the Food and Drug Administration a complete or partial denial or revocation of approval by the State authority unless the denial or revocation is based upon a State law or regulation. The appeal shall first be made to the Director of the Center for Drug Evaluation and Research, who shall hold an informal conference on the matter in accordance with Paragraph (h)(2) of this section. The State authority may participate in the conference. The appellant or the State authority may appeal the Director's decision to the Commissioner, who shall decide the matter in accordance with Paragraph (h)(3) of this section. If the Commissioner denies or revokes approval, such action shall be handled in accordance with Paragraph (h)(3) of this section. The Commissioner may not grant or retain Food and Drug Administration approval if the Commissioner finds that the appellant is not in compliance with all applicable State laws and regulations and with this section.

(i) Sanctions-

(1) Program sponsor or individual responsible for a particular program. If the program sponsor or the person responsible for a particular program fails to abide by all the requirements set forth in this regulation, or fails to adequately monitor the activities of those employed in the program, he or she may have the approval of his or her application revoked, his or her narcotic drug supply seized, an injunction granted precluding operation of his or her program, and criminal prosecution instituted against him or her.

(2) Persons responsible for administering or dispensing narcotic drugs. If a person responsible for administering or dispensing narcotic drugs for narcotic addict treatment fails to abide by all the requirements set forth in this regulation, criminal prosecution may be instituted against him or her, his or her drug supply may be seized, the approval of the program may be revoked, and an injunction may be granted precluding operation of the program.

(j) Requirements for distribution by manufacturers of narcotic drugs for narcotic addict treatment-

(1) Distribution requirements. Shipments of narcotic drugs for narcotic addict treatment are restricted to direct shipments by manufacturers of the drugs to approved treatment programs using the narcotic drugs and to approved hospital pharmacies. If requested by a manufacturer or State authority, wholesale pharmacy outlets in some regions or States may be authorized to stock narcotic drugs for narcotic addict treatment for that area and then transship the drug to approved narcotic treatment programs and approved hospital pharmacies. Alternative methods of distribution will be permitted if they are approved by the Food and Drug Administration and the State authority. Prior to any approval of an alternative method of distribution, there will be consultation with the Drug Enforcement Administration, Department of Justice, to assure compliance with its regulations regarding controlled substance distribution.

(2) Information regarding approved programs and hospitals. The Food and Drug Administration will provide manufacturer and the public with names and locations of programs and hospitals that have been approved to receive shipments of narcotic drugs for narcotic addiction treatment. All information contained in the forms required by Paragraph (k) of this section is available for public disclosure, except the names or other identifying information.

(3) Acceptance of delivery. Delivery shall only be made to a licensed practitioner or a licensed pharmacist employed at the facility. At the time of delivery, the licensed practitioner or licensed pharmacist shall sign for the drugs and place his or her specific title and identification number on any invoice. Copies of these signed invoices shall be kept by the manufacturer.

(k) Program forms. The program sponsor must ensure that the following forms are completed by the proper program staff and submitted to the appropriate State authority and the Division of Scientific Investigations, Regulatory Management Branch (HFD-342), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Forms are available upon request from the Regulatory Management Branch (HFD-352) at the same address.

## FORM

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| FDA-2632 | Application for Approval of Use of Methadone in a Treatment Program |
| FDA-2633 | Medical Responsibility Statement for Use of Methadone in a Treatment Program |
| FDA-2635 | Consent to Methadone Treatment |
| FDA-2636 | Hospital Request for Methadone Detoxification Treatment |

(Approved by the Office of Management and Budget under Number 0910-0140)

[54 FR 8960, Mar. 2, 1989; 54 FR 12531, Mar. 27, 1989]

## PART 291

## DRUGS USED FOR TREATMENT OF NARCOTIC ADDICTS [Revisions]

1. The authority citation for 21 CFR part 291 is revised to read as follows:

AUTHORITY: Secs. 505, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 371); 21 U.S.C. 823; secs. 301(d), 548, 1976 of the Public Health Service Act (42 U.S.C. 241(d), 290ee-3, 300y-11); 42 U.S.C. 257a.

2. Section 291.505 is amended by inserting the word "comprehensive" before the word "maintenance" everywhere it appears in paragraphs (d)(1)(i), (d)(1)(iii), (d)(1)(iv), (d)(2)(i), (d)(3)(v)(D), (d)(4)(i)(B)(2), (d)(5)(ii), (d)(6)(iv)(B)(6), (d)(6)(v)(A)(1) and (d)(6)(v)(A)(3), (d)(6)(v)(C), (d)(8)(i) introductory text and (d)(8)(i)(E), (d)(9)(i) introductory text and (d)(9)(i)(F), and by revising paragraph (a)(2), by adding paragraphs (a)(10), (b)(1)(v), (b)(2)(vi), (d)(4)(i)(C), and (d)(7), and by revising paragraph (d)(8)(i)(F) to read as follows:

Sec. 291.505 Conditions for the use of narcotic drugs; appropriate methods of professional practice for medical treatment of the narcotic addiction of various classes of narcotic addicts under section 4 of the Comprehensive Drug Abuse Prevention and Control Act of 1970.

(a) * * *

(2) Maintenance treatment means the dispensing of a narcotic drug, at relatively stable dosage levels, in the treatment of an individual for dependence on heroin or other morphine-like drug. There are two types of maintenance treatment: comprehensive maintenance treatment and interim maintenance treatment.

(i) Comprehensive maintenance treatment is maintenance treatment provided in conjunction with a comprehensive range of appropriate medical and rehabilitative services.

(ii) Interim maintenance treatment is maintenance treatment provided in conjunction with appropriate medical services while a patient is awaiting transfer to comprehensive maintenance treatment.

* * * * *

(10) The term HIV disease means infection with the etiologic agent for acquired immunodeficiency syndrome.

* * * * *

(b) * * *

(1) * * *

(v) Interim maintenance treatment. A public or nonprofit private narcotic treatment program may provide interim maintenance treatment only if the program also provides comprehensive maintenance treatment to which interim maintenance treatment patients may be transferred.

(2) * * *

(vi) Interim maintenance treatment program approval. Before a public or nonprofit private narcotic treatment program may provide interim maintenance treatment, the program must receive approval of both the Food and Drug Administration and the chief public health officer of the State. Before such approval is granted, the program must provide the Food and Drug Administration with certification from the chief public officer of the State that:

(A) Such officer does not object to the authorization of programs providing interim maintenance treatment in the State and that programs seeking such authorization are unable to place patients in a public or nonprofit private comprehensive treatment program within a reasonable geographic area within 14 days of the time patients seek admission to such programs;

(B) The authorization of programs providing interim maintenance treatment in the State will not reduce the capacity of comprehensive programs in the State to admit individuals to these programs (relative to the date on which such officer so certifies);

(C) The State guarantees that individuals enrolled in interim maintenance treatment will be transferred to comprehensive programs not later than 120 days, as provided by section 1923 of the Public Health Service Act (the PHS Act) and applicable regulations; and

(D) Requests for authorization should be submitted to the address specified in Sec. 291.505(k).

* * * * *

(d) * * *

(4) * * *

(i) * * *

(C) Counseling on HIV disease. A narcotic treatment program shall provide counseling on preventing exposure to, and the transmission of, HIV disease for each patient admitted or readmitted to maintenance or detoxification treatment. Although HIV testing is not required, an interim program shall inform patients of the availability of HIV testing. The program sponsor shall also ensure that HIV testing is accessible to patients who request such testing either on site or by the programs entering into agreements with HIV testing facilities to make HIV testing accessible to those patients who request it.

* * * * *

(7) Minimum standards for interim maintenance treatment. The person(s) responsible for a program may place an individual, who is eligible for admission to comprehensive maintenance treatment, in interim maintenance treatment if the individual cannot be placed in a public or nonprofit private comprehensive program within a reasonable geographic area and within 14 days of the individual's application for admission. An initial and at least two other urine screens shall be taken from interim patients during the maximum of 120 days permitted for such treatment. A program shall establish and follow reasonable criteria for establishing priorities for transferring patients from interim maintenance to comprehensive maintenance treatment. These transfer criteria shall be in writing and available for inspection and shall include, at a minimum, a preference for pregnant women in admitting patients to interim maintenance and in transferring patients from interim maintenance to comprehensive maintenance treatment. Interim maintenance shall be provided in a manner consistent with all applicable Federal and State laws including sections 1923 (mandatory transfer) and 1927(a) (pregnant patients) of the PHS Act. The program shall notify the State health officer when a patient begins interim treatment, when a patient leaves interim treatment, and before the date of mandatory transfer to a comprehensive program, and shall document such notifications. Programs in States not in compliance with provisions of this regulation risk loss of authorization for interim maintenance. All requirements for comprehensive maintenance treatment apply to interim maintenance treatment with the following exceptions:

(i) The narcotic drug is required to be administered daily under observation;

(ii) Take-home medication is not allowed;

(iii) The initial treatment plan and periodic treatment plan evaluation are,not [sic] required;

(iv) A primary counselor is not required to be assigned to a patient;

(v) Interim maintenance cannot be provided for longer than 120 days in any 12 month-period [sic]; and

(vi) The requirements and exceptions in paragraphs (b)(2)(iii) (as apply to rehabilitative services), in paragraphs (b)(3)(iv)(B) and (d)(4)(i)(A) (as apply to rehabilitative services), and in paragraphs (d)(4)(ii)(E), (d)(4)(ii)(F), (d)(4)(iv), (d)(6)(iv), (d)(6)(v), (d)(6)(vi), and (d)(6)(vii) of this section do not apply.

* * * * *

(8) * * *

(i) * * *

(F) The requirements of paragraph (d)(4) of this section, except paragraphs (d)(4)(i)(C), (d)(4)(ii)(A) through (d)(4)(ii)(D), and (d)(4)(iii) of this section, do not apply to short-term detoxification treatment.

## PART 291

## DRUGS USED FOR TREATMENT OF NARCOTIC ADDICTS [INTERIM RULE]

1. The authority citation for 21 CFR part 291 continues to read as follows:

AUTHORITY: Secs. 505, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 371); 21 U.S.C. 823; secs. 301(d), 548, 1976 of the Public Health Services Act (42 U.S.C. 241(d), 290ee–3, 300y–11); 42 U.S.C. 257a.

2. Section 291.501 is revised to read as follows:

**§ 291.501 Narcotic drugs in the maintenance treatment of narcotic addicts.**

(a) The Food and Drug Administration, the National Institute of Drug Abuse, and the Drug Enforcement Administration, Department of Justice, recognize that the use of narcotic drugs in the prolonged maintenance of narcotic dependence has been shown to be an effective part of a total treatment effort in the management and rehabilitation of selected narcotic addicts. It is also recognized that a number of dangers and possible abuses may arise from such efforts if professional services and controls are inadequately applied.

(b) Therefore, the Commissioner of Food and Drugs, the Director of the National Institute on Drug Abuse, and the Administrator of the Drug Enforcement Administration, Department of Justice, agree that interested professionals, municipalities, and organizations should be allowed to use narcotic drugs in the medical treatment of narcotic addiction within a framework of adequate controls designed to protect the individual patients and the community. Narcotic drugs that are to be used as part of the treatment of narcotic addiction must have an approved new drug application for use. To facilitate this purpose, the Food and Drug Administration, the National Institute on Drug Abuse, and the Drug Enforcement Administration, Department of Justice, have jointly agreed upon acceptable conditions for the use of narcotic drugs in a treatment program, which are set forth in § 291.505. In addition, such other provisions of the Federal narcotic laws and regulations as are applicable must also be observed.

3. Section 291.505 is amended by revising paragraphs (b)(2)(v), (b)(2)(vi)(D), (c)(4)(i), (c)(4)(ii), the last sentence in paragraph (d)(1)(i)(C), paragraph (d)(1)(ii), the first sentence in paragraph (d)(1)(iii)(B)(1) and by removing the word "methadone" in the two places it appears in paragraph (d)(1)(iii)(B)(1), by adding new paragraph (d)(1)(iii)(B)(*6*), by revising the second sentence in paragraph (d)(1)(iii)(C), paragraph (d)(1)(iv), by adding a new sentence after the second sentence in paragraph (d)(3)(i), by adding new paragraph (d)(4)(v), by revising the paragraph headings of paragraphs (d)(6) and (d)(6)(i), by removing paragraph (d)(6)(ii) and reserving it, by revising the second sentence in paragraph (d)(13)(i), in paragraph (f)(2)(viii) by removing the phrase "paragraph (k) of this section" and adding in in its place "paragraph (l) of this section", [sic] by revising paragraph (h)(1), by redesignating paragraph (k) as paragraph (l) and revising it, and by adding new paragraph (k) to read as follows:

**§ 291.505 Conditions for the use of narcotic drugs; appropriate methods of professional practice for medical treatment of the narcotic addiction of various classes of narcotic addicts under section 4 of the Comprehensive Drug Abuse Prevention and Control Act of 1970.**

* * * * *

(b) * * *

(2) * * *

(v) *Approved narcotic drugs for use in treatment programs.* The following narcotic drugs have been approved for use in the treatment of narcotic addiction: Methadone and Levo-*Alpha*-Acetyl-Methadol (LAAM).

(vi)* * *

(D) Requests for authorization should be submitted to the address specified in paragraph (l) of this section.

* * * * *

(c) * * *

(4) * * *

(i) Form FDA–2632 "Application for Approval of Use of Narcotic Drugs in a Treatment Program." This form, required by paragraph (l) of this section, shall be completed and signed by the program sponsor and submitted in duplicate to the Food and Drug Administration and the State authority.

(ii) Form FDA–2633 "Medical Responsibility Statement for Use of Narcotic Drugs in a Treatment Program." This form, required by paragraph (l) of this section, shall be completed and signed by each licensed physician authorized to administer or dispense narcotic drugs and submitted in duplicate to the Food and Drug Administration and the State authority. The names of any other persons licensed by law to administer or dispense narcotic drugs working in the program shall be listed even if they are not responsible for administering or dispensing the drug at the time the application is submitted.

* * * * *

(d)(1) * * * (i) * * *

(C) * * * The program physician shall complete and record the statement before the program administers any narcotic drug to the patient.

(ii) *Voluntary participation, informed consent.* The person responsible for the program shall ensure that: A patient voluntarily chooses to participate in a program; all relevant facts concerning the use of the narcotic drug used by the program are clearly and adequately explained to the patient; all patients, with full knowledge and understanding of its contents, sign the "Consent to Treatment with an Approved Narcotic Drug" Form FDA-2635 (see paragraph (l) of this section); a parent, legal guardian, or responsible adult designated by the State authority (e.g., "emancipated minor" laws) sign for patients under the age of 18 the second part of Form FDA–2635 "Consent to Treatment with an Approved Narcotic Drug."

(iii) * * *

(B) *Pregnant patients.* (1) Pregnant patients, regardless of age, who have had a documented narcotic dependency in the past and who may return to narcotic dependency, with all its attendant dangers during pregnancy, may be placed on a comprehensive maintenance regimen, except as provided in paragraph (d)(1)(iii)(B)(6) of this section. * * *

* * * * *

(6) Patients who are or become pregnant shall not be started or continued on LAAM, except by the written order of a physician who determines this to be the best choice of therapy for that patient. Clinics providing treatment with LAAM must advise all patients of childbearing potential of the risks of LAAM and make a medical evaluation available to all patients who become pregnant while taking the drug. An initial pregnancy test shall be performed for each prospective female patient of childbearing potential before admission to LAAM comprehensive maintenance treatment and monthly pregnancy tests performed thereafter on such female patients in LAAM comprehensive maintenance treatment. Analysis of such tests shall be performed in a laboratory approved under the Clinical Laboratory Improvement Amendments of 1988 or in a laboratory certified by a State or private accrediting body approved by the Health Care Financing Administration.

(C) * * * For patients meeting these criteria, the quantity of take-home medication, if take-home medication is permitted for the narcotic drug, will be determined in the reasonable clinical judgment of the program physician, but in no case may the quantity of take-home medication be greater than would have been allowed at the time the patient voluntarily terminated previous treatment. * * *

(iv) *Special limitation; treatment of patients under 18 years of age.* (A) A person under 18 years of age is required to have had two documented attempts at short-term detoxification or drug-free treatment to be eligible for maintenance treatment, except as provided in paragraph (d)(1)(iv)(B) of this section. A 1-week waiting period is required after such a detoxification attempt, however, before an attempt is repeated. The program physician shall document in the patient's record that the patient continues to be or is again physiologically dependent on narcotic drugs. No person under 18 years of age may be admitted to a maintenance treatment program unless a parent, legal guardian, or responsible adult designed by the State authority (e.g., "emancipated minor" laws) completes and signs consent form, Form FDA-2635 "Consent to Treatment with an Approved Narcotic Drug."

(B) A person under 18 years of age shall not be admitted to LAAM maintenance treatment.

* * * * *

(3) * * * (i) * * * A pregnancy test is required for any woman of childbearing potential before she may be administered LAAM as directed in paragraph (d)(1)(iii)(B)(1) of this section. * * *

* * * * *

(4) * * *

(v) *Authorized dispensers of narcotic drugs; responsibility.* A narcotic drug nay be administered or dispensed only by a practitioner licensed under the appropriate State law and registered under the appropriate State and Federal laws to order narcotic drugs for patients, or by an agent of such a practitioner, supervised by and under the order of the practitioner. This agent is required to be a pharmacist, registered nurse, or licensed practical nurse, or any other health care professional authorized by Federal and State law to administer or dispense narcotic drugs. The

licensed practitioner assumes responsibility for the amounts of narcotic drugs administered or dispensed and shall record and countersign all changes in dosage schedule.

* * * * *

(6) *Use of methadone in a treatment program; frequency of attendance; quantity of take-home medication; dosage of methadone; initial and stabilization—(i) Dosage and responsibility.* * * *

(ii) [Reserved]

* * * * *

(13) * * *

(i) * * * This system is required to comply with all Federal and State reporting requirements relevant to narcotic drugs approved for use in treatment of narcotic addiction. * * *

* * * * *

(h) *Denial or revocation of approval.* (1) Complete or partial denial or revocation of approval of an application to receive shipments of narcotic drugs (Forms FDA–2632 "Application for Approval of Use of Narcotic Drugs in a Treatment Program" and FDA–2636 "Hospital Request for Methadone Detoxification Treatment") may be proposed to the Commissioner of Food and Drugs by the Director of the Food and Drugs Administration's Center for Drug Evaluation and Research, on his or her own initiative or at the request of representatives of the Drug Enforcement Administration, Department of Justice, National Institute of Drug Abuse, the State authority, or any other interested person.

* * * * *

(k) *Use of narcotics other than methadone in a treatment program.* Narcotic drug products other than methadone that have been approved for treatment of narcotic addiction are listed in paragraph (b)(2)(v) of this section. Detailed information on the conditions for use of narcotic drug products other than methadone, with the exception of take-home and dosage form requirements, can be found in the respective approved product labeling. Treatment programs shall review the most recent approved product labeling for up-to-date information on important treatment parameters for each drug. Deviation from doses, frequencies, and conditions of usage described in the approved labeling shall be justified in the patient's record. Treatment programs that dispense narcotics other than methadone shall conform with the requirements set forth under paragraphs (a), (b), (c), (d)(1) through (d)(5), (d)(8) through (d)(14), and (e) through (l) of this section. Specifics regarding take-home and dosage form requirements along with any additional requirements are set forth in this paragraph.

(1) *LAAM*—(i) *Dosage and responsibility for administration.* After a patient's tolerance to LAAM is established, LAAM shall be administered no more frequently than every other day. Dosage of LAAM shall be individualized at doses, frequencies, and under conditions of usage described in approved labeling and as follows:

(A) *New Patients.* The persons responsible for the program shall ensure that the initial dose of LAAM to a patient whose tolerance for the drug is unknown does not exceed 40 milligrams.

(B) *Stabilized methadone maintenance patient.* The persons responsible for the program shall ensure that the initial dose of LAAM for a previously stabilized methadone maintenance patient is less than or equal to 1.3 times the patient's daily methadone dose, not to exceed 120 milligrams.

(C) A licensed physician shall assume responsibility for the amount of the narcotic drug administered or dispensed and shall record, date, and sign or countersign in each patient's record each change in dosage schedule.

(D) The administering licensed physician shall ensure that a single dose of LAAM greater than 140 milligrams is justified in the patient's record.

(ii) *Dosage form.* LAAM may be administered in oral form when used in a maintenance treatment program. Hospitalized patients under care for a medical or surgical condition are permitted to receive LAAM in oral form when the attending physician judges it advisable. Although syrup concentrate or other formulations may be distributed to the program, all oral medication is required to be administered in a liquid formulation. Clinics that administer both LAAM and methadone shall take appropriate measures, including contrasting color and taste, to ensure that dosage forms of LAAM and methadone are easily distinguished.

(iii) *Take-home medication.* Take-home doses of LAAM are not permitted. A Patient who is eligible for one or more take-home doses of methadone under paragraph (d)(6) of this section and who is unable to conform to the applicable mandatory LAAM dosing schedule because of exceptional circumstances such as illness, personal or family crises, travel, or other hardship, or official State holidays, may be temporarily transferred to methadone. Take-home doses of methadone for a patient eligible for a planned temporary discontinuation of treatment with

LAAM shall be individualized at doses, frequencies, and under conditions of usage described in the approved labeling and the applicable provisions for take-home methadone medication under paragraph (d)(6) of this section. The maximum number of take-home doses of methadone shall be determined in accordance with the provisions of 21 CFR 291.505(d)(6)(v) and (d)(6)(vi).

(2) [Reserved]

(l) *Program forms.* The program sponsor must ensure that the following forms are completed by the proper program staff and submitted to the appropriate State authority and the Division of Scientific Investigations, Regulatory Management Branch (HFD-342), Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855. The sponsor will indicate on the appropriate form which treatment drug is being utilized. Forms are available upon request from the Regulatory Management Branch (HFD-342) at the same address.

FORMS

FDA–2632 Application for Approval of Use of Narcotic Drugs in a Treatment Program.
FDA–2633 Medical Responsibility Statement for Use of Narcotic Drugs in a Treatment Program.
FDA–2635 Consent to Treatment with an Approved Narcotic Drug.
FDA–2636 Hospital Request for Methadone Detoxification Treatment.

(Approved by the Office of Management and Budget under number 0910–0140.)

**Michael R. Taylor,**
*Deputy Commissioner for Policy.*
Dated: April 8, 1993.
**Richard A. Millstein,**
*Acting Director, National Institute on Drug Abuse.*
[FR Doc. 93-17134 Filed 7-19-93; 8:45 am]
BILLING CODE 4160-01-P

# Appendix D—DEA Regulations

**Note to reader:** Only those Parts 1301–1307 that apply specifically to narcotic treatment programs are provided in this section. However, the reader is advised to review the DEA regulations in their entirety, as other parts may impact on compliance issues.

| | |
|---|---|
| § 1301.11 (f) | Fee amounts |
| § 1301.22 (a)(6),(11) | Separate registration for independent activities |
| § 1301.23 (a),(b) | Separate registrations for separate locations |
| § 1301.32 (a)(4)-(6),(9),(b)(9) | Application forms; contents; signature |
| § 1301.41 | Administrative review generally |
| § 1301.48 | Order to show cause |
| § 1301.55 | Burden of proof |
| § 1301.61 | Modification in registration |
| § 1301.71 through 1301.74 | Security requirements and physical security controls |
| § 1301.90 through 1301.93 | Employee screening—responsibility, illicit activities, employee checks |
| § 1304.03 | Persons required to keep records and file reports |
| § 1304.04 | Maintenance of records and inventories |
| § 1304.11 through 1304.13 | Inventory requirements |
| § 1304.17 | Inventories of dispensers and researchers |
| § 1304.21 | General requirements for continuing records |
| § 1304.28 through 1304.29 | Patient records |

| | |
|---|---|
| § 1305.08, 1305.09, 1305.11 through 1305.13 | Order forms |
| § 1307.14, 1307.21 | Disposal of controlled substance |
| § 1316.03 | Authority to make inspections |
| § 1316.06 | Notice of inspection |
| § 1316.31–34 | Enforcement proceedings |

# CHAPTER II — DRUG ENFORCEMENT ADMINISTRATION DEPARTMENT OF JUSTICE

## PART 1301—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

### GENERAL INFORMATION

Sec.



### FEES FOR REGISTRATION AND REREGISTRATION



### REQUIREMENTS FOR REGISTRATION



### APPLICATIONS FOR REGISTRATION



### ACTION ON APPLICATIONS FOR REGISTRATION: REVOCATION OR SUSPENSION OF REGISTRATION

HEARINGS



MODIFICATION, TRANSFER AND TERMINATION OF REGISTRATION



SECURITY REQUIREMENTS



EMPLOYEE SCREENING—NON-PRACTITIONERS



AUTHORITY: 21 U.S.C. 821, 822, 823, 824, 871(b), 875, 877.

SOURCE: 36 FR 7778 Apr. 24, 1971, unless otherwise noted. Redesignated at 38 FR 26609, Sept. 24, 1973.

**Note to reader:** Only those paragraphs in this Part that apply specifically to methadone maintenance treatment programs are provided.

FEES FOR REGISTRATION AND REREGISTRATION

**§1301.11 Fee amounts.**

(f) For each registration or reregistration to engage in a narcotic treatment program, including a compounder, the registrant shall pay an application fee of $20.

[48 FR 56043, Dec. 19, 1983, as amended at 52 FR 20598, June 2, 1987; 53 FR 4963, Feb. 19, 1988]

**§ 1301.22 Separate registration for independent activities.**

(a) The following groups of activities are deemed to be independent of each other:

(1) Manufacturing controlled substances;

(2) Distributing controlled substances;

(3) Dispensing controlled substances listed in Schedules II through V;

(4) Conducting research with controlled substances listed in Schedules II through V;

(5) Conducting instructional activities with controlled substances listed in schedules II through V;

(6) Conducting a narcotic treatment program using any narcotic drug listed in Schedules II, III, IV or V, however, pursuant to § 1301.24, employees, agents, or affiliated practitioners, in programs, need not register separately. Each program site located away from the principal location and at which place narcotic drugs are stored or dispensed must be separately registered and obtain narcotic drugs by use of order forms pursuant to § 1305.03;

(7) Conducting research and instructional activities with controlled substances listed in Schedule I;

(8) Conducting chemical analysis with controlled substances listed in any schedule;

(9) Importing controlled substances;

(10) Exporting controlled substances; and

(11) A compounder as defined by § 1301.02(d).

(b) Every person who engages in more than one group of independent activities shall obtain a separate registration for each group of activities, except as provided in this paragraph. Any person, when registered to engage in the group of activities described in each subparagraph in this paragraph, shall be authorized to engage in the coincident activities described in that subparagraph without obtaining a registration to engage in such coincident activities, provided that, unless specifically exempted, he complies with all requirements and duties prescribed by law for persons registered to engage in such coincident activities:

(1) A person registered to manufacture or import any controlled substance or basic class of controlled substance shall be authorized to distribute that substance or class, but no other substance or class which he is not registered to manufacture or import;

(2) A person registered to manufacture any controlled substance listed in Schedules II through V shall be authorized to conduct chemical analysis and preclinical research (including quality control analysis) with narcotic and non-narcotic controlled substances listed in those schedules in which he is authorized to manufacture;

(3) A person registered to conduct research with a basic class of controlled substance listed in Schedule I shall be authorized to manufacture or import such class if and to the extent that such manufacture or importation is set forth in the research protocol described in § 1301.33 and to distribute such class to other persons registered or authorized to conduct research with such class or registered or authorized to conduct chemical analysis with controlled substances;

(4) A person registered or authorized to conduct chemical analysis with controlled substances shall be authorized to manufacture and import such substances for analytical or instructional purposes, to distribute such substances to other persons registered or authorized to conduct chemical analysis or instructional activities or research with such substances and to persons exempted from registration pursuant to § 1301.26, to export such substances to persons in other countries performing chemical analysis or enforcing laws relating to controlled substances or drugs in those countries, and to conduct instructional activities with controlled substances; and

(5) A person registered or authorized to conduct research with controlled substances listed in Schedules II through V shall be authorized to conduct chemical analysis with controlled substances listed in those schedules in which he is authorized to conduct research, to manufacture such substances if and to the extent that such manufacture is set forth in a statement filed with the application for registration, to import such substances for research purposes, to distribute such substances to other persons registered or authorized to conduct chemical analysis, instructional activities, or research with such substances and to persons exempted from registration pursuant to § 1301.26, and to conduct instructional activities with controlled substances;

(6) A person registered to dispense controlled substances listed in Schedules II through V shall be authorized to conduct research and to conduct instructional activities with those substances.

(c) A single registration to engage in any group of independent activities may include one or more controlled substances listed in the schedules authorized in that group of independent activities. A person registered to conduct research with controlled substances listed in Schedule I may conduct research with any substance listed in Schedule I for which he has filed and had approved a research protocol.

[36 FR 7778, Apr. 24, 1971, as amended at 36 FR 18728, Sept. 21, 1971; 37 FR 15918, Aug. 8, 1972; 38 FR 756, Jan. 4, 1973. Redesignated at 38 FR 26609, Sept. 24, 1973.

EDITORIAL NOTE: For FR Citations affecting § 1301.22, see the List of CFR Sections Affected in the Finding Aids section of this volume.

**§1301.23 Separate registrations for separate locations.**

(a) A separate registration is required for each principal place of business or professional practice at one general physical location where controlled substances are manufactured, distributed, or dispensed by a person.

(b) The following locations shall be deemed not to be places where controlled substances are manufactured, distributed, or dispensed:

(1) A warehouse where controlled substances are stored by or on behalf of a registered person, unless such substances are distributed directly from such warehouse to registered locations other than the registered location from which the substances were delivered or to persons not required to register by virtue of subsection 302(c)(2) of the Act (21 U.S.C. 822(c)(2));

(2) An office used by agents of a registrant where sales of controlled substances are solicited, made, or supervised but which neither contains such substances (other than substances for display purposes or lawful distribution as samples only) nor serves as a distribution point for filling sales orders; and

(3) An office used by a practitioner (who is registered at another location) where controlled substances are prescribed but neither administered nor otherwise dispensed as a regular part of the professional practice of the practitioner at such office, and where no supplies of controlled substances are maintained.

[36 FR 7778, Apr. 24, 1971, as amended at 36 FR 18728, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973]

## APPLICATIONS FOR REGISTRATION

**§1301.32 Application forms; contents; signature.**

(a) If any person is required to be registered, and is not so registered and is applying for registration:

(4) To conduct research with controlled substances listed in Schedules II through V (other than research described in §§1301.22(a)(6), he shall apply on DEA Form 225;

(5) To conduct research with narcotic drugs listed in Schedules II through V, as described in §1301.22(a)(6), he shall apply on DEA Form 225;

(6) To conduct research with controlled substances listed in Schedule I, he shall apply on DEA Form 225, with three copies of a research protocol as described in §[1]301.33(a) attached to the form, or, in the case of a clinical investigation, with three copies of a certificate of submission of an IND as described in §1301.33(b) attached to the form (the researcher also submitting to the Food and Drug Administration three copies of a Notice of Claimed Investigational Exemption for a New Drug as required in §1301.33(b));

(9) To conduct a narcotic treatment program, including a compounder, shall apply on DEA Form 363.

(b) If any person is registered and is applying for reregistration:

(9) To conduct a narcotic treatment program, including a compounder, shall apply on DEA Form 363a (Renewal Form).

## ACTION ON APPLICATIONS FOR REGISTRATION; REVOCATION OR SUSPENSION OF REGISTRATION

**§1301.41 Administrative review generally.**

The Administrator may inspect, or cause to be inspected, the establishment of an applicant or registrant, pursuant to subpart A of part 1316 of this chapter. The Administrator shall review, [sic] the application for registration and other information gathered by the Administrator regarding an applicant in order to determine whether the applicable standards of section 1303 of the Act (21 U.S.C. 823) have been met by the applicant.

**§1301.48 Order to show cause.**

(a) If, upon examination of the application for registration from any applicant and other information gathered by the Administration regarding the applicant, the Administrator is unable to make the determinations required by the applicable provisions of section 303 of the Act (21 U.S.C. 823) to register the applicant, the Administrator shall serve upon the applicant an order to show cause why the registration should not be denied.

(b) If, upon information gathered by the Administration regarding any registrant, the Administrator determines that the registration of such registrant is subject to suspension or revocation pursuant to section 304 of the Act (21 U.S.C. 824), the Administrator shall serve upon the registrant an order to show cause why the registration should not be revoked or suspended.

(c) The order to show cause shall call upon the applicant or registrant to appear before the Administrator at a time and place stated in the order, which shall not be less than 30 days after the date of receipt of the order. The order to show cause shall also contain a statement of the legal basis for such hearing and for the denial, revocation, or suspension of registration and a summary of the matters of fact and law asserted.

(d) Upon receipt of an order to show cause, the applicant or registrant must, if he desires a hearing, file a request for a hearing pursuant to §1301.54. If a hearing is requested, the Administrator shall hold a hearing at the time and place stated in the order, pursuant to §1301.51.

(e) When authorized by the Administrator, any agent of the Administration may serve the order to show cause.

[36 FR 7778, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973]

## HEARINGS

**§1301.55 Burden of proof.**

(a) At any hearing on an application to manufacture any controlled substance listed in Schedule I or II, the applicant shall have the burden of proving that the requirements for such registration pursuant to section 303(a) of the Act (21 U.S.C. 823(a)) are satisfied. Any other person participating in the hearing pursuant to §1301.43 shall have the burden of proving any propositions of fact or law asserted by him in the hearing.

(b) At any hearing on the granting or denial of an applicant to be registered to conduct a narcotic treatment program or as a compounder, the applicant shall have the burden of proving that the requirements for each registration pursuant to section 303(g) of the Act (21 U.S.C. 823(g)) are satisfied.

(c) At any other hearing for the denial of a registration, the Administration shall have the burden of proving that the requirements for such registration pursuant to section 303 of the Act (21 U.S.C. 823) are not satisfied.

(d) At any hearing for the revocation or suspension of a registration, the Administration shall have the burden of proving that the requirements for such revocation or suspension to section 304(a) of the Act (21 U.S.C. 824(a)) are satisfied.

[36 FR 7778, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 41 FR 21448, May 26, 1976]

## MODIFICATION, TRANSFER, AND TERMINATION OF REGISTRATION

**§1301.61 Modification in registration.**

Any registrant may apply to modify his registration to authorize the handling of additional controlled substances or to change his name or address, by submitting a letter of request to the Registration Unit, Drug Enforcement Administration, Department of Justice, Post Office Box 28083, Central Station, Washington, DC 20005. The letter shall contain the registrant's name, address, and registration number as printud [sic] on the certificate of registration, and the substances and/or schedules to be added to his registration of the new name or address and shall be signed in accordance with §1301.32(f). If the registrant is seeking to handle additional controlled substances listed in Schedule I for the purpose of research or instructional activities, he shall attach three copies of a research protocol describing each research project involving the additional substances, or two copies of a statement describing the nature, extent, and duration of such instructional activities, as appropriate.

No fee shall be required to be paid for the modification. The request for modification shall be handled in the same manner as an application for registration. If the modification in registration is approved, the Administrator shall issue a new certificate of registration (DEA Form 223) to the registrant, who shall maintain it with the old certificate of registration until expiration.

[36 FR 18729, Sept. 21, 1971, as amended at 37 FR 15919, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 51 FR 5319, Feb. 13, 1986; 53 FR 4963, Feb. 19, 1988]

SECURITY REQUIREMENTS

**§ 1301.71 Security requirements generally.**

(a) All applicants and registrants shall provide effective controls and procedures to guard against theft and diversion of controlled substances. In order to determine whether a registrant has provided effective controls against diversion, the Administrator shall use the security requirements set forth in §§ 1301.72–1301.76 as standards for the physical security controls and operating procedures necessary to prevent diversion. Materials and construction which will provide a structural equivalent to the physical security controls set forth in §§ 1301.72, 1301.73 and 1301.75 may be used in lieu of the materials and construction described in those sections.

(b) Substantial compliance with the standards set forth in §§ 1301.72–1301.76 may be deemed sufficient by the Administrator after evaluation of the overall security system and needs of the applicant or registrant. In evaluating the overall security system of a registrant or applicant, the Administrator may consider any of the following factors as he may deem relevant to the need for strict compliance with security requirements:

(1) The type of activity conducted (e.g., processing of bulk chemicals, preparing dosage forms, packaging, labeling, cooperative buying, etc.);

(2) The type and form of controlled substances handled (e.g., bulk liquids or dosage units, usable powders or nonusable powders);

(3) The quantity of controlled substances handled;

(4) The location of the premises and the relationship such location bears on security needs;

(5) The type of building construction comprising the facility and the general characteristics of the building or buildings;

(6) The type of vault, safe, and secure enclosures or other storage system (e.g., automatic storage and retrieval system) used;

(7) The type of closures on vaults, safes, and secure enclosures;

(8) The adequacy of key control systems and/or combination lock control systems;

(9) The adequacy of electric detection and alarm systems, if any including use of supervised transmittal lines and standby power sources;

(10) The extent of unsupervised public access to the facility, including the presence and characteristics of perimeter fencing, if any;

(11) The adequacy of supervision over employees having access to manufacturing and storage areas;

(12) The procedures for handling business guests, visitors, maintenance personnel, and nonemployee service personnel;

(13) The availability of local police protection or of the registrant's or applicant's security personnel, and;

(14) The adequacy of the registrant's or applicant's system for monitoring the receipt, manufacture, distribution, and disposition of controlled substances in its operations.

(c) When physical security controls become inadequate as a result of a controlled substance being transferred to a different schedule, or as a result of a noncontrolled substance being listed on any schedule, or as a result of a significant increase in the quantity of controlled substances in the possession of the registrant during normal business operations, the physical security controls shall be expanded and extended accordingly. A registrant may adjust physical security controls within the requirements set forth in §§ 1301.72–1301.76 when the need for such controls decreases as a result of a controlled substance being transferred to a different schedule, or a result of a controlled substance being removed from control, or as a result of a significant decrease in the quantity of controlled substances in the possession of the registrant during normal business operations.

(d) Any registrant or applicant desiring to determine whether a proposed security system substantially complies with, or is the structural equivalent of, the requirements set forth in §§ 1301.72–1301.76 may submit

any plans, blueprints, sketches or other materials regarding the proposed security system either to the Special Agent in Charge in the region in which the system will be used, or to the Diversion Operations Section, Drug Enforcement Administration, Department of Justice, Washington, DC 20537.

(e) Physical security controls of locations registered under the Harrison Narcotic Act or the Narcotics Manufacturing Act of 1960 on April 30, 1971, shall be deemed to comply substantially with the standards set forth in §§ 1301.72, 1301.73 and 1301.75. Any new facilities or work or storage areas constructed or utilized for controlled substances, which facilities or work or storage areas have not been previously approved by the Administration, shall not necessarily be deemed to comply substantially with the standards set forth in §§ 1301.72, 1301.73 and 1301.75, notwithstanding that such facilities or work or storage areas have physical security controls similar to those previously approved by the Administration.

[36 FR 18729, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic], and amended at 46 FR 28841, May 29, 1981; 47 FR 41735, Sept. 22, 1982; 51 FR 5319, Feb. 13, 1986]

**§ 1301.72 Physical security controls for non-practitioners; narcotic treatment programs and compounders for narcotic treatment programs; storage areas.**

(a) *Schedules I and II.* Raw materials, bulk materials awaiting further processing, and finished products which are controlled substances listed in Schedule I or II shall be stored in one of the following secure storage areas:

(1) Where small quantities permit, a safe or steel cabinet;

(i) Which safe or steel cabinet shall have the following specifications or the equivalent: 30 man-minutes against surreptitious entry, 10 man-minutes against forced entry, 20 man-hours against lock manipulation, and 20 man-hours against radiological techniques;

(ii) Which safe or steel cabinet, if it weighs less than 750 pounds, is bolted or cemented to the floor or wall in such a way that it cannot be readily removed; and

(iii) Which safe or steel cabinet if necessary, depending upon the quantities and type of controlled substances stored, is equipped with an alarm system which, upon attempted unauthorized entry, shall transmit a signal directly to a central protection company or a local or State police agency which has a legal duty to respond or a 24-hour control station operated by the registrant, or such other protection as the Administrator may approve.

(2) A vault constructed before, or under construction on, September 1, 1971, which is of substantial construction with a steel door, combination or key lock, and an alarm system; or

(3) A vault constructed after September 1, 1971:

(i) The walls, floors, and ceilings of which vault are constructed of at least 8 inches of reinforced concrete or other substantial masonry, reinforced vertically and horizontally with 1/2- inch steel rods tied 6 inches on center, or the structural equivalent to such reinforced walls, floors, and ceilings;

(ii) The door and frame unit of which vault shall conform to the following specifications or the equivalent: 30 man-minutes against surreptitious entry, 10 man-minutes against forced entry, 20 man-hours against lock manipulation, and 20 man-hours against radiological techniques;

(iii) Which vault, if operations require it to remain open for frequent access, is equipped with a "day-gate" which is self-closing and self-locking, or the equivalent, for use during the hours of operation in which the vault door is open;

(iv) The walls or perimeter of which vault are equipped with an alarm, which upon unauthorized entry shall transmit a signal directly to a central station protection company, or a local or State police agency which has a legal duty to respond, or a 24-hour control station operated by the registrant, or such other protection as the Administrator may approve, and, if necessary, holdup buttons at strategic points of entry to the perimeter area of the vault;

(v) The door of which vault is equipped with contact switches; and

(vi) Which vault has one of the following: Complete electrical lacing of the walls, floor and ceilings; sensitive ultrasonic equipment within the vault; a sensitive sound accumulator system; or such other device designed to detect illegal entry as may be approved by the Administration.

(b) *Schedules III, IV and V.* Raw materials, bulk materials awaiting further processing, and finished products which are controlled substances listed in Schedules III, IV and V shall be stored in the following secure storage areas:

(1) A safe or steel cabinet as described in paragraph (a)(1) of this section;

(2) A vault as described in paragraph (a)(2) or (3) of this section equipped with an alarm system as described in paragraph (b)(4)(v) of this section;

(3) A building used for storage of Schedules III through V controlled substances with perimeter security which limits access during working hours and provides security after working hours and meets the following specifications:

(i) Has an electronic alarm system as described in paragraph (b)(4)(v) of this section,

(ii) Is equipped with self-closing, self-locking doors constructed of substantial material commensurate with the type of building construction, provided, however, a door which is kept closed and locked at all times when not in use and when in use is kept under direct observation of a responsible employee or agent of the registrant is permitted in lieu of a self-closing, self-locking door. Doors may be sliding or hinged. Regarding hinged doors, where hinges are mounted on the outside, such hinges shall be sealed, welded or otherwise constructed to inhibit removal. Locking devices for such doors shall be either of the multiple-position combination or key lock type and:

*(a)* In the case of key locks, shall require key control which limits access to a limited number of employees, or;

*(b)* In the case of combination locks, the combination shall be limited to a minimum number of employees and can be changed upon termination of employment of an employee having knowledge of the combination;

(4) A cage, located within a building on the premises, meeting the following specifications:

(i) Having walls constructed of not less than No. 10 gauge steel fabric mounted on steel posts, which posts are:

*(a)* At least one inch in diameter;

*(b)* Set in concrete or installed with lay bolts that are pinned or brazed; and

*(c)* Which are placed no more than ten feet apart with horizontal one and one-half inch reinforcements every sixty inches;

(ii) Having a mesh construction with openings of not more than two and one-half inches across the square,

(iii) Having a ceiling constructed of the same material, or in the alternative, a cage shall be erected which reaches and is securely attached to the structural ceiling of the building. A lighter gauge mesh may be used for the ceilings of large enclosed areas if walls are at least 14 feet in height,

(iv) Is equipped with a door constructed of No. 10 gauge steel fabric on a metal door frame in a metal door flange, and in all other respects conforms to all the requirements of 21 CFR 1301.72(b)(3)(ii), and

(v) Is equipped with an alarm system which upon unauthorized entry shall transmit a signal directly to a central station protection agency or a local or state police agency, each having a legal duty to respond, or to a 24-hour control station operated by the registrant, or to such other source of protection as the Administrator may approve;

(5) An enclosure of masonry or other material, approved in writing by the Administrator as providing security comparable to a cage;

(6) A building or enclosure within a building which has been inspected and approved by DEA or its predecessor agency, BNDD, and continues to provide adequate security against the diversion of Schedule III through V controlled substances, of which fact written acknowledgment has been made by the Special Agent in Charge of DEA for the area in which such building or enclosure is situated;

(7) Such other secure storage areas as may be approved by the Administrator after considering the factors listed in
§ 1301.71(b), (1) through (14);

(8) (i) Schedule III through V controlled substances may be stored with Schedules I and II controlled substances under security measures provided by 21 CFR 1301.72(a);

(ii) Non-controlled drugs, substances and other materials may be stored with Schedule III through V controlled substances in any of the secure storage areas required by 21 CFR 1301.72(b), provided that permission for such storage of non-controlled items is obtained in advance, in writing, from the Special Agent in Charge of DEA for the area in which such storage area is situated. Any such permission tendered must be upon the Special Agent in Charge's written determination that such non-segregated storage does not diminish security effectiveness for Schedules III through V controlled substances.

(c) *Multiple storage areas.* Where several types or classes of controlled substances are handled separately by the registrant or applicant for different purposes (e.g., returned goods, or goods in process), the controlled substances may be stored separately, provided that each storage area complies with the requirements set forth in this section.

(d) *Accessibility to storage areas.* The controlled substances storage areas shall be accessible only to an absolute minimum number of specifically authorized employees. When it is necessary for employee maintenance personnel, nonemployee maintenance personnel, business guests, or visitors to be present in or pass through controlled substances storage areas, the registrant shall provide for adequate observation of the area by an employee specifically authorized in writing.

[36 FR 18730, Sept. 21, 1971, as amended at 37 FR 15919, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic]].

EDITORIAL NOTE: For Federal Register citations affecting § 1301.72, see the List of CFR Sections Affected in the Finding Aids section of this volume.

**§ 1301.73 Physical security controls for non-practitioners; compounders for narcotic treatment programs; manufacturing and compounding areas.**

All manufacturing activities (including processing, packaging and labeling) involving controlled substances listed in any schedule and all activities of compounders shall be conducted in accordance with the following:

(a) All in-process substances shall be returned to the controlled substances storage area at the termination of the process. If the process is not terminated at the end of a workday (except where a continuous process or other normal manufacturing operation should not be interrupted), the processing area or tanks, vessels, bins or bulk containers containing such substances shall be securely locked, with adequate security for the area or building. If such security requires an alarm, such alarm, upon unauthorized entry, shall transmit a signal directly to a central station protection company, or local or state police agency which has a legal duty to respond, or a 24-hour control station operated by the registrant.

(b) Manufacturing activities with controlled substances shall be conducted in an area or areas of clearly defined limited access which is under surveillance by an employee or employees designated in writing as responsible for the area. "Limited access" may be provided, in the absence of physical dividers such as walls or partitions, by traffic control lines or restricted space designation. The employee designated as responsible for the area may be engaged in the particular manufacturing operation being conducted: *Provided*, That he is able to provide continuous surveillance of the area in order that unauthorized persons may not enter or leave the area without his knowledge.

(c) During the production of controlled substances, the manufacturing areas shall be accessible to only those employees required for efficient operation. When it is necessary for employee maintenance personnel, nonemployee maintenance personnel, business guests, or visitors to be present in or pass through manufacturing areas during production of controlled substances, the registrant shall provide for adequate observation of the area by an employee specifically authorized in writing.

36 FR 18731, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic] and amended at 39 FR 37984, Oct. 25, 1974]

**§ 1301.74 Other security controls for non-practitioners; narcotic treatment programs and compounders for narcotic treatment programs.**

(a) Before distributing a controlled substance to any person who the registrant does not know to be registered to possess the controlled substance, the registrant shall make a good faith inquiry either with the Administration or with the appropriate State controlled substances registration agency, if any, to determine that the person is registered to possess the controlled substance.

(b) The registrant shall design and operate a system to disclose to the registrant suspicious orders of controlled substances. The registrant shall inform the Field Division Office of the Administration in his area of suspicious orders when discovered by the registrant. Suspicious orders include orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency.

(c) The registrant shall notify the Field Division Office of the Administration in his area of any theft or significant loss of any controlled substances upon discovery of such theft or loss. The supplier shall be responsible for reporting in-transit losses of controlled substances by the common or contract carrier selected pursuant to § 1301.74(e), upon discovery of such theft or loss. The registrant shall also complete DEA Form 106 regarding such theft or loss. Thefts must be reported whether or not the controlled substances are subsequently recovered and/or the responsible parties are identified and action taken against them.

(d) The registrant shall not distribute any controlled substance listed in Schedules II through V as a complimentary sample to any potential or current customer (1) without the prior written request of the customer, (2) to be used only for satisfying the legitimate medical needs of patients of the customer, and (3) only in reasonable quantities. Such request must contain the name, address, and registration number of the customer and the name and quantity of the specific controlled substance desired. The request shall be preserved by the registrant with other records of distribution of controlled substances. In addition, the requirements of part 1305 of the chapter shall be complied with for any distribution of a controlled substance listed in Schedule II. For purposes of this paragraph, the term "customer" includes a person to whom a complimentary sample of a substance is given in order to encourage the prescribing or recommending of the substance by the person.

(e) When shipping controlled substances, a registrant is responsible for selecting common or contract carriers which provide adequate security to guard against in-transit losses. When storing controlled substances in a public warehouse, a registrant is responsible for selecting a warehouseman which will provide adequate security to guard against storage losses; wherever possible, the registrant shall store controlled substances in a public warehouse which complies with the requirements set forth in § 1301.72. In addition, the registrant shall employ precautions (e.g., assuring that shipping containers do not indicate that contents are controlled substances) to guard against storage or in-transit losses.

(f) When distributing controlled substances through agents (e.g., detailmen), a registrant is responsible for providing and requiring adequate security to guard against theft and diversion while the substances are being stored or handled by the agent or agents.

(g) Before the initial distribution of carfentanil etorphine hydrochloride and/or diprenorphine to any person, the registrant must verify that the person is authorized to handle the substances(s) [sic] by contacting the Drug Enforcement Administration.

(h) The acceptance of delivery of narcotic substances by a narcotic treatment program shall be made only by a licensed practitioner employed at the facility or other authorized individuals designated in writing. At the time of delivery, the licensed practitioner or other authorized individual designated in writing (excluding persons currently or previously dependent on narcotic drugs), shall sign for the narcotics and place his specific title (if any) on any invoice. Copies of these signed invoices shall be kept by the distributor.

(i) Narcotics dispensed or administered at a narcotic treatment program will be dispensed or administered directly to the patient by either (1) the licensed practitioner, (2) a registered nurse under the direction of the licensed practitioner, (3) a licensed practical nurse under the direction of the licensed practitioner, or (4) a pharmacist under the direction of the licensed practitioner.

(j) Persons enrolled in a narcotic treatment program will be required to wait in an area physically separated from the narcotic storage and dispensing area. This requirement will be enforced by the program physician and employees.

(k) All narcotic treatment programs must comply with standards established by the Secretary of Health and Human Services (after consultation with the Administration) respecting the quantities of narcotic drugs which may be provided to persons enrolled in a narcotic treatment program for unsupervised use.

(l) DEA may exercise discretion regarding the degree of security required in narcotic treatment programs based on such factors as the location of a program, the number of patients enrolled in a program and the number of physicians, staff members and security guards. Similarly, such factors will be taken into consideration when evaluating existing security or requiring new security at a narcotic treatment program.

[36 FR 7778, Apr. 24, 1971; 36 FR 13386, July 21, 1971, as amended at 36 FR 18731, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic]]

EDITORIAL NOTE: For Federal Register citations affecting § 1301.74, see the List of CFR Sections Affected in the Finding Aids section of this volume.

**§ 1301.90 Employee screening procedures.**

It is the position of DEA that the obtaining of certain information by non-practitioners is vital to fairly asses the likelihood of an employee committing a drug security breach. The need to know this information is a matter of business necessity, essential to overall controlled substances security. In this regard it is believed that conviction of crimes and unauthorized use to controlled substances are activities that are proper subjects for inquiry. It is, therefore, assumed that the following questions will become a part of an employer's comprehensive employee screening program:

*Question.* Within the past five years, have you been convicted of a felony, or within the past two years, of any misdemeanor or are you presently formally charged with committing a criminal offense? (Do not include any traffic violations, juvenile offenses or military convictions, except by general court-martial.) If the answer is yea, furnish details of convictions, offense, location, and date and sentence.

*Question.* In the past three years, have you ever knowingly used any narcotics, amphetamines or barbiturates, other than those prescribed to you by a physician? If the answer is yes, furnish details.

*Advice.* An authorization, in writing, that allows inquiries to be made of courts and law enforcement agencies for possible pending charges or convictions must be executed by a person who is allowed to work in an area where access to controlled substances clearly exists. A person must be advised that any false information or omission of information will jeopardize his or her position with respect to employment. the application for employment should inform a person that information furnished or recovered as a result of any inquiry will not necessarily preclude employment, but will be considered as part of an overall evaluation of the person's qualifications. The maintaining of fair employment practices, the protection of the person's right of privacy, and the assurance that the result of such inquiries will be treated by the employer in confidence will be explained to the employee.

[40 FR 17143, Apr. 17, 1975]

**§ 1301.91 Employee responsibility to report drug diversion.**

Reports of drug diversion by fellow employees is not only necessary part of an overall employee security program but also serves the public interest at large. It is, therefore, the position of DEA that an employee who has knowledge of drug diversion from his employer by a fellow employee has an obligation to report such information to a responsible security official of the employer. The employer shall treat such information as confidential and shall take all reasonable steps to protect the confidentiality of the information and the identity of the employee furnishing information. A failure to report information of drug diversion will be considered in determining the feasibility of continuing to allow an employee to work in a drug security area. The employer shall inform all employees concerning this policy.

[40 FR 17143, Apr. 17, 1975]

**§ 1301.92 Illicit activities by employees.**

It is the position of DEA that employees who possess, sell, use or divert controlled substances will subject themselves not only to State and Federal prosecution for any illicit activity, but shall also immediately become the subject of independent action regarding their continued employment. The employer will assess the seriousness of the employee's violation, the position of responsibility held by the employee, past record of employment, etc., in determining whether to suspend, transfer, terminate or take other action against the employee.

[40 FR 17143, Apr. 17, 1975]

**§ 1301.93 Sources of information for employee checks.**

DEA recommends that inquires concerning employees' criminal records be made as follows:

*Local inquiries.* Inquiries should be made by name, date and place of birth, and other identifying information, to local courts and law enforcement agencies for records of pending charges and convictions. Local practice may require such inquiries to be made in person, rather than by mail, and a copy of an authorization from the employee may be required by certain law enforcement agencies.

*DEA inquiries.* Inquiries supplying identifying information should also be furnished to DEA field Division Offices along with written consent from the concerned individual for a check of DEA files for records of convictions. The Regional check will result in a national check being made by the Field Division Office.

[40 FR 17143, Apr. 17, 1975, as amended at 47 FR 41735, Sept. 22, 1982]

# PART 1304—RECORDS AND REPORTS OF REGISTRANTS

## GENERAL INFORMATION

Sec.



## INVENTORY REQUIREMENTS



## CONTINUING RECORDS



## REPORTS



AUTHORITY: 21 U.S.C. 821, 827, 871(b), 958(d), 965, unless otherwise noted.

Note to reader: Only those paragraphs in this Part that apply specifically to methadone maintenance treatment programs are provided.

**§ 1304.03 Persons required to keep records and file reports.**

(a) Each registrant shall maintain the records and inventories and shall file the reports required by this part, except as exempted by this section. Any registrant who is authorized to conduct other activities without being registered to conduct those activities, either pursuant to § 1301.22(b) of this chapter or pursuant to § 1307.11-1307.15 of this chapter, shall maintain the records and inventories and shall file the reports required by

this part for persons registered to conduct such activities. This latter requirement should not be construed as requiring stocks of controlled substances being used in various activities under one registration to be stored separately nor that separate records are required for each activity. The intent of the Administration is to permit the registrant to keep one set of records which are adapted by the registrant to account for controlled substances used in any activity. Also, the Administration does not wish to acquire separate stocks of the same substance to be purchased and stored for separate activities. Otherwise, there is no advantage gained by permitting several activities under one registration. Thus, when a researcher manufactures a controlled item, he must keep a record of the quantity manufactured; when he distributes a quantity of the item, he must use and keep invoices or order forms to document the transfer; when he imports a substance, he keeps as part of his records the documentation required of an importer; and when substances are used in chemical analysis, he need not keep a record of this because such a record would not be required of him under a registration to do chemical analysis. All of these records may be maintained in one consolidated record system. Similarly, the researcher may store all of his controlled items in one place, and every two years take inventory of all items on hand, regardless of whether the substances were manufactured by him, imported by him, or purchased domestically by him, of whether the substances will be administered to subjects, distributed to other researchers, or destroyed during chemical analysis.

(b) A registered individual practitioner is required to keep records, as described in § 1304.04, of controlled substances in Schedules II, III, IV, and V which are dispensed, other than by prescribing or administering in the lawful course of professional practice.

(c) A registered individual practitioner is not required to keep records of controlled substances in Schedules II, III, IV, and V which are prescribed in the lawful course of professional practice, unless such substances are prescribed in the course of maintenance or detoxification treatment of an individual.

(d) A registered individual practitioner is not required to keep records of controlled substances listed in Schedules II, III, IV and V which are administered in the lawful course of professional practice unless the practitioner regularly engages in the dispensing or administering of controlled substances and charges patients, either separately or together with charges for other professional services, for substances so dispensed or administered. Records are required to be kept for controlled substances administered in the course of maintenance or detoxification treatment of an individual.

(e) A registered person using any controlled substance in research conducted in conformity with an exemption granted under section 505(i) or 512(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i) or 360b(j)) at a registered establishment which maintains records in accordance with either of those sections is not required to keep records if he notifies the Administration of the name, address, and registration number of the establishment maintaining such records.

(f) A registered person using any controlled substance in preclinical research or in teaching at a registered establishment which maintains records with respect to such substances is not required to keep records if he notifies the Administration of the name, address, and registration number of the establishment maintaining such records.

(g) Notice required by paragraphs (e) and (f) of this section shall be given at the time the person applies for registration or reregistration and shall be made in the form of an attachment to the application, which shall be filed with the application.

[36 FR 7790, Apr. 24, 1971, as amended at 36 FR 18731, Sept. 21, 1971; 37 FR 15920, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 50 FR 40523, Oct. 4, 1985; 51 FR 5320, Feb. 13, 1986; 51 FR 26154, July 21, 1986]

**§ 1304.04 Maintenance of records and inventories.**

(a) Every inventory and other records required to be kept under this part shall be kept by the registrant and be available, for at least 2 years from the date of such inventory or records, for inspection and copying by authorized employees of the Administration, except that financial and shipping records (such as invoices and packing slips but not excuted [sic] order forms subject to § 1305.13 of this chapter) may be kept at a central location, rather than at the registered location, if the registrant has notified the Administration of his intention to keep central records. Written notification must be submitted by registered or certified mail, return receipt requested, in triplicate, to the Special Agent in Charge of the Administration in the area in which the registrant is located. Unless the registrant is informed by the Special Agent in Charge that permission to keep central records is denied, the registrant may maintain central records commencing 14 days after receipt of his notification by the Special Agent in Charge.

All notifications must include:

(1) The nature of the records to be kept centrally.

(2) The exact location where the records will be kept.

(3) The name, address, DEA registration number and type of DEA registration of the registrant whose records are being maintained centrally.

(4) Whether central records will be maintained in a manual, or computed readable form.

(b) All registrants that are authorized to maintain a central recordkeeping system shall be subject to the following conditions:

(1) The records to be maintained at the central record location shall not include executed order forms, prescriptions and/or inventories which shall be maintained at each registered location.

(2) If the records are kept on microfilm, computer media or in any form requiring special equipment to render the records easily readable, the registrant shall provide access to such equipment with the records. If any code system is used (other than pricing information), a key to the code shall be provided to make the records understandable.

(3) The registrant agrees to deliver all or any part of such records to the registered location within two business days upon receipt of a written request from the Administration for such records, and if the Administration chooses to do so in lieu of requiring delivery of such records to the registered location, to allow authorized employees of the Administration to inspect such records at the central location upon request by such employees without a warrant of any kind.

(4) In the event that a registrant fails to comply with these conditions, the Special Agent in Charge may cancel such central recordkeeping authorization, and all other central recordkeeping authorizations held by the registrant without a hearing or other procedures. In the event of a cancellation of central recordkeeping authorizations under this paragraph the registrant shall, within the time specified by the Special Agent in Charge, comply with the requirements of this section that all records be kept at the registered location.

(c) Registrants need not notify the Special Agent in Charge or obtain central recordkeeping approval in order to maintain records on an in-house computer system.

(d) ARCOS participants who desire authorization to report from other than their registered locations must obtain a separate central reporting identifier. Request for central reporting identifiers will be submitted to: ARCOS Unit, P.0. Box 28293, Central Station, Washington, DC 20005.

(e) All central recordkeeping permits previously issued by the Administration will expire on September 30, 1980. Registrants who desire to continue maintaining central records will make notification to the local Special Agent in Charge as provided in paragraph (a) of this section.

(f) Each registered manufacturer, distributor, importer, exporter, narcotic treatment program and compounder for narcotic treatment program shall maintain inventories and records of controlled substances as follows:

(1) Inventories and records of controlled substances listed in Schedules I and II shall be maintained separately from all of the records of the registrant; and

(2) Inventories and records of controlled substances listed in Schedules III, IV, and V shall be maintained either separately from all other records of the registrant or in such form that the information required is readily retrievable from the ordinary business records of the registrant.

(g) Each registered individual practitioner required to keep records and institutional practitioner shall maintain inventories and records of controlled substances in the manner prescribed in paragraph (f) of this section.

(h) Each registered pharmacy shall maintain the inventories and records of controlled substances as follows:

(1) Inventories and records of all controlled substances listed in Schedules I and II shall be maintained separately from all other records of the pharmacy, and prescriptions for such substances shall be maintained in a separate prescription file; and

(2) Inventories and records of controlled substances listed in Schedules III, IV, and V shall be maintained either separately from all other records of the pharmacy or in such form that the information required is readily retrievable from ordinary business records of the pharmacy, and prescriptions for such substances shall be maintained either in separate prescription file for controlled substances listed in Schedules III, IV, and V only or in such form that they are readily retrievable from the other prescription records of the pharmacy. Prescriptions will be deemed readily retrievable if, at the time they are initially filed, the face of the prescription is stamped in red ink in the lower right corner with the letter "C" no less than 1-inch high and filed

either in the prescription file for controlled substances listed in Schedules I and II or in the usual consecutively numbered prescription file for non-controlled substances.

(21 U.S.C. 821 and 871(b); 28 CFR 0.100)

[36 FR 7790, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic], and amended at 39 PR 37985, Oct. 25, 1974; 45 FR 44266, July 1, 1980; 47 FR 41735, Sept. 22, 1982; 51 FR 5320, Feb. 13, 1986]

INVENTORY REQUIREMENTS

**§ 1304.11 General requirements for inventories.**

(a) Each inventory shall contain a complete and accurate record of all controlled substances on hand on the date the inventory is taken. Controlled substances shall be deemed to be "on hand" if they are in the possession of or under the control of the registrant, including substances returned by a customer, substances ordered by a customer but not yet invoiced, substances stored in a warehouse on behalf of the registrant, and substances in the possession of employees of the registrant and intended for distribution as complimentary samples.

(b) A separate inventory shall be made by a registrant for each registered location. In the event controlled substances in [sic] the possession or under the control of the registrant at a location for which he is not registered, the substances shall be included in the inventory of the registered location to which they are subject to control or to which the person possessing the substance is responsible. Each inventory for a registered location shall be kept at the registered location.

(c) A separate inventory shall be made by a registrant for each independent activity for which he is registered, except as provided in § 1304.18.

(d) A registrant may take an inventory on a date that is within 4 days of his biennial inventory date pursuant to § 1304.13 if he notifies in advance the Special Agent in Charge of the Administration in his area of the date on which he will take the inventory. A registrant may take an inventory either as of the opening of business or as of the close of business on the inventory date. The registrant shall indicate on the inventory records whether the inventory is taken as of the opening or as of the close of business and the date the inventory is taken.

(e) An inventory must be maintained in a written, typewritten or printed form. An inventory taken by use of an oral recording device must be promptly transcribed.

[36 FR 7790, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973 [sic], and amended at 47 FR 41735, Sept. 22, 1982]

**§ 1304.12 Initial inventory date.**

(a) Every person required to keep records who is provisionally registered on May 1, 1971, shall take an inventory of all stocks of controlled substances on hand on that date in accordance with §§ 1304.15-1304.19, as applicable.

(b) Every person required to keep records who is registered after May 1, 1971, and who was not provisionally registered on that date, shall take an inventory of all stocks of controlled substances on hand on the date he first engages in the manufacture, distribution, or dispensing of controlled substances, in accordance with §§ 1304.15-1304.19, as applicable. In the event a person commences business with no controlled substances on hand, he shall record this fact as his initial inventory.

[36 FR 7791, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971; 37 FR 15920, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973]

**§ 1304.13 Biennial inventory date.**

Every 2 years following the date on which the initial inventory is taken by a registrant pursuant to § 1304.12, the registrant shall take a new inventory of all stocks of controlled substances on hand. The biennial inventory may be taken (a) on the day of the year on which the initial inventory was taken or (b) on the registrant's regular general physical inventory date, if any, which is nearest to and does not vary by more than

6 months from the biennial date that would otherwise apply or (c) on any other fixed date which does not vary by more than 6 months from the biennial date that would otherwise apply. If the registrant elects to take the biennial inventory on his regular general physical inventory date or another fixed date, he shall notify the Administration of this election and of the date on which the biennial inventory will be taken.

[36 FR 7791, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973]

**§ 1304.17 Inventories of dispensers and researchers.**

Each person registered or authorized (by § 1301.22(b) of this chapter) to dispense or conduct research with controlled substances and required to keep records pursuant to § 1304.03 shall include in his inventory the same information required of manufacturers pursuant to § 1304.15 (c) and (d). In determining the number of units of each finished form of a controlled substance in a commercial container which has been opened, the dispenser shall do as follows:

(a) If the substance is listed in Schedule I or II, he shall make an exact count or measure of the contents; and

(b) If the substance is listed in Schedule III, IV, or V, he shall make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case he must make an exact count of the contents.

[36 FR 7791, Apr. 24, 1971, as amended at 36 FR 18732, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973]

CONTINUING RECORDS

**§ 1304.21 General requirements for continuing records.**

(a) On and after May 1, 1971, every registrant required to keep records pursuant to § 1304.03 shall maintain on a current basis a complete and accurate record of each such substance manufactured, imported, received, sold, delivered, exported, or otherwise disposed of by him, except that no registrant shall be required to maintain a perpetual inventory.

(b) Separate records shall be maintained by a registrant for each registered location except as provided in § 1304.04 (a). In the event controlled substances are in the possession or under the control of a registrant at a location for which he is not registered, the substances shall be included in the records of the registered location to which they are subject to control or to which the person possessing the substance is responsible.

(c) Separate records shall be maintained by a registrant for each independent activity for which he is registered, except as provided in §§ 1304.25 and 1304.26.

(d) In recording dates of receipt, importation, distribution, exportation, or other transfers, the date on which the controlled substances are actually received, imported, distributed, exported, or otherwise transferred shall be used as the date of receipt or distribution of any documents of transfer (e.g., invoices or packing slips).

[36 FR 7792, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973]

**§ 1304.28 Records for maintenance treatment programs and detoxification treatment programs.**

(a) Each person registered or authorized (by § 1301.22 of this chapter) to maintain and/or detoxify controlled substance users in a narcotic treatment program shall maintain records with the following information for each narcotic controlled substance:

(1) Name of substance;
(2) Strength of substance;
(3) Dosage form;
(4) Date dispensed;
(5) Adequate identification of patient (consumer);
(6) Amount consumed;
(7) Amount and dosage form taken home by patient; and
(8) Dispenser's initials.

(b) The records required by paragraph (a) of this section will be maintained in a dispensing log at the narcotic treatment program site and will be maintained in compliance with § 1304.24 without reference to § 1304.03.

(c) All sites which compound a bulk narcotic solution from bulk narcotic powder to liquid for on-site use must keep a separate batch record of the compounding.

(d) Records of identity, diagnosis, prognosis, or treatment of any patients which are maintained in connection with the performance of a narcotic treatment program shall be confidential, except that such records may be disclosed for purposes and under the circumstances authorized by part 310 and part 1401 of this title.

[39 FR 37985, Oct. 25, 1974]

**§ 1304.29 Records for treatment programs which compound narcotics for treatment programs and other locations.**

Each person registered or authorized by § 1301.22 of this chapter to compound narcotic drugs for off-site use in a narcotic treatment program shall maintain records which include the following information for each narcotic drug:

(a) For each narcotic controlled substance in bulk form to be used in or capable of use in, or being used in, the compounding of the same or other noncontrolled substance in finished form:

(1) The name of the substance;

(2) The quantity compounded in bulk form by the registrant, including the date, quantity and batch or other identifying number of each batch compounded;

(3) The quantity received from other persons, including the date and quantity of each receipt and the name, address and registration number of the other person from whom the substance was received;

(4) The quantity imported directly by the registrant (under a registration as an importer) for use in compounding by him, including the date, quantity and import permit or declaration number of each importation;

(5) The quantity used to compound the same substances in finished form, including:

(i) The date and batch or other identifying number of each compounding;

(ii) The quantity used in the compound;

(iii) The finished form (e.g., 10-milligram tablets or 10-milligram concentration per fluid ounce or milliliter;

(iv) The number of unites of finished form compounded;

(v) The quantity used in quality control;

(vi) The quantity lost during compounding and the causes therefore, if known;

(vii) The total quantity of the substance contained in the finished form;

(viii) The theoretical and actual yields; and

(ix) Such other information as is necessary to account for all controlled substance used int he compounding process;

(6) The quantity used to manufacture other controlled and non-controlled substances; including the name of each substance manufactured and the information required in paragraph (a)(5) of this section;

(7) The quantity distributed in bulk form to other programs, including the date and quantity of each distribution and the name, address and registration number of each program to whom a distribution was made;

(8) The quantity disposed of by destruction, including the reason, date and manner of destruction. All other destruction of narcotic controlled substances will comply with § 1307.22.

(9) The quantity disposed of the destruction, including the reason, date and manner of destruction, including the reason, date and manner of destruction. All other destruction of narcotic controlled substances with comply with § 1307.22.

(b) For each narcotic controlled substance in finished form:

(1) The name of the substance;

(2) Each finished form (e.g., 10-milligram tablet or 10 milligram concentration per fluid ounce or milliliter) and the number of units or volume or finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial);

(3) The number of containers of each such commercial finished form compounded from bulk form by the registrant, inclining the information required pursuant to paragraph (a)(5) of this section;

(4) The number of units of finished forms and/or commercial containers received from other person, including the date of and number of units and.or commercial containers in each receipt and the name, address and registration number of the person from whom the units were received;

(5) The number of units of finished forms and/or commercial containers imported directly by the person (under a registration or authorization to import), including the date of, the number of units and/or commercial containers in, and the import permit or declaration number for, each importation;

(6) The number of units and/or commercial containers compounded by the registrant from units in finished form received from other or imported, including:

(i) The date and batch or other identifying number of each compounding;

(ii) The operation performed (e.g., repackaging or relabeling);

(iii) The number of units of finished form used in the compound, the number compounded and the number lost during compounding, with the causes for such losses, if known; and

(iv) Such other information as is necessary tc account for all controlled substances used in the compounding process;

(7) The number of containers distributed to other programs, including the date, the number of containers in each distribution, and the name, address and registration number of the program to whom the containers were distributed;

(8) The number of commercial containers exported directly by the registrant (under a registration as an exporter), including the date, number of containers and export permit or declaration number for each exportation; and

(9) The number of units of finished forms and /or commercial containers destroyed in any manner by the registrant, including the reason, the date and manner of destruction. All other destruction of narcotic controlled substances will comply with § 1307.22.

[39 FR 37985, Oct. 25, 1974]

## PART 1305—ORDER FORMS

Sec.



AUTHORITY: 21 U.S.C. 821, 828, 871(b), unless otherwise noted.

SOURCE: 36 FR 7796, Apr. 24, 1971, unless otherwise noted. Redesignated at 38 FR 26609, Sept. 24, 1973.

**Note to reader:** Only those paragraphs in this Part that apply specifically to methadone maintenance treatment programs are provided.

**§ 1305.08 Persons entitled to fill order forms.**

An order form may be filled only by a person registered as a manufacturer or distributor of controlled substances listed in Schedule I or II under section 303 of the Act (21 U.S.C. 823) or as an importer of such substances under section 1008 of the Act (21 U.S.C. 958), except for the following:

(a) A person registered to dispense such substances under section 303 of the Act, or to export such substances under section 1008 of the Act, if he is discontinuing business or if his registration is expiring without reregistration, may dispose of any controlled substances listed in Schedule I or II in his possession pursuant to order forms in accordance with § 1307.14 of this chapter;

(b) A person who has obtained any controlled substance in Schedule I or II by order form may return such substance, or portion thereof, to the person from whom he obtained the substance or the manufacturer of the substance pursuant to the order form of the latter person;

(c) A person registered to dispense such substances may distribute such substances to another dispenser pursuant to, and only in the circumstances described in, § 1307.11 of this chapter; and

(d) A person registered or authorized to conduct chemical analysis or research with controlled substances may distribute a controlled substance listed in Schedule I or II to another person registered or authorized to conduct chemical analysis, instructional activities, or research with such substances pursuant to the order form of the latter person, if such distribution is for the purpose of furthering such chemical analysis, instructional activities, or research.

(e) A person registered as a compounder of narcotic substances for use at off-site locations in conjunction with a narcotic treatment program at the compounding location, who is authorized to handle Schedule II narcotics, is authorized to fill order forms for distribution of narcotic drugs to offsite narcotic treatment programs only.

[36 FR 7796, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971; 36 FR 18732, Sept. 21, 1971; 37 FR 15921, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973]

EDITORIAL NOTE: For FR citations affecting § 1305.08, see the List of CFR Sections Affected in the Finding Aids section of this volume.

**§ 1305.09 Procedure for filling order forms.**

(a) The purchaser shall submit Copy 1 and Copy 2 of the order form to the supplier, and retain Copy 3 in his own files.

(b) The supplier shall fill the order, if possible and if he desires to do so, and record on Copies 1 and 2 the number of commercial or bulk containers furnished on each item and the date on which such containers are shipped to the purchaser. If an order cannot be filled in its entirety, it may be filled in part and the balance supplied by additional shipments within 60 days following the date of the order form. No order form shall be valid more than 60 days after its execution by the purchaser, except as specified in paragraph (f) of this section.

(c) The controlled substances shall only be shipped to the purchaser and at the location printed by the Administration on the order form, except as specified in paragraph (f) of this section.

(d) The supplier shall retain Copy 1 of the order form for his own files and forward Copy 2 to the Special Agent in Charge of the Drug Enforcement Administration in the area in which the supplier is located. Copy 2 shall be forwarded at the close of the month during which the order is filled; if an order is filled by partial shipments, Copy 2 shall be forwarded at the close of the month during which the final shipment is made or during which the 60-day validity period expires.

(e) The purchaser shall record on Copy 3 of the order form the number of commercial or bulk containers furnished on each item and the dates on which such containers are received by the purchaser.

(f) Order forms submitted by registered procurement officers of the Defense Personnel Support Center of Defense Supply Agency for delivery to armed services establishments within the United States may be shipped to locations other than the location printed on the order form, and in partial shipments at different times not to exceed six months from the date of the order, as designated by the procurement officer when submitting the order.

[36 FR 7796, Apr. 24, 1971, as amended at 36 FR 18732, Sept. 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 47 FR 41735, Sept. 22, 1982]

**§ 1305.11 Unaccepted and defective order forms.**

(a) No order form shall be filled if it:

(1) Is not complete, legible, or properly prepared, executed, or endorsed; or

(2) Shows any alteration, erasure, or change of any description.

(b) If an order form cannot be filled for any reason under this section, the supplier shall return Copies 1 and 2 to purchaser with a statement as to the reason (e.g., illegible or altered). A supplier may for any reason refuse to accept any order and if a supplier refuses to accept the order, a statement that the order is not accepted shall be sufficient for purposes of this paragraph.

(c) When received by the purchaser, Copies 1 and 2 of the order form and the statement shall be attached to Copy 3 and retained in the files of the purchaser in accordance with § 1305.13. A defective order form may not be corrected; it must be replaced by a new order form in order for the order to be filled.

**§ 1305.12 Lost and stolen order forms.**

(a) If a purchaser ascertains that an unfilled order form has been lost, he shall execute another in triplicate and a statement containing the serial number and date of the lost form, and stating that the goods covered by the first order form were not received through loss of that order form. Copy 3 of the second form and a copy of the statement shall be retained with Copy 3 of the order form first executed. A copy of the statement shall be attached to Copies 1 and 2 of the second order form sent to the supplier. If the first order form is subsequently received by the supplier to whom it was directed, the supplier shall mark upon the face thereof "Not accepted" and return Copies 1 and 2 to the purchaser, who shall attach it to Copy 3 and the statement.

(b) Whenever any used or unused order forms are stolen form or lost (otherwise than in the course of transmission) by any purchaser or supplier, he shall immediately upon discovery of such theft or loss, report the same to the Registration Unit, Drug Enforcement Administration, Department of Justice, Post Office Box 28083, Central Station Washington, DC 20005, stating the serial number of each form stolen or lost. If the theft or loss includes any original order forms received from purchasers and the supplier is unable to state the serial numbers of such order forms, he shall report the date or approximate date of receipt thereof and the names and addresses of the purchaser is unable to state the serial numbers of the order forms contained therein, he shall report, in lieu of the numbers of the forms contained in such book, the date or approximate date of issuance thereof. If any unused order form reported stolen or lost is subsequently recovered or found, the Registration Branch of the Administration shall immediately be notified.

[36 FR 7796, Apr. 24, 1971, as amended at 36 FR 13386, July 21, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 51 FR 5319, Feb. 13, 1986]

**§ 1305.13 Preservation of order forms.**

(a) The purchaser shall retain Copy 3 of each order form which has been filled. He shall also retain in his files all copies of each unaccepted or defective order form and each statement attached thereto.

(b) The supplier shall retain Copy 1 of each order form which he has filled.

(c) Order forms must be maintained separately from all other records of the registrant. Order forms are required to be kept available for inspection for a period of 2 year. If a purchaser has several registered locations, he must retain Copy 3 of the executed order forms and any attached statements or other related documents (not including unexecuted order forms which may be kept elsewhere pursuant to §1305.06(e)) at the registered location printed on the order form.

(d) The supplier of carfentanil etorphine hydrochloride and diprenorphine shall maintain order forms for these substances separately from all other order forms and records required to be maintained by the registrant.

[36 FR 7796, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 39 FR 17839, May 21, 1974; 54 FR 33674, Aug. 16, 1989]

# PART 1307—MISCELLANEOUS

## General Information



## Special Exceptions for Manufacture and Distribution of Controlled Substances



## Disposal of Controlled Substances



## Special Exempt Persons



AUTHORITY: 21 U.S.C. 821, 822(d), 871(b), unless otherwise noted.

SOURCE: 36 FR 7801, Apr. 24, 1971, unless otherwise noted. Redesignated at 38 FR 26609, Sept. 24, 1973.

**Note to reader:** Only those paragraphs in this Part that apply specifically to methadone maintenance treatment programs are provided.

## Disposal of Controlled Substances

### § 1307.14 Distribution upon discontinuance or transfer of business.

(a) Any registrant desiring to discontinue business activities altogether or with respect to controlled substances (without transferring such business activities to another person) shall return for cancellation his certificate of registration, and any unexecuted order forms in his possession, to the Registration Unit, Drug Enforcement Administration, Department of Justice, Post Office Box 28083, Central Station, Washington, DC 20005. Any controlled substances in his possession may be disposed of in accordance with § 1307.21.

### § 1307.21 Procedure for disposing of controlled substances.

(a) Any person in possession of any controlled substance and desiring or required to dispose of such substance may request the Special Agent in Charge of the Administration in the area in which the person is located for authority and instructions to dispose of such substance. The request should be made as follows:

(1) If the person is a registrant required to make reports pursuant to part 1304 of this chapter, he shall list the controlled substance or substances which he desires to dispose of on the "b" subpart of the report normally filed by him, and submit three copies of that subpart to the Special Agent in Charge of the Administration in his area.

(2) If the person is a registrant not required to make reports pursuant to part 1304 of this chapter, he shall list the controlled substance or substances which he desires to dispose of on DEA Form 41, and submit three copies of that form to the Special Agent in Charge in his area; and

(3) If the person is not a registrant, he shall submit to the Special Agent in Charge a letter stating:

(i) The name and address of the person;

(ii) The name and quantity of each controlled substance to be disposed of;

(iii) How the applicant obtained the substance, if known; and

(iv) The name, address, and registration number, if known, of the person who possessed the controlled substances prior to the applicant, if known.

(b) The Special Agent in Charge shall authorize and instruct the applicant to dispose of the controlled substance in one of the following manners:

(1) By transfer to person registered under the Act and authorized to possess the substance;

(2) By delivery to an agent of the Administration or to the nearest office of the Administration;

(3) By destruction in the presence of an agent of the Administration or other authorized person; or

(4) By such other means as the Special Agent in Charge may determine to assure that the substance does not become available to unauthorized persons.

(c) In the event that a registrant is required regularly to dispose of controlled substances, the Special Agent in Charge may authorize the registrant to dispose of such substances, in accordance with paragraph (b) of this section, without prior approval of the Administration in each instance, on the condition that the registrant keep records of such disposals and file periodic reports with the Special Agent in Charge summarizing the disposals made by the registrant. In granting such authority, the Special Agent in Charge may place such conditions as he deems proper on the disposal of controlled substances, including the method of disposal and the frequency and detail of reports.

(d) This section shall not be construed as affecting or altering in any way the disposal of controlled substances through procedures provided in laws and regulations adopted by the State.

[36 FR 7801, Apr. 24, 1971, as amended at 37 FR 15922, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 47 FR 41735, Sept. 22, 1982]

# PART 1316—ADMINISTRATIVE FUNCTIONS, PRACTICES, AND PROCEDURES

## SUBPART A—ADMINISTRATIVE INSPECTIONS

Sec.



## SUBPART B—PROTECTION OF RESEARCHERS AND RESEARCH SUBJECTS

Sec.



## SUBPART C—ENFORCEMENT PROCEEDINGS

Sec.



## SUBPART D—ADMINISTRATIVE HEARINGS

Sec.

SUBPART E—SEIZURE, FORFEITURE, AND DISPOSITION OF PROPERTY

Sec.



SUBPART F—EXPEDITED FORFEITURE PROCEEDINGS FOR CERTAIN PROPERTY

Sec.



SOURCE: 36 FR 7820 Apr. 24, 1971, unless otherwise noted. Redesignated at 38 FR 26609, Sept. 24, 1973.

SUBPART A—ADMINISTRATIVE INSPECTIONS

**§1316.03 Authority to make inspections.**

In carrying out his functions under the Act, the Administrator, through his inspectors, is authorized in accordance with sections 510 and 1015 of the Act (21 U.S.C. 880 and 965) to enter controlled premises and conduct administrative inspections thereof, for the purpose of:

(a) Inspecting, copying, and verifying the correctness of records, reports, or other documents required to be kept or made under the Act and regulations promulgated under the Act, including, but not limited to, inventory and other records required to be kept pursuant to part 1304 of this chapter, order form records required to be kept pursuant to part 1305 of this chapter, prescription and distribution records required to be kept pursuant to part 1306 of this chapter, records of listed chemicals, tableting machines, and encapsulating machines required to be kept pursuant to part 1310 of this chapter, import/export records of listed chemicals required to be kept pursuant to part 1313 of this chapter, shipping records identifying the name of each carrier used and the date and quantity of each shipment, and storage records identifying the name of each warehouse used and the date and quantity of each storage.

(b) Inspecting within reasonable limits and to a reasonable manner all pertinent equipment, finished and unfinished controlled substances and other substances or materials, containers, and labeling found at the controlled premises relating to this Act;

(c) Making a physical inventory of all controlled substances on-hand [sic] at the premises;

(d) Collecting samples of controlled substances or precursors (in the event any samples are collected during an inspection, the inspector shall issue a receipt for such samples on DEA Form 84 to the owner, operator, or agent in charge of the premises);

(e) Checking of records and information on distribution of controlled substances by the registrant as they relate to total distribution of the registrant (i.e., has the distribution in controlled substances increased markedly within the past year, and if so why); and

(f) Except as provided in §1316.04, all other things therein (including records, files, papers, processes, controls, and facilities) appropriate for verification of the records, reports, documents referred to above or otherwise bearing on the provisions of the Act and the regulations thereunder.

[36 FR 7820, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 51 FR 5319, Feb. 13, 1986; 55 FR 50827, Dec. 11, 1990]

**§1316.06 Notice of inspection.**

The notice of inspection (DEA (or DNB) Form 82) shall contain:

(a) The name and title of the owner, operator, or agent in charge of the controlled premises;

(b) The controlled premises name;

(c) The address of the controlled premises to be inspected;

(d) The date and time of the inspection;

(e) A statement that a notice of inspection is given pursuant to section 510 of the Act (21 U.S.C. 880);

(f) A reproduction of the pertinent parts of section 510 of the Act; and

(g) The signature of the inspector.

## SUBPART C—ENFORCEMENT PROCEEDINGS

AUTHORITY: 21 U.S.C. 871(B), 883.

**§1316.31 Authority for enforcement proceeding.**

A hearing may be ordered or granted by any Special Agent in Charge of the Drug Enforcement Administration, at his discretion, to permit any person against whom criminal and/or civil action is contemplated under the Controlled Substances Act (84 Stat. 1242; 21 U.S.C. 801) or the Controlled Substances Import and Export Act (84 Stat. 1285; 21 U.S.C. 951) an opportunity to present his views and his proposals for bringing his alleged violations into compliance with the law. Such hearing will also permit him to show cause why prosecution should not be instituted, or to present his views on the contemplated proceeding.

[36 FR 7820, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 47 FR 41735, Sept. 22, 1982]

**§1316.32 Notice of proceeding; time and place.**

Appropriate notice designating the time and place for the hearing shall be given to the person. Upon request, timely and properly made, by the person to whom notice has been given, the time or place of the hearing, or both, may be changed if the request states reasonable grounds for such change. Such request shall be addressed to the Special Agent in Charge who issued the notice.

[36 FR 7820, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 47 FR 41735, Sept. 22, 1982]

**§1316.33 Conduct of proceeding.**

Presentation of views at a hearing under this subpart shall be private and informal. The views presented shall be confined to matters relevant to bringing violations into compliance with the Act or to other contemplated proceedings under the Act. These views may be presented orally or in writing by the person to whom the notice was given, or by his authorized representative.

**§1316.34 Records of proceeding.**

A formal record, either verbatim or summarized, of the hearing may be made at the discretion of the Special Agent in Charge. If a verbatim record is to be made, the person attending the hearing will be so advised prior to the start of the hearing.

[37 FR 15924, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973, and amended at 47 FR 41735, Sept. 22, 1982]

# Appendix E—Confidentiality Regulations

42 CFR Part 2—Confidentiality of Alcohol and Drug Abuse Patient Records

**Public Health Service, HHS**

## SUBCHAPTER A—GENERAL PROVISIONS
## PART 1—[RESERVED]

## PART 2—CONFIDENTIALITY OF ALCOHOL AND DRUG ABUSE PATIENT RECORDS

### Subpart A—Introduction



### Subpart B—General Provisions



### Subpart C—Disclosures With Patient's Consent



### Subpart D—Disclosures Without Patient Consent



### Subpart E—Court Orders Authorizing Disclosures and Use

2.65 Procedures and criteria for orders authorizing disclosure and use of records to criminally investigate or prosecute patients.
2.66 Procedures and criteria for orders authorizing disclosure and use of records to investigate or prosecute a program or the person holding the records.
2.67 Orders authorizing the use of undercover agents and informants to criminally investigate employees or agents of a program.

AUTHORITY: Sec. 408 of Pub. L. 92-255, 86 Stat. 79, 9s amended by sec. 303 (a), (b) of Pub. L. 93-282, 83 Stat. 137, 138; sec. 4(c)(5)(A) of Pub. L. 94-237, 90 Stat. 244; sec. 111(c)(3) of Pub. L. 94-581, 90 Stat. 2852; sec. 509 of Pub. L. 96-88, 93 Stat. 695; sec. 973(d) of Pub. L. 97-35, 95 Stat. 598; and transferred to sec. 527 of the Public Health Service Act by sec. 2(b)(16)(B) of Pub. L. 98-24, 97 Stat. 182 and as amended by sec. 106 of Pub. L. 99-401, 100 Stat. 907 (42 U.S.C. 290ee-3) and sec. 333 of Pub. L. 91-616, 84 Stat. 1853, as amended by sec. 122(a) of Pub. L. 93-282, 88 Stat. 131; and sec. 111(c)(4) of Pub. L. 94-581, 90 Stat. 2852 and transferred to sec. 523 of the Public Health Service Act by sec. 2(b)(13) of Pub. L. 98-24, 97 Stat. 181 and as amended by sec. 106 of Pub. L. 99-401, 100 Stat. 907 (42 U.S.C. 290dd-3).

SOURCE: 52 FR 21809, June 9, 1987, unless otherwise noted.

## Subpart A—Introduction

### § 2.1 Statutory authority for confidentiality of drug abuse patient records.

The restrictions of these regulations upon the disclosure and use of drug abuse patient records were initially authorized by section 408 of the Drug Abuse Prevention, Treatment, and Rehabilitation Act (21 U.S.C. 1175). That section as amended was transferred by Pub. L. 98-24 to section 527 of the Public Health Service Act which is codified at 42 U.S.C. 290ee-3. The amended statutory authority is set forth below:

§ 290ee-3. CONFIDENTIALITY OF PATIENT RECORDS.

(a) Disclosure authorization

Records of the identity, diagnosis, prognosis, or treatment of any patient which are maintained in connection with the performance of any drug abuse prevention function conducted, regulated, or directly or indirectly assisted by any department or agency of the United States shall, except as provided in subsection (e) of this section, be confidential and be disclosed only for the purposes and under the circumstances expressly authorized under subsection (b) of this section.

(b) Purposes and circumstances of disclosure affecting consenting patient and patient regardless of consent

(1) The content of any record referred to in subsection (a) of this section may be disclosed in accordance with the prior written consent of the patient with respect to whom such record is maintained, but only to such extent, under such circumstances, and for such purposes as may be allowed under regulations prescribed pursuant to subsection (g) of this section.

(2) Whether or not the patient, with respect to whom any given record referred to in subsection (a) of this section is maintained, gives his written consent, the content of such record may be disclosed as follows:

(A) To medical personnel to the extent necessary to meet a bona fide medical emergency.

(B) To qualified personnel for the purpose of conducting scientific research, management audits, financial audits, or program evaluation, but such personnel may not identify, directly or indirectly, any individual patient in any report of such research, audit, or evaluation, or otherwise disclose patient identities in any manner.

(C) If authorized by an appropriate order of a court of competent jurisdiction granted after application showing good cause therefor. In assessing good cause the court shall weigh the public interest and the need for disclosure against the injury to the patient, to the physician-patient relationship, and to the treatment services. Upon the granting of such order, the court, in determining the extent to which any disclosure of all or any part of any record is necessary, shall impose appropriate safeguards against unauthorized disclosure.

(c) Prohibition against use of record in making criminal charges or investigation of patient

Except as authorized by a court order granted under subsection (b)(2)(C) of this section, no record referred to in subsection (a) of this section may be used to initiate or substantiate any criminal charges against a patient or to conduct any investigation of a patient.

(d) Continuing prohibition against disclosure irrespective of status as patient

The prohibitions of this section continue to apply to records concerning any individual who has been a patient, irrespective of whether or when he ceases to be a patient.

(e) Armed Forces and Veterans' Administration; interchange of records; report of suspected child abuse and neglect to State or local authorities

The prohibitions of this section do not apply to any interchange of records—

(1) within the Armed Forces or witrhin [sic] those components of the Veterans' Administration furnishing health care to veterans, or

(2) between such components and the Armed Forces.

The prohibitions of this section do not apply to the reporting under State law of incidents of suspected child abuse and neglect to the appropriate State or local authorities.

(f) Penalty for first and subsequent offenses

Any person who violates any provision of this section or any regulation issued pursuant to this section shall be fined not nore [sic] than $500 in the case of a first offense, and not more than $5,000 in the case of each subsequent offense.

(g) Regulations; interagency consultations; definitions, safeguards, and procedures, including procedures and criteria for issuance and scope of orders

Except as provided in subsection (h) of this section, the Secretary, after consultation with the Administrator of Veterans' Affairs and the heads of other Federal departments and agencies substantially affected thereby, shall prescribe regulations to carry out the purposes of this section. These regulations may contain such definitions, and may provide for such safeguards and procedures, including procedures and criteria for the issuance and scope of orders under subsection (b)(2)(C) of this section, as in the judgment of the Secretary are necessary or proper to effectuate the purposes of this section, to prevent circumvention or evasion thereof, or to facilitate compliance therewith. (Subsection (h) was superseded by section 111(c)(3) of Pub. L. 94-581. The responsibility of the Administrator of Veterans' Affairs to write regulations to provide for confidentiality of drug abuse patient records under Title 38 was moved from 21 U.S.C. 1175 to 38 U.S.C. 4134.)

**§ 2.2 Statutory authority for confidentiality of alcohol abuse patient records.**

The restrictions of these regulations upon the disclosure and use of alcohol abuse patient records were initially authorized by section 333 of the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation Act of 1970 (42 U.S.C. 4582). The section as amended was transferred by Pub. L. 98-24 to section 523 of the Public Health Service Act which is codified at 42 U.S.C. 290dd-3. The amended statutory authority is set forth below:

§ 290dd-3. CONFIDENTIALITY OF PATIENT RECORDS

(a) Disclosure authorization

Records of the identity, diagnosis, prognosis, or treatment of any patient which are maintained in connection with the performance of any program or activity relating to alcoholism or alcohol abuse education, training, treatment, rehabilitation, or research, which is conducted, regulated, or directly or indirectly assisted by any department or agency of the United States shall, except as provided in subsection (e) of this section, be confidential and be disclosed only for the purposes and under the circumstances expressly authorized under subsection (b) of this section.

(b) Purposes and circumstances of disclosure affecting consenting patient and patient regardless of consent

(1) The content of any record referred to in subsection (a) of this section may be disclosed in accordance with the prior written consent of the patient with respect to whom such record is maintained, but only to such extent, under such circumstances, and for such purposes as may be allowed under regulations prescribed pursuant to subsection (g) of this section.

(2) Whether or not the patient, with respect to whom any given record referred to in subsection (a) of this section is maintained, gives his written consent, the content of such record may be disclosed as follows:

(A) To medical personnel to the extent necessary to meet a bona fide medical emergency.

(B) To qualified personnel for the purpose of conducting scientific research, management audits, financial audits, or program evaluation, but such personnel may not identify, directly or indirectly, any individual patient in any report of such research, audit, or evaluation, or otherwise disclose patient identities in any manner.

(C) If authorized by an appropriate order of a court of competent jurisdiction granted after application showing good cause therefor. In assessing good cause the court shall weigh the public interest and the need for disclosure against the injury to the patient, to the physician-patient relationship, and to the treatment services. Upon the granting of such order, the court, in determining the extent to which any disclosure of all or any part of any record is necessary, shall impose appropriate safeguards against unauthorized disclosure.

(c) Prohibition against use of record in making criminal charges or investigation of patient

Except as authorized by a court order granted under subsection (b)(2)(C) of this section, no record referred to in subsection (a) of this section may be used to initiate or substantiate any criminal charges against a patient or to conduct any investigation of a patient.

(d) Continuing prohibition against disclosure irrespective of status as patient

The prohibitions of this section continue to apply to records concerning any individual who has been a patient, irrespective of whether or when he ceases to be a patient.

(e) Armed Forces and Veterans' Administration; interchange of record of suspected child abuse and neglect to State or local authorities

The prohibitions of this section do not apply to any interchange of records-

(1) within the Armed Forces or within those components of the Veterans' Administration furnishing health care to veterans, or

(2) between such components and the Armed Forces.

The prohibitions of this section do not apply to the reporting under State law of incidents of suspected child abuse and neglect to the appropriate State or local authorities.

(f) Penalty for first and subsequent offenses

Any person who violates any provision of this section or any regulation issued pursuant to this section shall be fined not more than $500 in the case of a first offense, and not more than $5,000 in the case of each subsequent offense.

(g) Regulations of Secretary; definitions, safeguards, and procedures, including procedures and criteria for issuance and scope of orders

Except as provided in subsection (h) of this section, the Secretary shall prescribe regulations to carry out the purposes of this section. These regulations may contain such definitions, and may provide for such safeguards and procedures, including procedures and criteria for the issuance and scope of orders under subsection(b)(2)(C) of this section, as in the judgment of the Secretary are necessary or proper to effectuate the purposes of this section, to prevent circumvention or evasion thereof, or to facilitate compliance therewith. (Subsection (h) was superseded by section 111(c)(4) of Pub. L. 94-581. The responsibility of the Administrator of Veterans' Affairs to write regulations to provide for confidentiality of alcohol abuse patient records under Title 38 was moved from 42 U.S.C. 4582 to 38 U.S.C. 4134.)

**§ 2.3 Purpose and effect.**

(a) *Purpose.* Under the statutory provisions quoted in §§ 2.1 and 2.2, these regulations impose restrictions upon the disclosure and use of alcohol and drug abuse patient records which are maintained in connection with the performance of any federally assisted alcohol and drug abuse program. The regulations specify:

(1) Definitions, applicability, and general restrictions in subpart B (definitions applicable to § 2.34 only appear in that section);

(2) Disclosures which may be made with written patient consent and the form of the written consent in subpart C;

(3) Disclosures which may be made without written patient consent or an authorizing court order in subpart D; and

(4) Disclosures and uses of patient records which may be made with an authorizing court order and the procedures and criteria for the entry and scope of those orders in subpart E.

(b) *Effect.* (1) These regulations prohibit the disclosure and use of patient records unless certain circumstances exist. If any circumstances exists [sic] under which disclosure is permitted, that circumstance acts to remove the prohibition on disclosure but it does not compel disclosure. Thus, the regulations do not require disclosure under any circumstances.

(2) These regulations are not intended to direct the manner in which substantive functions such as research, treatment, and evaluation are carried out. They are intended to insure that an alcohol or drug abuse patient in a federally assisted alcohol or drug abuse program is not made more vulnerable by reason of the availability of his or her patient record than an individual who has an alcohol or drug problem and who does not seek treatment.

(3) Because there is a criminal penalty (a fine—see 42 U.S.C. 290ee-3(f), 42 U.S.C. 290dd-3(f) and 42 CFR 2.4) for violating the regulations, they are to be construed strictly in favor of the potential violator in the same manner as a criminal statute (see *M. Kraus & Brothers v. United States*, 327 U.S. 614, 621-22, 66 S. Ct. 705, 707-08 (1946)).

**§ 2.4 Criminal penalty for violation.**

Under 42 U.S.C. 290ee-3(f) and 42 U.S.C. 290dd-3(f), any person who violates any provision of those statutes or these regulations shall be fined not more than $500 in the case of a first offense, and not more than $5,000 in the case of each subsequent offense.

**§ 2.6 Reports of violations.**

(a) The report of any violation of these regulations may be directed to the United States Attorney for the judicial district in which the violation occurs.

(b) The report of any violation of these regulations by a methadone program may be directed to the Regional Offices of the Food and Drug Administration.

## Subpart B—General Provisions

### § 2.11 Definitions.

For purposes of these regulations:

*Alcohol abuse* means the use of an alcoholic beverage which impairs the physical, mental, emotional, or social well-being of the user.

*Drug abuse* means the use of a psychoactive substance for other than medicinal purposes which impairs the physical, mental, emotional, or social well-being of the user.

*Diagnosis* means any reference to an individual's alcohol or drug abuse or to a condition which is identified as having been caused by that abuse which is made for the purpose of treatment or referral for treatment.

*Disclose or disclosure* means a communication of patient indentifying [sic] information, the affirmative verification of another person's communication of patient identifying information, or the communication of any information from the record of a patient who has been identified.

*Informant* means an individual:

(a) Who is a patient or employee of a program or who becomes a patient or employee of a program at the request of a law enforcement agency or official; and

(b) Who at the request of a law enforcement agency or official observes one or more patients or employees of the program for the purpose of reporting the information obtained to the law enforcement agency or official.

*Patient* means any individual who has applied for or been given diagnosis or treatment for alcohol or drug abuse at a federally assisted program and includes any individual who, after arrest on a criminal charge, is identified as an alcohol or drug abuser in order to determine that individual's eligibility to participate in a program.

*Patient identifying information* means the name, address, social security number, fingerprints, photograph, or similar information by which the identity of a patient can be determined with reasonable accuracy and speed either directly or by reference to other publicly available information. The term does not include a number assigned to a patient by a program, if that number does not consist of, or contain numbers (such as a social security, or driver's license number) which could be used to identify a patient with reasonable accuracy and speed from sources external to the program.

*Person* means an individual, partnership, corporation, Federal, State or local government agency, or any other legal entity.

*Program* means a person which in whole or in part holds itself out as providing, and provides, alcohol or drug abuse diagnosis, treatment, or referral for treatment. For a general medical care facility or any part thereof to be a program, it must have:

(a) An identified unit which provides alcohol or drug abuse diagnosis, treatment, or referral for treatment or

(b) Medical personnel or other staff whose primary function is the provision of alcohol or drug abuse diagnosis, treatment, or referral for treatment and who are identified as such providers.

*Program director* means:

(a) In the case of a program which is an individual, that individual;

(b) In the case of a program which is an organization, the individual designated as director, managing director, or otherwise vested with authority to act as chief executive of the organization.

*Qualified service organization* means a person which:

(a) Provides services to a program, such as data processing, bill collecting, dosage preparation, laboratory analyses, or legal, medical, accounting, or other professional services, or services to prevent or treat child abuse or neglect, including training on nutrition and child care and individual and group therapy, and

(b) Has entered into a written agreement with a program under which that person:

(1) Acknowledges that in receiving, storing, processing or otherwise dealing with any patient records from the programs, it is fully bound by these regulations; and

(2) If necessary, will resist in judicial proceedings any efforts to obtain access to patient records except as permitted by these regulations.

*Records* means any information, whether recorded or not, relating to a patient received or acquired by a federally assisted alcohol or drug program.

*Third party payer* means a person who pays, or agrees to pay, for diagnosis or treatment furnished to a patient on the basis of a contractual relationship with the patient or a member of his family or on the basis of the patient's eligibility for Federal, State, or local governmental benefits.

*Treatment* means the management and care of a patient suffering from alcohol or drug abuse, a condition which is identified as having been caused by that abuse, or both, in order to reduce or eliminate the adverse effects upon the patient.

*Undercover agent* means an officer of any Federal, State, or local law enforcement agency who enrolls in or becomes an employee of a program for the purpose of investigating a suspected violation of law or who pursues that purpose after enrolling or becoming employed for other purposes.

**§ 2.12 Applicability.**

(a) *General*—(1) *Restrictions on disclosure.* The restrictions on disclosure in these regulations apply to any information, whether or not recorded, which:

(i) Would identify a patient as an alcohol or drug abuser either directly, by reference to other publicly available information, or through verification of such an identification by another person; and

(ii) Is drug abuse information obtained by a federally assisted drug abuse program after March 20, 1972, or is alcohol abuse information obtained by a federally assisted alcohol abuse program after May 13, 1974 (or if obtained before the pertinent date, is maintained by a federally assisted alcohol or drug abuse program after that date as part of an ongoing treatment episode which extends past that date) for the purpose of treating alcohol or drug abuse, making a diagnosis for that treatment, or making a referral for that treatment.

(2) *Restriction on use.* The restriction on use of information to initiate or substantiate any criminal charges against a patient or to conduct any criminal investigation of a patient (42 U.S.C. 290ee-3(c), 42 U.S.C. 290dd-3(c)) applies to any information, whether or not recorded which is drug abuse information obtained by a federally assisted drug abuse program after March 20, 1972, or is alcohol abuse information obtained by a federally assisted alcohol abuse program after May 13, 1974 (or if obtained before the pertinent date, is maintained by a federally assisted alcohol or drug abuse program after that date as part of an ongoing treatment episode which extends past that date), for the purpose of treating alcohol or drug abuse, making a diagnosis for the treatment, or making a referral for the treatment.

(b) *Federal assistance.* An alcohol abuse or drug abuse program is considered to be federally assisted if:

(1) It is conducted in whole or in part, whether directly or by contract or otherwise by any department or agency of the United States (but see paragraphs (c)(1) and (c)(2) of this section relating to the Veterans' Administration and the Armed Forces);

(2) It is being carried out under a license, certification, registration, or other authorization granted by any department or agency of the United States including but not limited to:

(i) Certification of provider status under the Medicare program;

(ii) Authorization to conduct methadone maintenance treatment (see 21 CFR 291.505); or

(iii) Registration to dispense a substance under the Controlled Substances Act to the extent the controlled substance is used in the treatment of alcohol or drug abuse;

(3) It is supported by funds provided by any department or agency of the United States by being:

(i) A recipient of Federal financial assistance in any form, including financial assistance which does not directly pay for the alcohol or drug abuse diagnosis, treatment, or referral activities; or

(ii) Conducted by a State or local government unit which, through general or special revenue sharing or other forms of assistance, receives Federal funds which could be (but are not necessarily) spent for the alcohol or drug abuse program; or

(4) It is assisted by the Internal Revenue Service of the Department of the Treasury through the allowance of income tax deductions for contributions to the program or through the granting of tax exempt status to the program.

(c) *Exceptions*—(1) *Veterans' Administration.* These regulations do not apply to information on alcohol and drug abuse patients maintained in connection with the Veterans' Administration provisions of hospital care, nursing home care, domiciliary care, and medical services under title 38, United States Code. Those records are governed by 38 U.S.C. 4132 and regulations issued under that authority by the Administrator of Veterans' Affairs.

(2) *Armed Forces.* These regulations apply to any information described in paragraph (a) of this section which was obtained by any component of the Armed Forces during a period when the patient was subject to the Uniform Code of Military Justice except:

(i) Any interchange of that information within the Armed Forces; and

(ii) Any interchange of that information between the Armed Forces and those components of the Veterans Administration furnishing health care to veterans.

(3) *Communication within a program or between a program and an entity having direct administrative control over that program.* The restrictions on disclosure in these regulations do not apply to communications of information between or among personnel having a need for the information in connection with their duties that arise out of the provision of diagnosis, treatment, or referral for treatment of alcohol or drug abuse if the communications are

(i) Within a program or

(ii) Between a program and an entity that has direct administrative control over the program.

(4) *Qualified Service Organizations.* The restrictions on disclosure in these regulations do not apply to communications between a program and a qualified service organization of information needed by the organization to provide services to the program.

(5) *Crimes on program premises or against program personnel.* The restrictions on disclosure and use in these regulations do not apply to communications from program personnel to law enforcement officers which—

(i) Are directly related to a patient's commission of a crime on the premises of the program or against program personnel or to a threat to commit such a crime; and

(ii) Are limited to the circumstances of the incident, including the patient status of the individual committing or threatening to commit the crime, that individual's name and address, and that individual's last known whereabouts.

(6) *Reports of suspected child abuse and neglect.* The restrictions on disclosure and use in these regulations do not apply to the reporting under State law of incidents of suspected child abuse and neglect to the appropriate State or local authorities. However, the restrictions continue to apply to the original alcohol or drug abuse patient records maintained by the program including their disclosure and use for civil or criminal proceedings which may arise out of the report of suspected child abuse and neglect.

(d) *Applicability to recipients of information*—(1) *Restriction on use of information.* The restriction on the use of any information subject to these regulations to initiate or substantiate any criminal charges against a patient or to conduct any criminal investigation of a patient applies to any person who obtains that information from a federally assisted alcohol or drug abuse program, regardless of the status of the person obtaining the information or of whether the information was obtained in accordance with these regulations. This restriction on use bars, among other things, the introduction of that information as evidence in a criminal proceeding and any other use of the information to investigate or prosecute a patient with respect to a suspected crime. Information obtained by undercover agents or informants (see § 2.17) or through patient access (see § 2.23) is subject to the restriction on use.

(2) *Restrictions on disclosures—Third party payers, administrative entities, and others.* The restrictions on disclosure in these regulations apply to:

(i) Third party payers with regard to records disclosed to them by federally assisted alcohol or drug abuse programs;

(ii) Entities having direct administrative control over programs with regard to information communicated to them by the program under § 2.12(c)(3); and

(iii) Persons who receive patient records directly from a federally assisted alcohol or drug abuse program and who are notified of the restrictions on redisclosure of the records in accordance with § 2.32 of these regulations.

(e) *Explanation of applicability*—(1) *Coverage.* These regulations cover any information (including information on referral and intake) about alcohol and drug abuse patients obtained by a program (as the terms "patient" and "program" are defined in § 2.11) if the program is federally assisted in any manner described in § 2.12(b). Coverage includes, but is not limited to, those treatment or rehabilitation programs, employee assistance programs, programs within general hospitals, school-based programs, and private practitioners who hold themselves out as providing, and provide alcohol or drug abuse diagnosis, treatment, or referral for treatment.

(2) *Federal assistance to program required.* If a patient's alcohol or drug abuse diagnosis, treatment, or referral for treatment is not provided by a program which is federally conducted, regulated or supported in a manner which constitutes Federal assistance under § 2.12(b), that patient's record is not covered by these regulations. Thus, it is possible for an individual patient to benefit from Federal support and not be covered by the confidentiality regulations because the program in which the patient is enrolled is not federally assisted as defined in § 2.12(b). For example, if a Federal court placed an individual in a private for-profit program and made a payment to the program on behalf of that individual, that patient's record would not be covered by these regulations unless the program itself received Federal assistance as defined by § 2.12(b).

(3) *Information to which restrictions are applicable.* Whether a restriction is on use or disclosure affects the type of information which may be available. The restrictions on disclosure apply to any information which would identify a patient as an alcohol or drug abuser. The restriction on use of information to bring criminal charges against a patient for a crime applies

to any information obtained by the program for the purpose of diagnosis, treatment, or referral for treatment of alcohol or drug abuse. (Note that restrictions on use and disclosure apply to recipients of information under § 2.12(d).)

(4) *How type of diagnosis affects coverage.* These regulations cover any record of a diagnosis identifying a patient as an alcohol or drug abuser which is prepared in connection with the treatment or referral for treatment of alcohol or drug abuse. A diagnosis prepared for the purpose of treatment or referral for treatment but which is not so used is covered by these regulations. The following are not covered by these regulations:

(i) Diagnosis which is made solely for the purpose of providing evidence for use by law enforcement authorities; or

(ii) A diagnosis of drug overdose or alcohol intoxication which clearly shows that the individual involved is not an alcohol or drug abuser (e.g., involuntary ingestion of alcohol or drugs or reaction to a prescribed dosage of one or more drugs). [52 FR 21809, June 9, 1987; 52 FR 42061, Nov. 2, 1987]

**§ 2.13 Confidentiality restrictions.**

(a) *General.* The patient records to which these regulations apply may be disclosed or used only as permitted by these regulations and may not otherwise be disclosed or used in any civil, criminal, administrative, or legislative proceedings conducted by any Federal, State, or local authority. Any disclosure made under these regulations must be limited to that information which is necessary to carry out the purpose of the disclosure.

(b) *Unconditional compliance required.* The restrictions on disclosure and use in these regulations apply whether the holder of the information believes that the person seeking the information already has it, has other means of obtaining it, is a law enforcement or other official, has obtained a subpoena, or asserts any other justification for a disclosure or use which is not permitted by these regulations.

(c) *Acknowledging the presence of patients: Responding to requests.* (1) The presence of an identified patient in a facility or component of a facility which is publicly identified as a place where only alcohol or drug abuse diagnosis, treatment, or referral is provided may be acknowledged only if the patient's written consent is obtained in accordance with subpart C of these regulations or if an authorizing court order is entered in accordance with subpart E of these regulations. The regulations permit acknowledgment of the presence of an identified patient in a facility or part of a facility if the facility is not publicy [sic] identified as only an alcohol or drug abuse diagnosis, treatment or referral facility, and if the acknowledgment does not reveal that the patient is an alcohol or drug abuser.

(2) Any answer to a request for a disclosure of patient records which is not permissible under these regulations must be made in a way that will not affirmatively reveal that an identified individual has been, or is being diagnosed or treated for alcohol or drug abuse. An inquiring party may be given a copy of these regulations and advised that they restrict the disclosure of alcohol or drug abuse patient records, but may not be told affirmatively that the regulations restrict the disclosure of the records of an identified patient. The regulations do not restrict a disclosure that an identified individual is not and never has been a patient.

**§ 2.14 Minor patients.**

(a) *Definition of minor.* As used in these regulations the term "minor" means a person who has not attained the age of majority specified in the applicable State law, or if no age of majority is specified in the applicable State law, the age of eighteen years.

(b) *State law not requiring parental consent to treatment.* If a minor patient acting alone has the legal capacity under the applicable State law to apply for and obtain alcohol or drug abuse treatment, any written consent for disclosure authorized under subpart C of these regulations may be given only by the minor patient. This restriction includes, but is not limited to, any disclosure of patient identifying information to the parent or guardian of a minor patient for the purpose of obtaining financial reimbursement. These regulations do not prohibit a program from refusing to provide treatment until the minor patient consents to the disclosure necessary to obtain reimbursement, but refusal to provide treatment may be prohibited under a State or local law requiring the program to furnish the service irrespective of ability to pay.

(c) *State law requiring parental consent to treatment.* (1) Where State law requires consent of a parent, guardian, or other person for a minor to obtain alcohol or drug abuse treatment, any written consent for disclosure authorized under subpart C of these regulations must be given by both the minor and his or her parent, guardian, or other person authorized under State law to act in the minor's behalf.

(2) Where State law requires parental consent to treatment the fact of a minor's application for treatment may be communicated to the, minor's parent, guardian, or other person authorized under State law to act in the minor's behalf only if:

(i) The minor has given written consent to the disclosure in accordance with subpart C of these regulations or

(ii) The minor lacks the capacity to make a rational choice regarding such consent as judged by the program director under paragraph (d) of this section.

(d) *Minor applicant for services lacks capacity for rational choice.* Facts relevant to reducing a threat to the life or physical well being of the applicant or any other individual may be disclosed to the parent, guardian, or other person authorized under State law to act in the minor's behalf if the program director judges that:

(1) A minor applicant for services lacks capacity because of extreme youth or mental or physical condition to make a rational decision on whether to consent to a disclosure under subpart C of these regulations to his or her parent, guardian, or other person authorized under State law to act in the minor's behalf, and

(2) The applicant's situation poses a substantial threat to the life or physical well being of the applicant or any other individual which may be reduced by communicating relevant facts to the minor's parent, guardian, or other person authorized under State law to act in the minor's behalf.

**§ 2.15 Incompetent and deceased patients.**

(a) *Incompetent patients other than minors*—(1) *Adjudication of incompetence.* In the case of a patient who has been adjudicated as lacking the capacity, for any reason other than insufficient age, to manage his or her own affairs, any consent which is required under these regulations may be given by the guardian or other person authorized under State law to act in the patient's behalf.

(2) *No adjudication of incompetency.* For any period for which the program director determines that a patient, other than a minor or one who has been adjudicated incompetent, suffers from a medical condition that prevents knowing or effective action on his or her own behalf, the program director may exercise the right of the patient to consent to a disclosure under subpart C of these regulations for the sole purpose of obtaining payment for services from a third party payer.

(b) *Deceased patients*—(1) *Vital statistics.* These regulations do not restrict the disclosure of patient identifying information relating to the cause of death of a patient under laws requiring the collection of death or other vital statistics or permitting inquiry into the cause of death.

(2) *Consent by personal representative.* Any other disclosure of information identifying a deceased patient as an alcohol or drug abuser is subject to these regulations. If a written consent to the disclosure is required, that consent may be given by an executor, administrator, or other personal representative appointed under applicable State law. If there is no such appointment the consent may be given by the patient's spouse or, if none, by any responsible member of the patient's family.

**§ 2.16 Security for written records.**

(a) Written records which are subject to these regulations must be maintained in a secure room, locked file cabinet, safe or other similar container when not in use; and

(b) Each program shall adopt in writing procedures which regulate and control access to and use of written records which are subject to these regulations.

**§ 2.17 Undercover agents and informants.**

(a) *Restrictions on placement.* Except as specifically authorized by a court order granted under § 2.67 of these regulations, no program may knowingly employ, or enroll as a patient, any undercover agent or informant.

(b) *Restriction on use of information.* No information obtained by an undercover agent or informant, whether or not that undercover agent or informant is placed in a program pursuant to an authorizing court order, may be used to criminally investigate or prosecute any patient.

[52 FR 21809, June 9, 1987; 52 FR 42061, Nov. 2, 1987]

**§ 2.18 Restrictions on the use of identification cards.**

No person may require any patient to carry on his or her person while away from the program premises any card or other object which would identify the patient as an alcohol or drug abuser. This section does not prohibit a person from requiring patients to use or carry cards or other identification objects on the premises of a program.

**§ 2.19 Disposition of records by discontinued programs.**

(a) *General.* If a program discontinues operations or is taken over or acquired by another program, it must purge patient identifying information from its records or destroy the records unless—

(1) The patient who is the subject of the records gives written consent (meeting the requirements of § 2.31) to a transfer of the records to the acquiring program or to any other program designated in the consent (the manner of obtaining this consent must minimize the likelihood of a disclosure of patient identifying information to a third party); or

(2) There is a legal requirement that the records be kept for a period specified by law which does not expire until after the discontinuation or acquisition of the program.

(b) *Procedure where retention period required by law.* If paragraph (a)(2) of this section applies, the records must be:

(1) Sealed in envelopes or other containers labeled as follows: "Records of [insert name of program] required to be maintained under [insert citation to statute, regulation, court order or other legal authority requiring that records be kept] until a date not later than [insert appropriate date]"; and

(2) Held under the restrictions of these regulations by a responsible person who must, as soon as practicable after the end of the retention period specified on the label, destroy the records.

**§ 2.20 Relationship to State laws.**

The statutes authorizing these regulations (42 U.S.C. 290ee-3 and 42 U.S.C. 290dd-3) do not preempt the field of law which they cover to the exclusion of all State laws in that field. If a disclosure permitted under these regulations is prohibited under State law, neither these regulations nor the authorizing statutes may be construed to authorize any violation of that State law. However, no State law may either authorize or compel any disclosure prohibited by these regulations.

**§ 2.21 Relationship to Federal statutes protecting research subjects against compulsory disclosure of their identity.**

(a) *Research privilege description.* There may be concurrent coverage of patient identifying information by these regulations and by administrative action taken under: Section 303(a) of the Public Health Service Act (42 U.S.C. 242a(a) and the implementing regulations at 42 CFR part 2a); [sic] or section 502(c) of the Controlled Substances Act (21 U.S.C. 872(c) and the implementing regulations at 21 CFR 1316.21). These "research privilege" statutes confer on the Secretary of Health and Human Services and on the Attorney General, respectively, the power to authorize researchers conducting certain types of research to withhold from all persons not connected with the research the names and other identifying information concerning individuals who are the subjects of the research.

(b) *Effect of concurrent coverage.* These regulations restrict the disclosure and use of information about patients, while administrative action taken under the research privilege statutes and implementing regulations protects a person engaged in applicable research from being compelled to disclose any identifying characteristics of the individuals who are the subjects of that research. The issuance under subpart E of these regulations of a court order authorizing a disclosure of information about a patient does not affect an exercise of authority under these research privilege statutes. However, the research privilage [sic] granted under 21 CFR 291.505(g) to treatment programs using methadone for maintenance treatment does not protect from compulsory disclosure any imformation [sic] which is permitted to be disclosed under those regulations. Thus, if a court order entered in accordance with subpart E of these regulations authorizes a methadone maintenance treatment program to disclose certain information about its patients, that program may not invoke the research privilege under 21 CFR 291.505(g) as a defense to a subpoena for that information.

**§ 2.22 Notice to patients of Federal confidentiality requirements.**

(a) *Notice required.* At the time of admission or as soon threreafter [sic] as the patient is capable of rational communication. [sic] each program shall:

(1) Communicate to the patient that Federal law and regulations protect the confidentiality of alcohol and drug abuse patient records; and

(2) Give to the patient a summary in writing of the Federal law and regulations.

(b) *Required elements of written summary.* The written summary of the Federal law and regulations must include:

(1) A general description of the limited circumstances under which a program may acknowledge that an individual is present at a facility or disclose outside the program information identifying a patient as an alcohol or drug abuser.

(2) A statement that violation of the Federal law and regulations by a program is a crime and that suspected violations may be reported to appropriate authorities in accordance with these regulations.

(3) A statement that information related to a patient's commission of a crime on the premises of the program or against personnel of the program is not protected.

(4) A statement that reports of suspected child abuse and neglect made under State law to appropriate State or local authorities are not protected.

(5) A citation to the Federal law and regulations.

(c) *Program options.* The program may devise its own notice or may use the sample notice in paragraph (d) to comply with the requirement to provide the patient with a summary in writing of the Federal law and regulations. In addition, the program may include in the written summary information concerning State law and any program policy not inconsistent with State and Federal law on the subject of confidentiality of alcohol and drug abuse patient records.

(d) *Sample notice.*

CONFIDENTIALITY OF ALCOHOL AND DRUG ABUSE PATIENT RECORDS

The confidentiality of alcohol and drug abuse patient records maintained by this program is protected by Federal law and regulations. Generally, the program may not say to a person outside the program that a patient attends the program, or disclose any information identifying a patient as an alcohol or drug abuser Unless:

(1) The patient consents in writing:

(2) The disclosure is allowed by a court order; or

(3) The disclosure is made to medical personnel in a medical emergency or to qualified personnel for research, audit, or program evaluation.

Violation of the Federal law and regulations by a program is a crime. Suspected violations may be reported to appropriate authorities in accordance with Federal regulations.

Federal law and regulations do not protect any information about a crime committed by a patient either at the program or against any person who works for the program or about any threat to commit such a crime.

Federal laws and regulations do not protect any information about suspected child abuse or neglect from being reported under State law to appropriate State or local authorities. (See 42 U.S.C. 290dd-3 and 42 U.S.C. 290ee-3 for Federal laws and 42 CFR part 2 for Federal regulations.) (Approved by the Office of Management and Budget under control number 0930-0099)

**§ 2.23 Patient access and restrictions on use.**

(a) *Patient access not prohibited.* These regulations do not prohibit a program from giving a patient access to his or her own records, including the opportunity to inspect and copy any records that the program maintains about the patient. The program is not required to obtain a patient's written consent or other authorization under these regulations in order to provide such access to the patient.

(b) *Restriction on use of information.* Information obtained by patient access to his or her patient record is subject to the restriction on use of his information to initiate or substantiate any criminal charges against the patient or to conduct any criminal investigation of the patient as provided for under § 2.12(d)(1).

## Subpart C—Disclosures With Patient's Consent

**§ 2.31 Form of written consent.**

(a) *Required elements.* A written consent to a disclosure under these regulations must include:

(1) The specific name or general designation of the program or person permitted to make the disclosure.

(2) The name or title of the individual or the name of the organization to which disclosure is to be made.

(3) The name of the patient.

(4) The purpose of the disclosure.

(5) How much and what kind of information is to be disclosed.

(6) The signature of the patient and, when required for a patient who is a minor, the signature of a person authorized to give consent under § 2.14; or, when required for a patient who is incompetent or deceased, the signature of a person authorized to sign under § 2.15 in lieu of the patient.

(7) The date on which the consent is signed.

(8) A statement that the consent is subject to revocation at any time except to the extent that the program or person which is to make the disclosure has already acted in reliance on it. Acting in reliance includes the provision of treatment services in reliance on a valid consent to disclose information to a third party payer.

(9) The date, event, or condition upon which the consent will expire if not revoked before. This date, event, or condition must insure that the consent will last no longer than reasonably necessary to serve the purpose for which it is given.

(b) *Sample consent form.* The following form complies with paragraph (a) of this section, but other elements may be added.

1. I (name of patient) ☐ Request ☐ Authorize:
2. (name or general designation of program which is to make the disclosure)

3. To disclose: (kind and amount of information to be disclosed)

4. To: (name or title of the person or organization to which disclosure is to be made)

5. For (purpose of the disclosure)

6. Date (on which this consent is signed)

7. Signature of patient

8. Signature of parent or guardian (where required)

9. Signature of person authorized to sign in lieu of the patient (where required)

10. This consent is subject to revocation at any time except to the extent that the program which is to make the disclosure has already taken action in reliance on it. If not previously revoked, this consent will terminate upon: (specific date, event, or condition)

(c) *Expired, deficient, or false consent.* A disclosure may not be made on the basis of a consent which:
(1) Has expired:
(2) On its face substantially fails to conform to any of the requirements set forth in paragraph (a) of this section;
(3) Is known to have been revoked; or
(4) Is known, or through a reasonable effort could be known, by the person holding the records to be materially false.

(Approved by the Office of Management and Budget under control number 0930-0099)

**§ 2.32 Prohibition on redisclosure.**

*Notice to accompany disclosure.* Each disclosure made with the patient's written consent must be accompanied by the following written statement:

This information has been disclosed to you from records protected by Federal confidentiality rules (42 CFR part 2). The Federal rules prohibit you from making any further disclosure of this information unless further disclosure is expressly permitted by the written consent of the person to whom it pertains or as otherwise permitted by 42 CFR part 2. A general authorization for the release of medical or other information is NOT sufficient for this purpose. The Federal rules restrict any use of the information to criminally investigate or prosecute any alcohol or drug abuse patient.

[52 FR 21809, June 9, 1987; 52 FR 41997, Nov. 2, 1987]

**§ 2.33 Disclosures permitted with written consent.**

If a patient consents to a disclosure of his or her records under § 2.31, a program may disclose those records in accordance with that consent to any individual or organization named in the consent, except that disclosures to central registries and in connection with criminal justice referrals must meet the requirements of §§ 2.34 and 2.35, respectively.

**§ 2.34 Disclosures to prevent multiple enrollments in detoxification and maintenance treatment programs.**

(a) *Definitions.* For purposes of this section:

*Central registry* means an organization which obtains from two or more member programs patient identifying information about individuals applying for maintenance treatment or detoxification treatment for the purpose of avoiding an individual's concurrent enrollment in more than one program.

*Detoxification treatment* means the dispensing of a narcotic drug in decreasing doses to an individual in order to reduce or eliminate adverse physiological or psychological effects incident to withdrawal from the sustained use of a narcotic drug.

*Maintenance treatment* means the dispensing of anarcotic drug in the treatment of an individual for dependence upon heroin or other morphine-like drugs.

*Member program* means a detoxification treatment or maintenance treatment or maintenance treatment program which reports patient identifying information to a central registry and which is in the same State as that central registry or is not more than 125 miles from any border of the State in which the central registry is located.

(b) *Restrictions on disclosure.* A program may disclose patient records to a central registry or to any detoxification or maintenance treatment program not more than 200 miles away for the purpose of preventing the multiple enrollment of a patient only if:

(1) The disclosure is made when:

(i) The patient is accepted for treatment;

(ii) The type or dosage of the drug is changed; or

(iii) The treatment is interrupted, resumed or terminated.

(2) The disclosure is limited to:

(i) Patient identifying information:

(ii) Type and dosage of the drug; and

(iii) Relevant dates.

(3) The disclosure is made with the patient's written consent meeting the requirements of § 2.31, except that:

(i) The consent must list the name and address of each central registry and each known detoxification or maintenance treatment program to which a disclosure will be made; and

(ii) The consent may authorize a disclosure to any detoxification or maintenance treatment program established within 200 miles of the program after the consent is given without naming any such program.

(c) *Use of information limited to prevention of multiple enrollments.* A central registry and any detoxification or maintenance treatment program to which information is disclosed to prevent multiple enrollments may not redisclose or use patient identifying information for any purpose other than the prevention of multiple enrollments unless authorized by a court order under subpart E of these regulations.

(d) *Permitted disclosure by a central registry to prevent a multiple enrollment.* When a member program asks a central registry if an identified patient is enrolled in another member program and the registry determines that the patient is so enrolled, the registry may disclose—

(1) The name, address, and telephone number of the member program(s) in which the patient is already enrolled to the inquiring member program; and

(2) The name, address, and telephone number of the inquiring member program to the member program(s) in which the patient is already enrolled. The member programs may communicate as necessary to verify that no error has been made and to prevent or eliminate any multiple enrollment.

(e) *Permitted disclosure by a detoxification or maintenance treatment program to prevent a multiple enrollment.* A detoxification or maintenance treatment program which has received a disclosure under this section and has determined that the patient is already enrolled may communicate as necessary with the program making the disclosure to verify that no error has been made and to prevent or eliminate any multiple enrollment.

**§ 2.35 Disclosures to elements of the criminal justice system which have referred patients.**

(a) A program may disclose information about a patient to those persons within the criminal justice system which have made participation in the program a condition of the disposition of any criminal proceedings against the patient or of the patient's parole or other release from custody if:

(1) The disclosure is made only to those individuals within the criminal justice system who have a need for the information in connection with their duty to monitor the patient's progress (e.g., a prosecuting attorney who is withholding charges against the patient, a court granting pretrial or post-trial release, probation or parole, officers responsible for supervision of the patient); and

(2) The patient has signed a written consent meeting the requirements of § 2.31 (except paragraph (a)(8) which is inconsistent with the revocation provisions of paragraph (c) of this section) and the requirements of paragraphs (b) and (c) of this section.

(b) *Duration of consent.* The written consent must state the period during which it remains in effect. This period must be reasonable, taking into account:

(1) The anticipated length of the treatment;

(2) The type of criminal proceeding involved, the need for the information in connection with the final disposition of that proceeding, and when the final disposition will occur; and

(3) Such other factors as the program, the patient, and the person(s) who will receive the disclosure consider pertinent.

(c) *Revocation of consent.* The written consent must state that it is revocable upon the passage of a specified amount of time or the occurrence of a specified, ascertainable event. The time or occurrence upon which consent becomes revocable may be no later than the final disposition of the conditional release or other action in connection with which consent was given.

(d) *Restrictions on redisclosure and use.* A person who receives patient information under this section may redisclose and use it only to carry out that person's official duties with regard to the patient's conditional release or other action in connection with which the consent was given.

## Subpart D—Disclosure Without Patient Consent

### § 2.51 Medical emergencies.

(a) *General Rule.* Under the procedures required by paragraph (c) of this section, patient identifying information may be disclosed to medical personnel who have a need for information about a patient for the purpose of treating a condition which poses an immediate threat to the health of any individual and which requires immediate medical intervention.

(b) *Special Rule.* Patient identifying information may be disclosed to medical personnel of the Food and Drug Administration (FDA) who assert a reason to believe that the health of any individual may be threatened by an error in the manufacture, labeling, or sale of a product under FDA jurisdiction, and that the information will be used for the exclusive purpose of notifying patients or their physicians of potential dangers.

(c) *Procedures.* Immediately following disclosure, the program shall document the disclosure in the patient's records, setting forth in writing:

(1) The name of the medical personnel to whom disclosure was made and their affiliation with any health care facility;

(2) The name of the individual making the disclosure;

(3) The date and time of the disclosure; and

(4) The nature of the emergency (or error, if the report was to FDA).

(Approved by the Office of Management and Budget under control number 0930-0099)

### § 2.52 Research activities.

(a) Patient identifying information may be disclosed for the purpose of conducting scientific research if the program director makes a determination that the recipient of the patient identifying information:

(1) Is qualified to conduct the research;

(2) Has a research protocol under which the patient identifying information:

(i) Will be maintained in accordance with the security requirements of § 2.16 of these regulations (or more stringent requirements); and

(ii) Will not be redisclosed except as permitted under paragraph (b) of this section; and

(3) Has provided a satisfactory written statement that a group of three or more individuals who are independent of the research project has reviewed the protocol and determined that:

(i) The rights and welfare of patients will be adequately protected; and

(ii) The risks in disclosing patient identifying information are outweighed by the potential benefits of the research.

(b) A person conducting research may disclose patient identifying information obtained under paragraph (a) of this section only back to the program from which that information was obtained and may not identify any individual patient in any report of that research or otherwise disclose patient identities.

[52 FR 21809, June 9, 1987, as amended at 52 FR 41997, Nov. 2, 1987]

### § 2.53 Audit and evaluation activities

(a) *Records not copied or removed.* If patient records are not copied or removed, patient identifying information may be disclosed in the course of a review of records on program premises to any person who agrees in writing to comply with the limitations on redisclosure and use in paragraph (d) of this section and who:

(1) Performs the audit or evaluation activity on behalf of:

(i) Any Federal, State, or local governmental agency which provides financial assistance to the program or is authorized by law to regulate its activities; or

(ii) Any private person which provides financial assistance to the program, which is a third party payer covering patients in the program, or which is a peer review organization performing a utilization or quality control review; or

(2) Is determined by the program director to be qualified to conduct the audit or evaluation activities.

(b) *Copying or removal of records.* Records containing patient identifying information may be copied or removed from program premises by any person who:

(1) Agrees in writing to:

(i) Maintain the patient identifying information in accordance with the security requirements provided in § 2.16 of these regulations (or more stringent requirements);

(ii) Destroy all the patient identifying information upon completion of the audit or evaluation; and

(iii) Comply with the limitations on disclosure and use in paragraph (d) of this section;

and

(2) Performs the audit or evaluation activity on behalf of:

(i) Any Federal, State, or local governmental agency which provides financial assistance to the program or is authorized by law to regulate its activities; or

(ii) Any private person which provides financial assistance to the program, which is a third part [sic] payer covering patients in the program, or which is a peer review organization performing a utilization or quality control review.

(c) *Medicare or Medicaid audit or evaluation.* (1) For purposes of Medicare or Medicaid audit or evaluation under this section, audit or evaluation includes a civil or administrative investigation of the program by any Federal, State, or local agency responsible for oversight of the Medicare or Medicaid program and includes administrative enforcement, against the program by the agency, of any remedy authorized by law to be imposed as a result of the findings of the investigation.

(2) Consistent with the definition of program in § 2.11, program includes an employee of, or provider of medical services under, the program when the employee or provider is the subject of a civil investigation or administrative remedy, as those terms are used in paragraph (c)(1) of this section.

(3) If a disclosure to a person is authorized under this section for a Medicare or Medicaid audit or evaluation, including a civil investigation or administrative remedy, as those terms are used in paragraph (c)(1) of this section, then a peer review organization which obtains the information under paragraph (a) or (b) may disclose the information to that person but only for purposes of Medicare or Medicaid audit or evaluation.

(4) The provisions of this paragraph do not authorize the agency, the program, or any other person to disclose or use patient identifying information obtained during the audit or evaluation for any purposes other than those necessary to complete the Medicare or Medicaid audit or evaluation activity as specified in this paragraph.

(d) *Limitations on disclosure and use.* Except as provided in paragraph (c) of this section, patient identifying information disclosed under this section may be disclosed only back to the program from which it was obtained and used only to carry out an audit or evaluation purpose or two investigate or prosecute criminal or other activities, as authorized by a court order entered under § 2.66 of these regulations.

## Subpart E—Court Orders Authorizing Disclosure and Use

### § 2.61 Legal effect of order

(a) *Effect.* An order of a court of competent jurisdiction entered under this subpart is a unique kind of court order. Its only purpose is to authorize a disclosure or use of patient information which would otherwise be prohibited by 42 U.S.C. 290ee-3, 42 U.S.C. 290dd-3 and these regulations. Such an order does not compel disclosure. A subpoena or a similar legal mandate must be issued in order to compel disclosure. This mandate may be entered at the same time as and accompany an authorizing court order entered under these regulations.

(b) *Examples.* (1) A person holding records subject to these regulations receives a subpoena for those records: a response to the subpoena is not permitted under the regulations unless an authorizing court order is entered. The person may not disclose the records in response to the subpoena unless a court of competent jurisdiction enters an authorizing order under these regulations.

(2) An authorizing court order is entered under these regulations, but the person authorized does not want to make the disclosure. If there is no subpoena or other compulsory process or a subpoena for the records has expired or been quashed, that person may refuse to make the disclosure. Upon the entry of a valid subpoena or other compulsory process the person authorized to disclose must disclose, unless there is a valid legal defense to the process other than the confidentiality restrictions of these regulations.

[52 FR 21809, June 9, 1987; 52 FR 42061, Nov. 2, 1987]

**§ 2.62 Order not applicable to records disclosed without consent to researchers, auditors and evaluators.**

A court order under these regulations may not authorize qualified personnel, who have received patient identifying information without consent for the purpose of conducting research, audit or evaluation, to disclose that information or use it to conduct any criminal investigation or prosecution of a patient. However, a court order under § 2.66 may authorize disclosure and use of records to investigate or prosecute qualified personnel holding the records.

**§ 2.63 Confidential communications.**

(a) A court order under these regulations may authorize disclosure of confidential communications made by a patient to a program in the course of diagnosis, treatment, or referral for treatment only if:

(1) The disclosure is necessary to protect against an existing threat to life or of serious bodily injury, including circumstances which constitute suspected child abuse and neglect and verbal threats against third parties;

(2) The disclosure is necessary in connection with investigation or prosecution of an extremely serious crime, such as one which directly threatens loss of life or serious bodily injury, including homicide, rape, kidnapping, armed robbery, assault with a deadly weapon, or child abuse and neglect; or

(3) The disclosure is in connection with litigation or an administrative proceeding in which the patient offers testimony or other evidence pertaining to the content of the confidential communications.

(b) [Reserved]

**§ 2.64 Procedures and criteria for orders authorizing disclosures for noncriminal purposes.**

(a) *Application.* An order authorizing the disclosure of patient records for purposes other than criminal investigation or prosecution may be applied for by any person having a legally recognized interest in the disclosure which is sought. The application may be filed separately or as part of a pending civil action in which it appears that the patient records are needed to provide evidence. An application mst [sic] use a fictitious name, such as John Doe, to refer to any patient and may not contain or otherwise disclose any patient identifying information unless the patient is the applicant or has given a written consent (meeting the requirements of these regulations) to disclosure or the court has ordered the record of the proceeding sealed from public scrutiny.

(b) *Notice.* The patient and the person holding the records from whom disclosure is sought must be given:

(1) Adequate notice in a manner which will not disclose patient identifying information to other persons; and

(2) An opportunity to file a written response to the application, or to appear in person, for the limited purpose of providing evidence on the statutory and regulatory criteria for the issuance of the court order.

(c) *Review of evidence: Conduct of hearing.* Any oral argument, review of evidence, or hearing on the application must be held in the judge's chambers or in some manner which ensures that patient identifying information is not disclosed to anyone other than a party to the proceeding, the patient, or the person holding the record, unless the patient requests an open hearing in a manner which meets the written consent requirements of these regulations. The proceeding may include an examination by the judge of the patient records referred to in the application.

(d) *Criteria for entry of order.* An order under this section may be entered only if the court determines that good cause exists. To make this determination the court must find that:

(1) Other ways of obtaining the information are not available or would not be effective; and

(2) The public interest and need for the disclosure outweigh the potential injury to the patient, the physician-patient relationship and the treatment services.

(e) *Content of order.* An order authorizing a disclosure must:

(1) Limit disclosure to those parts of the patient's record which are essential to fulfill the objective of the order.

(2) Limit disclosure to those persons whose need for information is the basis for the order; and

(3) Include such other measures as are necessary to limit disclosure for the protection of the patient, the physician-patient relationship and the treatment services; for example, sealing from public scrutiny the record of any proceeding for which disclosure of a patient's record has been ordered.

**§ 2.65 Procedures and criteria for orders authorizing disclosure and use of records to criminally investigate or prosecute patients.**

(a) *Application.* An order authorizing the disclosure or use of patient records to criminally investigate or prosecute a patient may be applied for by the person holding the records or by any person conducting investigative or prosecutorial activities with respect to the enforcement of criminal laws. The application may be filed separately, as part of an application for a subpoena or other compulsory process, or in a pending criminal action. An application must use a fictitious name such

as John Doe, to refer to any patient and may no contain or otherwise disclose patient identifying information unless the court has ordered the record of the proceeding sealed from public scrutiny.

(b) *Notice and hearing.* Unless an order under § 2.66 is sought with an order under this section, the person holding the records must be given:

(1) Adequate notice (in a manner which will not disclose patient identifying information to third parties) of an application by a person performing a law enforcement function;

(2) An opportunity to appear and be heard for the limited purpose of providing evidence on the statutory and regulatory criteria for the issuance of the court order; and

(3) An opportunity to be represented by counsel independent of counsel for an applicant who is a person performing a law enforcement function.

(c) *Review of evidence: Conduct of hearings.* Any oral argument, review of evidence, or hearing on the application shall be held in the judge's chambers or in some other manner which ensures that patient identifying information is not disclosed to anyone other than a party to the proceedings, the patient, or the person holding the records. The proceeding may include an examination by the judge of the patient records referred to in the application.

(d) *Criteria.* A court may authorize the disclosure and use of patient records for the purpose of conducting a criminal investigation or prosecution of a patient only if the court finds that all of the following criteria are met:

(1) The crime involved is extremely serious, such as one which causes or directly threatens loss of life or serious bodily injury including homicide, rape, kidnapping, armed robbery, assault with a deadly weapon, and child abuse and neglect.

(2) There is a reasonable likelihood that the records will disclose information of substantial value in the investigation or prosecution.

(3) Other ways of obtaining the information are not available or would not be effective.

(4) The potential injury to the patient, to the physician-patient relationship and to the ability of the program to provide services to other patients is outweighed by the public interest and the need for the disclosure.

(5) If the applicant is a person performing a law enforcement function that:

(i) The person holding the records has been afforded the opportunity to be represented by independent counsel; and

(ii) Any person holding the records which is an entity within Federal, State, or local government has in fact been represented by counsel independent of the applicant.

(e) *Content of order.* Any order authorizing a disclosure or use of patient records under this section must:

(1) Limit disclosure and use to those parts of the patient's record which are essential to fulfill the objective of the order;

(2) Limit disclosure to those law enforcement and prosecutorial officials who are responsible for, or are conducting, the investigation or prosecution, and limit their use of the records to investigation and prosecution of extremely serious crime or suspected crime specified in the application; and

(3) Include such other measures as are necessary to limit disclosure and use to the fulfillment of only that public interest and need found by the court.

[52 FR 21809, June 9, 1987; 52 FR 42061, Nov. 2, 1987]

**§ 2.66 Procedures and criteria for orders authorizing disclosure and use of records to investigate or prosecute a program or the person holding the records.**

(a) *Application.*

(1) An order authorizing the disclosure or use of patient records to criminally or administratively investigate or prosecute a program or the person holding the records (or employees or agents of that program or person) may be applied for by any administrative, regulatory, supervisory, investigative, law enforcement, or prosecutorial agency having jurisdiction over the program's or person's activities.

(2) The application may be filed separately or as part of a pending civil or criminal action against a program or the person holding the records (or agents or employees of the program or person) in which it appears that the patient records are needed to provide material evidence. The application must use a fictitious name, such as John Doe, to refer to any patient and may not contain or otherwise disclose any patient identifying information unless the court has ordered the record of the proceeding sealed from public scrutiny or the patient has given a written consent (meeting the requirements of § 2.31 of these regulations) to that disclosure.

(b) *Notice not required.* An application under this section may, in the discretion of the court, be granted without notice. Although no express notice is required to the program, to the person holding the records, or to any patient whose records are to be disclosed, upon implementation of an order so granted any of the above persons must be afforded an opportunity to seek

revocation or amendment of that order, limited to the presentation of evidence on the statutory and regulatory criteria for the issuance of the court order.

(c) *Requirements for order.* An order under this section must be entered in accordance with, and comply with the requirements of, paragraphs (d) and (e) of § 2.64 of these regulations.

(d) *Limitations on disclosure and use of patient identifying information:* (1) An order entered under this section must require the deletion of patient identifying information from any documents made available to the public.

(2) No information obtained under this section may be used to conduct any investigation or prosecution of a patient, or be used as the basis for an application for an order under § 2.65 of these regulations.

**§ 2.67 Orders authorizing the use of undercover agents and informants to criminally investigate employees or agents of a program.**

(a) *Application.* A court order authorizing the placement of an undercover agent or informant in a program as an employee or patient may be applied for by any law enforcement or prosecutorial agency which has reason to believe that employees or agents of the program are engaged in criminal misconduct.

(b) *Notice.* The program director must be given adequate notice of the application and an opportunity to appear and be heard (for the limited purpose of providing evidence on the statutory and regulatory criteria for the issuance of the court order), unless the application asserts a belief that:

(1) The program director is involved in the criminal activities to be investigated by the undercover agent or informant; or

(2) The program director will intentionally or unintentionally disclose the proposed placement of an undercover agent or informant to the employees or agents who are suspected of criminal activities.

(c) *Criteria.* An order under this section may be entered only if the court determines that good cause exists. To make this determination the court must find:

(1) There is reason to believe that an employee or agent of the program is engaged in criminal activity;

(2) Other ways of obtaining evidence of this criminal activity are not available or would not be effective; and

(3) The public interest and need for the placement of an undercover agent or informant in the program outweigh the potential injury to patients of the program, physician patient relationships and the treatment services.

(d) *Content of order.* An order authorizing the placement of an undercover agent or informant in a program must:

(1) Specifically authorize the placement of an undercover agent or an informant;

(2) Limit the total period of the placement to six months;

(3) Prohibit the undercover agent or informant from disclosing any patient identifying information obtained from the placement except as necessary to criminally investigate or prosecute employees or agents of the program; and

(4) Include any other measures which are appropriate to limit any potential disruption of the program by the placement and any potential for a real or apparent breach of patient confidentiality; for example, sealing from public scrutiny the record of any proceeding for which disclosure of a patient's record has been ordered.

(e) *Limitation on use of information.* No information obtained by an undercover agent or informant placed under this section may be used to criminally investigate or prosecute any patient or as the basis for an application for an order under § 2.65 of these regulations.

## PART 2a—PROTECTION OF IDENTITY—RESEARCH SUBJECTS

Sec.



AUTHORITY: Sec. 3(a), Pub. L. 91-513 as amended by sec. 122(b), Pub. L. 93-282; 84 Stat. 1241 (42 U.S.C. 242a(a)), as amended by 88 Stat. 132.

SOURCE: 44 FR 20384, Apr. 4, 1979, unless otherwise noted.

**§ 2a.1 Applicability.**

(a) Section 303(a) of the Public Health Service Act (42 U.S.C. 242a(a) provides that "[t]he Secretary [of Health and Human Services] may authorize persons engaged in research on mental health, including research on the use and effect of alcohol and other psychoactive drugs, to protect the privacy of individuals who are the subject of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals." The regulations in this part establish procedures under which any person engaged in research on mental health including research on the use and effect of alcohol and other psychoactive drugs (whether or not the research is federally funded) may, subject to the exceptions set forth in paragraph (b) of this section, apply for such an authorization of confidentiality.

(b) These regulations do not apply to:

(1) Authorizations of confidentiality for research requiring an Investigational New Drug exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or to approved new drugs, such as methadone, requiring continuation of long-term studies, records, and reports. Attention is called to 21 CFR 291.505(g) relating to authorizations of confidentiality for patient records maintained by methadone treatment programs.

(2) Authorizations of confidentiality for research which are related to law enforcement activities or otherwise within the purview of the Attorney General's authority to issue authorizations of confidentiality pursuant to section 502(c) of the Controlled Substances Act (21 U.S.C. 872(c) and 21 CFR 1316.21.

(c) The Secretary's regulations on confidentiality of alcohol and drug abuse patient records (42 CFR part 2) and the regulations of this part may, in some instances, concurrently cover the same transaction. As explained in 42 CFR 2.24 and 2.24-1, 42 CFR part 2 restricts voluntary disclosures of information from applicable patient records while a Confidentiality Certificate issued pursuant to the regulations of this part protects a person engaged in applicable research from being compelled to disclose identifying characteristics of individuals who are the subject of such research.

**§ 2a.2 Definitions.**

(a) *Secretary* means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom the authority involved has been delegated.

(b) *Person* means any individual, corporation, government, or governmental subdivision or agency, business trust, partnership, association, or other legal entity.

(c) *Research* means systematic study directed toward new or fuller knowledge and understanding of the subject studied. The term includes, but is not limited to, behavioral science studies, surveys, evaluations, and clinical investigations.

(d) *Drug* has the meaning given that term by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(g)(1).

(e) *Controlled drug* means a drug which is included in schedule I, II, III, IV, or V of part B of the Controlled Substances Act (21 U.S.C. 811-812).

(f) *Administer* refers to the direct application of a drug to the body of a human research subject, whether such application be by injection, inhalation, ingestion, or any other means, by (1) a qualified person engaged in research (or, in his or her presence, by his or her authorized agent), or (2) a research subject in accordance with instructions of a qualified person engaged in research, whether or not in the presence of a qualified person engaged in research.

(g) *Identifying characteristics* refers to the name, address, any identifying number, fingerprints, voiceprints, photographs or any other item or combination of data about a research subject which could reasonably lead directly or indirectly by reference to other information to identification of that research subject.

(h) *Psychoactive drug* means, in addition to alcohol, any drug which has as its principal action an effect on thought, mood, or behavior.

**§ 2a.3 Application; coordination.**

(a) Any person engaged in (or who intends to engage in) the research to which this part applies, who desires authorization to withhold the names and other identifying characteristics of individuals who are the subject of such research from any person or authority not connected with the conduct of such research may apply to the Office of the Director, National Institute on Drug Abuse, the Office of the Director, National Institute of Mental Health, or the Office of the Director, National Institute on Alcohol Abuse and Alcoholism, 5600 Fishers Lane, Rockville, Maryland 20857 for an authorization of confidentiality.

(b) If there is uncertainty with regard to which Institute is appropriate or if the research project falls within the purview of more than one Institute, an application need be submitted only to one Institute. Persons who are uncertain with regard to the

applicability of these regulations to a particular type of research may apply for an authorization of confidentiality under the regulations of this part to one of the Institutes. Requests which are within the scope of the authorities described in § 2a.1(b) will be forwarded to the appropriate agency for consideration and the person will be advised accordingly.

(c) An application may accompany, precede, or follow the sumission [sic] of a request for DHHS grant or contract assistance, though it is not necessary to request DHHS grant or contract assistance in order to apply for a Confidentiality Certificate. If a person has previously submitted any information required in this part in connection with a DHHS grant or contract, he or she may substitute a copy of information thus submitted, if the information is current and accurate. If a person requests a Confidentiality Certificate at the same time he or she submits an application for DHHS grant or contract assistance, the application for a Confidentiality Certificate may refer to the pertinent section(s) of the DHHS grant or contract application which provide(s) the information required to be submitted under this part. (See §§ 2a.4 and 2a.5.)

(d) A separate application is required for each research project for which an authorization of confidentiality is requested.

**§ 2a.4 Contents of application; in general.**

In addition to any other pertinent information which the Secretary may require, each application for an authorization of confidentiality for a research project shall contain:

(a) The name and address of the individual primarily responsible for the conduct of the research and the sponsor or institution with which he or she is affiliated, if any. Any application from a person affiliated with an institution will be considered only if it contains or is accompanied by documentation of institutional approval. This documentation may consist of a written statement signed by a responsible official of the institution or of a copy of or reference to a valid certification submitted in accordance with 45 CFR part 46.

(b) The location of the research project and a description of the facilities available for conducting the research, including the name and address of any hospital, institution, or clinical laboratory facility to be utilized in connection with the research.

(c) The names, addresses, and summaries of the scientific or other appropriate training and experience of all personnel having major responsibilities in the research project and the training and experience requirements for major positions not yet filled.

(d) An outline of the research protocol for the project including a clear and concise statement of the purpose and rationale of the research project and the general research methods to be used.

(e) The date on which research will begin or has begun and the estimated date for completion of the project.

(f) A specific request, signed by the individual primarily responsible for the conduct of the research, for authority to withhold the names and other identifying characteristics of the research subjects and the reasons supporting such request.

(g) An assurance (1) From persons making application for a Confidentiality Certificate for a research project for which DHHS grant or contract support is received or sought that they will comply with all the requirements of 45 CFR part 46, "Protection of Human Subjects," or

(2) From all other persons making application that they will comply with the informed consent requirements of 45 CFR 46.103(c) and document legally effective informed consent in a manner consistent with the principles stated in 45 CFR 46.110, if it is determined by the Secretary, on the basis of information submitted by the person making application, that subjects will be placed at risk. If a modification of paragraphs (a) or (b) of 45 CFR 46.110 is to be used, as permitted under paragraph (c) of that section, the applicant will describe the proposed modification and submit it for approval by the Secretary.

(h) An assurance that if an authorization of confidentiality is given it will not be represented as an endorsement of the research project by the Secretary or used to coerce individuals to participate in the research project.

(i) An assurance that any person who is authorized by the Secretary to protect the privacy of research subjects will use that authority to refuse to disclose identifying characteristics of research subjects in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to compel disclosure of the identifying characteristics of research subjects.

(j) An assurance that all research subjects who participate in the project during the period the Confidentiality Certificate is in effect will be informed that:

(1) A Confidentiality Certificate has been issued;

(2) The persons authorized by the Confidentiality Certificate to protect the identity of research subjects may not be compelled to identify research subjects in any civil, criminal, administrative, legislative, or other proceedings whether Federal, State, or local;

(3) If any of the following conditions exist the Confidentiality Certificate does not authorize any person to which it applies to refuse to reveal identifying information concerning research subjects:

(i) The subject consents in writing to disclosure of identifying information,

(ii) Release is required by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301) or regulations promulgated thereunder (title 21, Code of Federal Regulations), or

(iii) Authorized personnel of DHHS request identifying information for audit or program evaluation of a research project funded by DHHS or for investigation of DHHS grantees or contractors and their employees or agents carrying out such a project. (See § 2a.7(b));

(4) The Confidentiality Certificate does not govern the voluntary disclosure of identifying characteristics of research subjects;

(5) The Confidentiality Certificate does not represent an endorsement of the research project by the Secretary.

(k) An assurance that all research subjects who enter the project after the termination of the Confidentiality Certificate will be informed that the authorization of confidentiality has ended and that the persons authorized to protect the identity of research subjects by the Confidentiality Certificate may not rely on the Certificate to refuse to disclose identifying characteristics of research subjects who were not participants in the project during the period the Certificate was in effect. (See § 2a.8(c)). [sic]

**§ 2a.5 Contents of application; research projects in which drugs will be administered.**

(a) In addition to the information required by § 2a.4 and any other pertinent information which the Secretary may require, each application for an authorization of confidentiality for a research project which involves the administering of a drug shall contain:

(1) Identification of the drugs to be administered in the research project and a description of the methods for such administration, which shall include a statement of the dosages to be administered to the research subjects;

(2) Evidence that individuals who administer drugs are authorized to do so under applicable Federal and State law; and

(3) In the case of a controlled drug, a copy of the Drug Enforcement Administration Certificate of Registration (BND Form 223) under which the research project will be conducted.

(b) An application for an authorization of confidentiality with respect to a research project which involves the administering of a controlled drug may include a request for exemption of persons engaged in the research from State or Federal prosecution for possession, distribution, and dispensing of controlled drugs as authorized under section 502(d) of the Controlled Substances Act (21 U.S.C. 872(d)) and 21 CFR 1316.22. If the request is in such form, and is supported by such information, as is required by 21 CFR 1316.22, the Secretary will forward it, together with his or her recommendation that such request be approved or disapproved, for the consideration of the Administrator of the Drug Enforcement Administration.

**§ 2a.6 Issuance of Confidentiality Certificates; single project limitation.**

(a) In reviewing the information provided in the application for a Confidentiality Certificate, the Secretary will take into account:

(1) The scientific or other appropriate training and experience of all personnel having major responsibilities in the research project;

(2) Whether the project constitutes bona fide "research" which is within the scope of the regulations of this part; and

(3) Such other factors as he or she may consider necessary and appropriate. All applications for Confidentiality Certificates shall be evaluated by the Secretary through such officers and employees of the Department and such experts or consultants engaged for this purpose as he or she determines to be appropriate.

(b) After consideration and evaluation of an application for an authorization of confidentiality, the Secretary will either issue a Confidentiality Certificate or a letter denying a Confidentiality Certificate, which will set forth the reasons for such denial, or will request additional information from the person making application. The Confidentiality Certificate will include:

(1) The name and address of the person making application;

(2) The name and address of the individual primarily responsible for conducting the research, if such individual is not the person making application;

(3) The location of the research project;

(4) A brief description of the research project;

(5) A statement that the Certificate does not represent an endorsement of the research project by the Secretary;

(6) The Drug Enforcement Administration registration number for the project, if any; and

(7) The date or event upon which the Confidentiality Certificate becomes effective, which shall not be before the later of either the commencement of the research project or the date of issuance of the Certificate, and the date or event upon which the Certificate will expire.

(c) A Confidentiality Certificate is not transferable and is effective only with respect to the names and other identifying characteristics of those individuals who are the subjects of the single research project specified in the Confidentiality Certificate. The recipient of a Confidentiality Certificate shall, within 15 days of any completion or discontinuance of the research project which occurs prior to the expiration date set forth in the Certificate, provide written notification to the

Director of the Institute to which application was made. If the recipient determines that the research project will not be completed by the expiration date set forth in the Confidentiality Certificate he or she may submit a written request for an extension of the expiration date which shall include a justification for such extension and a revised estimate of the date for completion of the project. Upon approval of such a request, the Secretary will issue an amended Confidentiality Certificate.

(d) The protection afforded by a Confidentiality Certificate does not extend to significant changes in the research project as it is described in the application for such Certificate (e.g., changes in the personnel having major responsibilities in the research project, major changes in the scope or direction of the research protocol, or changes in the drugs to be administered and the persons who will administer them). The recipient of a Confidentiality Certificate shall notify the Director of the Institute to which application was made of any proposal for such a significant change by submitting an amended application for a Confidentiality Certificate in the same form and manner as an original application. On the basis of such application and other pertinent information the Secretary will either:

(1) Approve the amended application and issue an amended Confidentiality Certificate together with a Notice of Cancellation terminating original the [sic] Confidentiality Certificate in accordance with § 2a.8; or

(2) Disapprove the amended application and notify the applicant in writing that adoption of the proposed significant changes will result in the issuance of a Notice of Cancellation terminating the original Confidentiality Certificate in accordance with § 2a.8.

**§ 2a.7 Effect of Confidentiality Certificate.**

(a) A Confidentiality Certificate authorizes the withholding of the names and other identifying characteristics of individuals who participate as subjects in the research project specified in the Certificate while the Certificate is in effect. The authorization applies to all persons who, in the performance of their duties in connection with the research project, have access to information which would identify the subjects of the research. Persons so authorized may not, at any time, be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify the research subjects encompassed by the Certificate, except in those circumstances specified in paragraph (b) of this section.

(b) A Confidentiality Certificate granted under this part does not authorize any person to refuse to reveal the name or other identifying characteristics of any research subject in the following circumstances:

(1) The subject (or, if he or she is legally incompetent, his or her guardian) consents, in writing, to the disclosure of such information,

(2) Authorized personnel of DHHS request such information for audit or program evaluation of a research project funded by DHHS or for investigation of DHHS grantees or contractors and their employees or agents carrying out such a project. (See 45 CFR 5.71 far confidentiality standards imposed on such DHHS personnel), or

(3) Release of such information is required by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301) or the regulations promulgated thereunder (title 21, Code of Federal Regulations).

(c) Neither a Confidentiality Certificate nor the regulations of this part govern the voluntary disclosure of identifying characteristics of research subjects.

**§ 2a.8 Termination.**

(a) A Confidentiality Certificate is in effect from the date of its issuance until the effective date of its termination. The effective date of termination shall be the earlier of:

(1) The expiration date set forth in the Confidentiality Certificate; or

(2) Ten days from the date of mailing a Notice of Cancellation to the applicant, pursuant to a determination by the Secretary that the research project has been completed or discontinued or that retention of the Confidentiality Certificate is otherwise no longer necessary or desirable.

(b) A Notice of Cancellation shall include: an identification of the Confidentiality Certificate to which it applies; the effective date of its termination; and the grounds for cancellation. Upon receipt of a Notice of Cancellation the applicant shall return the Confidentiality Certificate to the Secretary.

(c) Any termination of a Confidentiality Certificate pursuant to this section is operative only with respect to the names and other identifying characteristics of individuals who begin their participation as research subjects after the effective date of such termination. (See § 2a.4(k) requiring researchers to notify subjects who enter the project after the termination of the Confidentiality Certificate of termination of the Certificate). The protection afforded by a Confidentiality Certificate is permanent with respect to subjects who participated in research during any time the authorization was in effect.

# Appendix F—Standard Definitions Used During Application and Monitoring

**Definitions Used by FDA (21 CFR § 291.505 (a)):**

*Detoxification Treatment*

The dispensing of a narcotic drug in decreasing doses to an individual to alleviate adverse physiological or psychological effects incident to withdrawal from the continuous or sustained use of narcotic drug and as a method of bringing the individual to a narcotic drug-free state.

*Short-term Detoxification Treatment*

Detoxification treatment for a period not in excess of 30 days.

*Long-term Detoxification Treatment*

Detoxification treatment for a period more than 30 days but not in excess of 180 days..

*Maintenance Treatment*

The dispensing of a narcotic drug, at relatively stable dosage levels, in the treatment of an individual for dependence on heroin or other morphine-like drug. There are two types of maintenance treatment: comprehensive maintenance treatment and interim maintenance treatment.

(i) *Comprehenisve maintenance treatment* is maintenance treatment provided in conjunction with a comprehensive range of appropriate medical and rehabilitative services.

(ii) *Interim maintenance treatment* is maintenance treatment provided in conjunction with appropriate medical services while a patient is awaiting transfer to comprehensive maintenance treatment.

*Medical Director*

A physician licensed to practice medicine in the jurisdiction in which the program is located, who assumes responsibility for the administration of all medical services performed by the narcotic treatment program including ensuring that the program is in compliance with all Federal, State, and local laws and regulations regarding the medical treatment of narcotic addiction with a narcotic drug.

*Medication Unit*

A facility established as part of, but geographically dispersed, i.e., separate from a narcotic treatment program from which licensed private practitioners and community pharmacists : (1) are permitted to administer and dispense a narcotic drug; (2) are authorized to collect samples for drug testing or analysis for narcotic drugs.

*Narcotic Dependent*

An individual who physiologically needs heroin or a morphine-like drug to prevent the onset of signs of withdrawal.

*Narcotic Treatment Program*

An organization (or person, including a private physician) that administers or dispenses a narcotic drug to a narcotic addict for maintenance or detoxification treatment, provides when appropriate and necessary, a comprehensive range of medical and rehabilitative services, is approved by the State authority and the Food and Drug Administration, and is registered with the Drug Enforcement Administration to use a narcotic drug for the treatment of narcotic addiction.

*Program Sponsor*

A person (or a representative of an organization) who is responsible for the operation of a narcotic treatment program and who assumes responsibility for all its employees including any practitioners, agents, or other persons providing services at the program (including its medication units).

*Services*

Medical evaluations, counseling, rehabilitative and other social programs (e.g., vocational and educational guidance, employment placement), which help the patient become a productive member of society.

*State Authority*

The agency designated by the governor or other appropriate official to exercise the responsibility and authority within the State or territory for governing the treatment of narcotic addiction with a narcotic drug.

**Definitions Used by the DEA (21 CFR §1301.02 (a)):**

*Act*

The Controlled Substances Act (84 Stat. 1242; 21 U.S.C. 801) and/or the Controlled Substances Import and Export Act (84 Stat.1285; 21 U.S.C. 951).

*Basic Class*

The controlled substances listed in Schedules I and II including each of the opiates; each of the opium derivatives; each of the hallucinogenic substances; various substances produced directly or indirectly by extraction from substances of vegetable origin, or independently by combination of extraction and chemical synthesis; methamphetamine; amphetamine; phenmetrazine and its salts; methylphenidate; each of the substances having depressant effects on the central nervous system.

*Administration*

The Drug Enforcement Administration

*Compounder*

Any person engaging in maintenance or detoxification treatment who also mixes, prepares, packages, or changes the dosage form of a narcotic drug listed in Schedules II, III, IV or V for use in maintenance or detoxification treatment by another narcotic treatment program.

*Detoxification Treatment*

The dispensing of a narcotic drug in decreasing doses to an individual to alleviate adverse physiological or psychological effects incident to withdrawal from the continuous or sustained use of a narcotic drug and as a method of bringing the individual to a narcotic drug-free state.

*Short-term Detoxification Treatment*

Detoxification treatment for a period not in excess of 30 days.

*Long-term Detoxification Treatment*

Detoxification treatment for a period more than 30 days but not in excess of 180 days.

*Administrator*

The administrator of the Drug enforcement Administration with delegated authority under the Act of the Attorney General (28 CFR § 0.100).

*Hearing*

Any hearing held pursuant to the granting, denial, revocation, or suspension of a registration.

*Maintenance Treatment*

The dispensing for a period in excess of 21 days, of a narcotic drug or narcotic drugs in the treatment of an individual for dependence on heroin or other morphine-like drug.

*Narcotic Treatment Program*

A program engaged in maintenance and/or detoxification treatment with narcotic drugs.

*Register/Registration*

The registration required and permitted by section 303 os the Act (21 U.S.C. 823).

*Registrant*

Any person (individual, corporation, government, or governmental subdivision or agency, business trust, partnership, association, or other legal entity) who is registered.

**Definitions Used by the Public Health Service, HHS for Confidentiality (42 CFR § 2.11):**

*Alcohol Abuse*

The use of an alcoholic beverage which impairs the physical, mental, emotional, or social well-being of the user.

*Drug Abuse*

The use of a psychoactive substance for other than medicinal purposes which impairs the physical, mental, emotional, or social well-being of the user.

*Diagnosis*

Any reference to an individual's alcohol or drug abuse or to a condition which is identified as having been caused by that abuse which is made for the purpose of treatment or referral for treatment.

*Disclose or disclosure*

A communication of patient identifying information, the affirmative verification of another person's communication of patient identifying information, or the communication of any information from the record of a patient who has been identified.

*Informant*

An individual who is a patient or employee of a program or who becomes a patient or employee of a program at the request of a law enforcement agency or official, who at the request of a law enforcement agency or official observes one or more patients or employees of the program for the purpose of reporting the information obtained to the law enforcement agency or official.

*Patient*

Any individual who has applied for or been given diagnosis or treatment for alcohol or drug abuse at a Federally assisted program and includes any individual who, after arrest on a criminal charge, is identified as an alcohol or drug abuser in order to determine that individual's eligibility to participate in a program.

*Patient Identifying Information*

The name, address, social security number, fingerprints, photograph, or similar information by which the identity of a patient can be determined with reasonable accuracy and speed either directly or by reference to other publicly available information. This does not include a number assigned to the patient by a program, if that number does not consist of, or contain numbers which could be used to identify the patient with reasonable accuracy and speed.

*Person*

An individual, partnership, corporation, Federal, State, local government agency, or any other legal entity.

*Program*

A person, as defined above, that provides alcohol or drug abuse diagnosis, treatment, or referral for treatment. For a general medical care facility to be a program it must have an identified unit that provides alcohol, or drug abuse diagnosis, treatment, or referral for treatment or medical personnel or other staff to provide these services.

*Program Director*

For a program that is an individual, the program director is that individual. For a program that is an organization, the individual designated as director, managing director, or otherwise vested with authority to act as chief executive of the organization.

*Qualified Service Organization*

A person that provides services to a program such as data processing, bill collecting, dosage preparation, laboratory analysis, or legal or medical, accounting, or other professional services, or services to prevent or treat child abuse or neglect including training on nutrition and child care, and individual and group therapy, who has entered into a written agreement with a program. In the written agreement, the person acknowledges that receiving, storing, processing, or other dealing with any patient records from the program is bound by regulation and will resist in judicial proceedings any efforts to obtain access to patient records except as permitted by regulations.

*Records*

Any information, whether recorded or not, relating to a patient receiving or acquired by a Federally assisted alcohol or drug program.

*Third Party Payer*

A person who pays, or agrees to pay, for diagnosis or treatment furnished to a patient on the basis of a contractual relationship with the patient or a member of the patient's family or on the basis of the patient's eligibility for Federal, State, or local governmental benefits.

*Treatment*

The management and care of a patient suffering from alcohol or drug abuse, a condition identified as having been caused by that abuse, or both, in order to reduce or eliminate the adverse effects upon the patient.

*Undercover Agent*

An officer of any Federal, State, or local law enforcement agency who enrolls in or becomes an employee of a program for the purpose of investigating a suspected violation of law or who pursues that purpose after enrolling or becoming employed for other purposes.

**Definitions Used by HHS for Research Subjects (45 CFR § 46.101):**

*Department of Agency Head*

The head of any Federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

*Institution*

Any public or private entity or agency including Federal, State, or other agencies.

*Legally Authorized Representative*

Individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

*Research*

A systematic investigation including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

*Research Subject to Regulation*

Research activities for which a Federal department or agency has specific responsibility for regulating as a research activity.

*Human Subject*

A living individual about whom an investigation conducting research obtains data and identifiable private information.

*Intervention*

Both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes. This includes communication or interpersonal contact between investigator and subject.

*Private Information*

Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public. Such information must be individually identifiable in order for obtaining the information to constitute research information involving human subjects.

*IRB*

An institutional review board established in accord with and for the purposes expressed in the research using human subjects policy (45 CFR § 46.103).

*IRB Approval*

The determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

*Minimal Risk*

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

*Certification*

The official notification by the institution to the supporting department or agency that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

# Appendix G—State Authorities

## ALABAMA

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# Appendix I—Investigational New Drug Application Regulations

21 CFR Part 312

proved new drug application, such product is also misbranded under section 502 of the act.

(c) Clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for the OTC uses and containing any active ingredient(s) as specified in paragraph (a) of this section is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs set forth in part 312 of this chapter.

(d) Any OTC drug product that is not in compliance with this section is subject to regulatory action if initially introduced or initially delivered for introduction into interstate commerce after the dates specified in paragraphs (d)(1) and (d)(2) of this section.

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(19) of this section; and

(2) February 10, 1992, for products subject to paragraph (a)(20) of this section.

[55 FR 46919, Nov. 7, 1990; 55 FR 49973, Dec. 3, 1990, as amended at 56 FR 37798, Aug. 8, 1991; 56 FR 46823, Sept. 16, 1991; 56 FR 63568, Dec. 4, 1991; 57 FR 3526, Jan. 30, 1992]

EFFECTIVE DATE NOTE: At 56 FR 63568, Dec. 4, 1991, in § 310.545 paragraph (a)(7) was amended by removing the entry "Methol" including the parenthetical statement and alphabetically adding the entry "Menthol", the introductory text of paragraph (d) was revised, and paragraph (d)(3) was added, effective December 4, 1992. For the convenience of the reader, the text in effect as of December 4, 1992 appears as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

* * * * *

(d) Any OTC drug product that is not in compliance with this section is subject to regulatory action if initially introduced or initially delivered for introduction into interstate commerce after the dates specified in paragraphs (d)(1), (d)(2), and (d)(3) of this section.

* * * * *

(3) December 4, 1992, for products subject to paragraph (a)(7) of this section that contain menthol as an antipruritic in combination with the antidandruff ingredient coal tar identified in § 358.710(a)(1) of this chapter.

## PART 312—INVESTIGATIONAL NEW DRUG APPLICATION

### Subpart A—General Provisions



### Subpart B—Investigational New Drug Application (IND)



### Subpart C—Administrative Actions



### Subpart D—Responsibilities of Sponsors and Investigators









### Subpart E—Drugs Intended to Treat Life-threatening and Severely-debilitating Illnesses



### Subpart F—Miscellaneous



### Subpart G—Drugs for Investigational Use in Laboratory Research Animals or in Vitro Tests



AUTHORITY: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 371); sec. 351 of the Public Health Service Act (42 U.S.C. 262).

SOURCE: 52 FR 8831, Mar. 19, 1987, unless otherwise noted.

### Subpart A—General Provisions

#### § 312.1 Scope.

(a) This part contains procedures and requirements governing the use of investigational new drugs, including procedures and requirements for the submission to, and review by, the Food and Drug Administration of investigational new drug applications (IND's). An investigational new drug for which an IND is in effect in accordance with this part is exempt from the premarketing approval requirements that are otherwise applicable and may be shipped lawfully for the purpose of conducting clinical investigations of that drug.

(b) References in this part to regulations in the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

#### § 312.2 Applicability.

(a) *Applicability.* Except as provided in this section, this part applies to all clinical investigations of products that are subject to section 505 or 507 of the Federal Food, Drug, and Cosmetic Act or to the licensing provisions of the Public Health Service Act (58 Stat. 632, as amended (42 U.S.C. 201 et seq.)).

(b) *Exemptions.* (1) The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all the following apply:

(i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

(ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

(iii) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

(iv) The investigation is conducted in compliance with the requirements for institutional review set forth in Part 56 and with the requirements for informed consent set forth in Part 50; and

(v) The investigation is conducted in compliance with the requirements of § 312.7.

(2)(i) A clinical investigation involving an in vitro diagnostic biological product listed in paragraph (b)(2)(ii) of this section is exempt from the requirements of this part if (*a*) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and (*b*) it is shipped in compliance with § 312.160.

(ii) In accordance with paragraph (b)(2)(i) of this section, the following products are exempt from the requirements of this part: (*a*) blood grouping serum; (*b*) reagent red blood cells; and (*c*) anti-human globulin.

(3) A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with § 312.160.

(4) FDA will not accept an application for an investigation that is exempt under the provisions of paragraph (b)(1) of this section.

(5) A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

(c) *Bioavailability studies.* The applicability of this part to in vivo bioavailability studies in humans is subject to the provisions of § 320.31.

(d) *Unlabeled indication.* This part does not apply to the use in the practice of medicine for an unlabeled indication of a new drug or antibiotic drug product approved under Part 314 or of a licensed biological product.

(e) *Guidance.* FDA may, on its own initiative, issue guidance on the applicability of this part to particular investigational uses of drugs. On request, FDA will advise on the applicability of this part to a planned clinical investigation.

### § 312.3 Definitions and interpretations.

(a) The definitions and interpretations of terms contained in section 201 of the act apply to those terms when used in this part:

(b) The following definitions of terms also apply to this part:

*Act* means the Federal Food, Drug, and Cosmetic Act (secs. 201-902, 52 Stat. 1040 et seq., as amended (21 U.S.C. 301-392)).

*Clinical investigation* means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.

*Contract research organization* means a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration.

*FDA* means the Food and Drug Administration.

*IND* means an investigational new drug application. For purposes of this part, "IND" is synonymous with "Notice of Claimed Investigational Exemption for a New Drug."

*Investigational new drug* means a new drug, antibiotic drug, or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this part.

*Investigator* means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.

*Marketing application* means an application for a new drug submitted under section 505(b) of the act, a request to provide for certification of an antibiotic submitted under section 507 of the act, or a product license application for a biological product submitted under the Public Health Service Act.

*Sponsor* means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

*Sponsor-investigator* means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.

*Subject* means a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.





### § 312.6 Labeling of an investigational new drug.

(a) The immediate package of an investigational new drug intended for human use shall bear a label with the statement "Caution: New Drug—Limited by Federal (or United States) law to investigational use."

(b) The label or labeling of an investigational new drug shall not bear any statement that is false or misleading in any particular and shall not represent that the investigational new drug is safe or effective for the purposes for which it is being investigated.

### § 312.7 Promotion and charging for investigational drugs.

(a) *Promotion of an investigational new drug.* A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.

(b) *Commercial distribution of an investigational new drug.* A sponsor or investigator shall not commercially distribute or test market an investigational new drug.

(c) *Prolonging an investigation.* A sponsor shall not unduly prolong an investigation after finding that the results of the investigation appear to establish sufficient data to support a marketing application.

(d) *Charging for and commercialization of investigational drugs—(1) Clinical trials under an IND.* Charging for an investigational drug in a clinical trial under an IND is not permitted without the prior written approval of FDA. In requesting such approval, the sponsor shall provide a full written explanation of why charging is necessary in order for the sponsor to undertake or continue the clinical trial, e.g., why distribution of the drug to test subjects should not be considered part of the normal cost of doing business.

(2) *Treatment protocol or treatment IND.* A sponsor or investigator may charge for an investigational drug for a treatment use under a treatment protocol or treatment IND provided: (i) There is adequate enrollment in the ongoing clinical investigations under the authorized IND; (ii) charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved; (iii) the drug is not being commercially promoted or advertised; and (iv) the sponsor of the drug is actively pursuing marketing approval with due diligence. FDA must be notified in writing in advance of commencing any such charges, in an information amendment submitted under § 312.31. Authorization for charging goes into effect automatically 30 days after receipt by FDA of the information amendment, unless the sponsor is notified to the contrary.

(3) *Noncommercialization of investigational drug.* Under this section, the

sponsor may not commercialize an investigational drug by charging a price larger than that necessary to recover costs of manufacture, research, development, and handling of the investigational drug.

(4) *Withdrawal of authorization.* Authorization to charge for an investigational drug under this section may be withdrawn by FDA if the agency finds that the conditions underlying the authorization are no longer satisfied.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 19476, May 22, 1987]

### § 312.10 Waivers.

(a) A sponsor may request FDA to waive applicable requirement under this part. A waiver request may be submitted either in an IND or in an information amendment to an IND. In an emergency, a request may be made by telephone or other rapid communication means. A waiver request is required to contain at least one of the following:

(1) An explanation why the sponsor's compliance with the requirement is unnecessary or cannot be achieved;

(2) A description of an alternative submission or course of action that satisfies the purpose of the requirement; or

(3) Other information justifying a waiver.

(b) FDA may grant a waiver if it finds that the sponsor's noncompliance would not pose a significant and unreasonable risk to human subjects of the investigation and that one of the following is met:

(1) The sponsor's compliance with the requirement is unnecessary for the agency to evaluate the application, or compliance cannot be achieved;

(2) The sponsor's proposed alternative satisfies the requirement; or

(3) The applicant's submission otherwise justifies a waiver.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

## Subpart B—Investigational New Drug Application (IND)

### § 312.20 Requirement for an IND.

(a) A sponsor shall submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug that is subject to § 312.2(a).

(b) A sponsor shall not begin a clinical investigation subject to § 312.2(a) until the investigation is subject to an IND which is in effect in accordance with § 312.40.

### § 312.21 Phases of an investigation.

An IND may be submitted for one or more phases of an investigation. The clinical investigation of a previously untested drug is generally divided into three phases. Although in general the phases are conducted sequentially, they may overlap. These three phases of an investigation are a follows:

(a) *Phase 1.* (1) Phase 1 includes the initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80.

(2) Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

(b) *Phase 2.* Phase 2 includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.

(c) *Phase 3.* Phase 3 studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundred to several thousand subjects.

### § 312.22 General principles of the IND submission.

(a) FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety. Therefore, although FDA's review of Phase 1 submissions will focus on assessing the safety of Phase 1 investigations, FDA's review of Phases 2 and 3 submissions will also include an assessment of the scientific quality of the clinical investigations and the likelihood that the investigations will yield data capable of meeting statutory standards for marketing approval.

(b) The amount of information on a particular drug that must be submitted in an IND to assure the accomplishment of the objectives described in paragraph (a) of this section depends upon such factors as the novelty of the drug, the extent to which it has been studied previously, the known or suspected risks, and the developmental phase of the drug.

(c) The central focus of the initial IND submission should be on the general investigational plan and the protocols for specific human studies. Subsequent amendments to the IND that contain new or revised protocols should build logically on previous submissions and should be supported by additional information, including the results of animal toxicology studies or other human studies as appropriate. Annual reports to the IND should serve as the focus for reporting the status of studies being conducted under the IND and should update the general investigational plan for the coming year.

(d) The IND format set forth in § 312.23 should be followed routinely by sponsors in the interest of fostering an efficient review of applications. Sponsors are expected to exercise considerable discretion, however, regarding the content of information submitted in each section, depending upon the kind of drug being studied and the nature of the available information. Section 312.23 outlines the information needed for a commercially sponsored IND for a new molecular entity. A sponsor-investigator who uses, as a research tool, an investigational new drug that is already subject to a manufacturer's IND or marketing application should follow the same general format, but ordinarily may, if authorized by the manufacturer, refer to the manufacturer's IND or marketing application in providing the technical information supporting the proposed clinical investigation. A sponsor-investigator who uses an investigational drug not subject to a manufacturer's IND or marketing application is ordinarily required to submit all technical information supporting the IND, unless such information may be referenced from the scientific literature.

### § 312.23 IND content and format.

(a) A sponsor who intends to conduct a clinical investigation subject to this part shall submit an "Investigational New Drug Application" (IND) including, in the following order:

(1) *Cover sheet (Form FDA-1571).* A cover sheet for the application containing the following:

(i) The name, address, and telephone number of the sponsor, the date of the application, and the name of the investigational new drug.

(ii) Identification of the phase or phases of the clinical investigation to be conducted.

(iii) A commitment not to begin clinical investigations until an IND covering the investigations is in effect.

(iv) A commitment that an Institutional Review Board (IRB) that complies with the requirements set forth in Part 56 will be responsible for the initial and continuing review and approval of each of the studies in the proposed clinical investigation and that the investigator will report to the IRB proposed changes in the research activity in accordance with the requirements of Part 56.

(v) A commitment to conduct the investigation in accordance with all other applicable regulatory requirements.

(vi) The name and title of the person responsible for monitoring the conduct and progress of the clinical investigations.

(vii) The name(s) and title(s) of the person(s) responsible under § 312.32 for review and evaluation of information relevant to the safety of the drug.

(viii) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred. If all obligations governing the conduct of the study have been transferred, a general statement of this transfer—in lieu of a listing of the specific obligations transferred—may be submitted.

(ix) The signature of the sponsor or the sponsor's authorized representative. If the person signing the application does not reside or have a place of business within the United States, the IND is required to contain the name and address of, and be countersigned by, an attorney, agent, or other authorized official who resides or maintains a place of business within the United States.

(2) *A table of contents.*

(3) *Introductory statement and general investigational plan.* (i) A brief introductory statement giving the name of the drug and all active ingredients, the drug's pharmacological class, the structural formula of the drug (if known), the formulation of the dosage form(s) to be used, the route of administration, and the broad objectives and planned duration of the proposed clinical investigation(s).

(ii) A brief summary of previous human experience with the drug, with reference to other IND's if pertinent, and to investigational or marketing experience in other countries that may be relevant to the safety of the proposed clinical investigation(s).

(iii) If the drug has been withdrawn from investigation or marketing in any country for any reason related to safety or effectiveness, identification of the country(ies) where the drug was withdrawn and the reasons for the withdrawal.

(iv) A brief description of the overall plan for investigating the drug product for the following year. The plan should include the following: (*a*) The rationale for the drug or the research study; (*b*) the indication(s) to be studied; (*c*) the general approach to be followed in evaluating the drug; (*d*) the kinds of clinical trials to be conducted in the first year following the submission (if plans are not developed for the entire year, the sponsor should so indicate); (*e*) the estimated number of patients to be given the drug in those studies; and (*f*) any risks of particular severity or seriousness anticipated on the basis of the toxicological data in animals or prior studies in humans with the drug or related drugs.

(4) [Reserved]

(5) *Investigator's brochure.* If required under § 312.55, a copy of the investigator's brochure, containing the following information:

(i) A brief description of the drug substance and the formulation, including the structural formula, if known.

(ii) A summary of the pharmacological and toxicological effects of the drug in animals and, to the extent known, in humans.

(iii) A summary of the pharmacokinetics and biological disposition of the drug in animals and, if known, in humans.

(iv) A summary of information relating to safety and effectiveness in humans obtained from prior clinical studies. (Reprints of published articles on such studies may be appended when useful.)





(v) A description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug.

(6) *Protocols.* (i) A protocol for each planned study. (Protocols for studies not submitted initially in the IND should be submitted in accordance with § 312.30(a).) In general, protocols for Phase 1 studies may be less detailed and more flexible than protocols for Phase 2 and 3 studies. Phase 1 protocols should be directed primarily at providing an outline of the investigation—an estimate of the number of patients to be involved, a description of safety exclusions, and a description of the dosing plan including duration, dose, or method to be used in determining dose—and should specify in detail only those elements of the study that are critical to safety, such as necessary monitoring of vital signs and blood chemistries. Modifications of the experimental design of Phase 1 studies that do not affect critical safety assessments are required to be reported to FDA only in the annual report.

(ii) In Phases 2 and 3, detailed protocols describing all aspects of the study should be submitted. A protocol for a Phase 2 or 3 investigation should be designed in such a way that, if the sponsor anticipates that some deviation from the study design may become necessary as the investigation progresses, alternatives or contingencies to provide for such deviation are built into the protocols at the outset. For example, a protocol for a controlled short-term study might include a plan for an early crossover of nonresponders to an alternative therapy.

(iii) A protocol is required to contain the following, with the specific elements and detail of the protocol reflecting the above distinctions depending on the phase of study:

(*a*) A statement of the objectives and purpose of the study.

(*b*) The name and address and a statement of the qualifications (curriculum vitae or other statement of qualifications) of each investigator, and the name of each subinvestigator (e.g., research fellow, resident) working under the supervision of the investigator; the name and address of the research facilities to be used; and the name and address of each reviewing Institutional Review Board.

(*c*) The criteria for patient selection and for exclusion of patients and an estimate of the number of patients to be studied.

(*d*) A description of the design of the study, including the kind of control group to be used, if any, and a description of methods to be used to minimize bias on the part of subjects, investigators, and analysts.

(*e*) The method for determining the dose(s) to be administered, the planned maximum dosage, and the duration of individual patient exposure to the drug.

(*f*) A description of the observations and measurements to be made to fulfill the objectives of the study.

(*g*) A description of clinical procedures, laboratory tests, or other measures to be taken to monitor the effects of the drug in human subjects and to minimize risk.

(7) *Chemistry, manufacturing, and control information.* (i) As appropriate for the particular investigations covered by the IND, a section describing the composition, manufacture, and control of the drug substance and the drug product. Although in each phase of the investigation sufficient information is required to be submitted to assure the proper identification, quality, purity, and strength of the investigational drug, the amount of information needed to make that assurance will vary with the phase of the investigation, the proposed duration of the investigation, the dosage form, and the amount of information otherwise available. FDA recognizes that modifications to the method of preparation of the new drug substance and dosage form and changes in the dosage form itself are likely as the investigation progresses. Therefore, the emphasis in an initial Phase 1 submission should generally be placed on the identification and control of the raw materials and the new drug substance. Final specifications for the drug substance and drug product are not expected

until the end of the investigational process.

(ii) It should be emphasized that the amount of information to be submitted depends upon the scope of the proposed clinical investigation. For example, although stability data are required in all phases of the IND to demonstrate that the new drug substance and drug product are within acceptable chemical and physical limits for the planned duration of the proposed clinical investigation, if very short-term tests are proposed, the supporting stability data can be correspondingly limited.

(iii) As drug development proceeds and as the scale or production is changed from the pilot-scale production appropriate for the limited initial clinical investigations to the larger-scale production needed for expanded clinical trials, the sponsor should submit information amendments to supplement the initial information submitted on the chemistry, manufacturing, and control processes with information appropriate to the expanded scope of the investigation.

(iv) Reflecting the distinctions described in this paragraph (a)(7), and based on the phase(s) to be studied, the submission is required to contain the following:

(*a*) *Drug substance.* A description of the drug substance, including its physical, chemical, or biological characteristics; the name and address of its manufacturer; the general method of preparation of the drug substance; the acceptable limits and analytical methods used to assure the identity, strength, quality, and purity of the drug substance; and information sufficient to support stability of the drug substance during the toxicological studies and the planned clinical studies. Reference to the current edition of the United States Pharmacopeia—National Formulary may satisfy relevant requirements in this paragraph.

(*b*) *Drug product.* A list of all components, which may include reasonable alternatives for inactive compounds, used in the manufacture of the investigational drug product, including both those components intended to appear in the drug product and those which may not appear but which are used in the manufacturing process, and, where applicable, the quantitative composition of the investigational drug product, including any reasonable variations that may be expected during the investigational stage; the name and address of the drug product manufacturer; a brief general description of the manufacturing and packaging procedure as appropriate for the product; the acceptable limits and analytical methods used to assure the identity, strength, quality, and purity of the drug product; and information sufficient to assure the product's stability during the planned clinical studies. Reference to the current edition of the United States Pharmacopeia—National Formulary may satisfy certain requirements in this paragraph.

(*c*) A brief general description of the composition, manufacture, and control of any placebo used in a controlled clinical trial.

(*d*) *Labeling.* A copy of all labels and labeling to be provided to each investigator.

(*e*) *Environmental analysis requirements.* A claim for categorical exclusion under § 25.24 or an environmental assessment under § 25.31.

(8) *Pharmacology and toxicology information.* Adequate information about pharmacological and toxicological studies of the drug involving laboratory animals or in vitro, on the basis of which the sponsor has concluded that it is reasonably safe to conduct the proposed clinical investigations. The kind, duration, and scope of animal and other tests required varies with the duration and nature of the proposed clinical investigations. Guidelines are available from FDA that describe ways in which these requirements may be met. Such information is required to include the identification and qualifications of the individuals who evaluated the results of such studies and concluded that it is reasonably safe to begin the proposed investigations and a statement of where the investigations were conducted and where the records are available for inspection. As drug development proceeds, the sponsor is required to submit informational amendments, as appropriate, with additional information pertinent to safety.





(i) *Pharmacology and drug disposition.* A section describing the pharmacological effects and mechanism(s) of action of the drug in animals, and information on the absorption, distribution, metabolism, and excretion of the drug, if known.

(ii) *Toxicology.* (*a*) An integrated summary of the toxicological effects of the drug in animals and in vitro. Depending on the nature of the drug and the phase of the investigation, the description is to include the results of acute, subacute, and chronic toxicity tests; tests of the drug's effects on reproduction and the developing fetus; any special toxicity test related to the drug's particular mode of administration or conditions of use (e.g., inhalation, dermal, or ocular toxicology); and any in vitro studies intended to evaluate drug toxicity.

(*b*) For each toxicology study that is intended primarily to support the safety of the proposed clinical investigation, a full tabulation of data suitable for detailed review.

(iii) For each nonclinical laboratory study subject to the good laboratory practice regulations under Part 58, a statement that the study was conducted in compliance with the good laboratory practice regulations in Part 58, or, if the study was not conducted in compliance with those regulations, a brief statement of the reason for the noncompliance.

(9) *Previous human experience with the investigational drug.* A summary of previous human experience known to the applicant, if any, with the investigational drug. The information is required to include the following:

(i) If the investigational drug has been investigated or marketed previously, either in the United States or other countries, detailed information about such experience that is relevant to the safety of the proposed investigation or to the investigation's rationale. If the durg has been the subject of controlled trials, detailed information on such trials that is relevant to an assessment of the drug's effectiveness for the proposed investigational use(s) should also be provided. Any published material that is relevant to the safety of the proposed investigation or to an assessment of the drug's effectiveness for its proposed investigational use should be provided in full. Published material that is less directly relevant may be supplied by a bibliography.

(ii) If the drug is a combination of drugs previously investigated or marketed, the information required under paragraph (a)(9)(i) of this section should be provided for each active drug component. However, if any component in such combination is subject to an approved marketing application or is otherwise lawfully marketed in the United States, the sponsor is not required to submit published material concerning that active drug component unless such material relates directly to the proposed investigational use (including publications relevant to component-component interaction).

(iii) If the drug has been marketed outside the United States, a list of the countries in which the drug has been marketed and a list of the countries in which the drug has been withdrawn from marketing for reasons potentially related to safety or effectiveness.

(10) *Additional information.* In certain applications, as described below, information on special topics may be needed. Such information shall be submitted in this section as follows:

(i) *Drug dependence and abuse potential.* If the drug is a psychotropic substance or otherwise has abuse potential, a section describing relevant clinical studies and experience and studies in test animals.

(ii) *Radioactive drugs.* If the drug is a radioactive drug, sufficient data from animal or human studies to allow a reasonable calculation of radiation-absorbed dose to the whole body and critical organs upon administration to a human subject. Phase 1 studies of radioactive drugs must include studies which will obtain sufficient data for dosimetry calculations.

(iii) *Other information.* A brief statement of any other information that would aid evaluation of the proposed clinical investigations with respect to their safety or their design and potential as controlled clinical trials to support marketing of the drug.

(11) *Relevant information.* If requested by FDA, any other relevant

information needed for review of the application.

(b) *Information previously submitted.* The sponsor ordinarily is not required to resubmit information previously submitted, but may incorporate the information by reference. A reference to information submitted previously must identify the file by name, reference number, volume, and page number where the information can be found. A reference to information submitted to the agency by a person other than the sponsor is required to contain a written statement that authorizes the reference and that is signed by the person who submitted the information.

(c) *Material in a foreign language.* The sponsor shall submit an accurate and complete English translation of each part of the IND that is not in English. The sponsor shall also submit a copy of each original literature publication for which an English translation is submitted.

(d) *Number of copies.* The sponsor shall submit an original and two copies of all submissions to the IND file, including the original submission and all amendments and reports.

(e) *Numbering of IND submissions.* Each submission relating to an IND is required to be numbered serially using a single, three-digit serial number. The initial IND is required to be numbered 000; each subsequent submission (e.g., amendment, report, or correspondence) is required to be numbered chronologically in sequence.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 53 FR 1918, Jan. 25, 1988]

### § 312.30 Protocol amendments.

Once an IND is in effect, a sponsor shall amend it as needed to ensure that the clinical investigations are conducted according to protocols included in the application. This section sets forth the provisions under which new protocols may be submitted and changes in previously submitted protocols may be made.

(a) *New protocol.* Whenever a sponsor intends to conduct a study that is not covered by a protocol already contained in the IND, the sponsor shall submit to FDA a protocol amendment containing the protocol for the study. Such study may begin provided two conditions are met: (1) The sponsor has submitted the protocol to FDA for its review; and (2) the protocol has been approved by the Institutional Review Board (IRB) with responsibility for review and approval of the study in accordance with the requirements of Part 56. The sponsor may comply with these two conditions in either order.

(b) *Changes in a protocol.* (1) A sponsor shall submit a protocol amendment describing any change in a Phase 1 protocol that significantly affects the safety of subjects or any change in a Phase 2 or 3 protocol that significantly affects the safety of subjects, the scope of the investigation, or the scientific quality of the study. Examples of changes requiring an amendment under this paragraph include:

(i) Any increase in drug dosage or duration of exposure of individual subjects to the drug beyond that in the current protocol, or any significant increase in the number of subjects under study.

(ii) Any significant change in the design of a protocol (such as the addition or dropping of a control group).

(iii) The addition of a new test or procedure that is intended to improve monitoring for, or reduce the risk of, a side effect or adverse event; or the dropping of a test intended to monitor safety.

(2)(i) A protocol change under paragraph (b)(1) of this section may be made provided two conditions are met:

(*a*) The sponsor has submitted the change to FDA for its review; and

(*b*) The change has been approved by the IRB with responsibility for review and approval of the study. The sponsor may comply with these two conditions in either order.

(ii) Notwithstanding paragraph (b)(2)(i) of this section, a protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately provided FDA is subsequently notified by protocol amendment and the reviewing IRB is notified in accordance with § 56.104(c).

(c) *New investigator.* A sponsor shall submit a protocol amendment when a new investigator is added to carry out a previously submitted protocol, except that a protocol amendment is not required when a licensed practitioner is added in the case of a treatment protocol under § 312.34. Once the investigator is added to the study, the investigational drug may be shipped to the investigator and the investigator may begin participating in the study. The sponsor shall notify FDA of the new investigator within 30 days of the investigator being added.

(d) *Content and format.* A protocol amendment is required to be prominently identified as such (i.e., "Protocol Amendment: New Protocol", "Protocol Amendment: Change in Protocol", or "Protocol Amendment: New Investigator"), and to contain the following:

(1)(i) In the case of a new protocol, a copy of the new protocol and a brief description of the most clinically significant differences between it and previous protocols.

(ii) In the case of a change in protocol, a brief description of the change and reference (date and number) to the submission that contained the protocol.

(iii) In the case of a new investigator, the investigator's name, the qualifications to conduct the investigation, reference to the previously submitted protocol, and all additional information about the investigator's study as is required under § 312.23(a)(6)(iii)(*b*).

(2) Reference, if necessary, to specific technical information in the IND or in a concurrently submitted information amendment to the IND that the sponsor relies on to support any clinically significant change in the new or amended protocol. If the reference is made to supporting information already in the IND, the sponsor shall identify by name, reference number, volume, and page number the location of the information.

(3) If the sponsor desires FDA to comment on the submission, a request for such comment and the specific questions FDA's response should address.

(e) *When submitted.* A sponsor shall submit a protocol amendment for a new protocol or a change in protocol before its implementation. Protocol amendments to add a new investigator or to provide additional information about investigators may be grouped and submitted at 30-day intervals. When several submissions of new protocols or protocol changes are anticipated during a short period, the sponsor is encouraged, to the extent feasible, to include these all in a single submission.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 53 FR 1918, Jan. 25, 1988]

### § 312.31 Information amendments.

(a) *Requirement for information amendment.* A sponsor shall report in an information amendment essential information on the IND that is not within the scope of a protocol amendment, IND safety reports, or annual report. Examples of information requiring an information amendment include:

(1) New toxicology, chemistry, or other technical information; or

(2) A report regarding the discontinuance of a clinical investigation.

(b) *Content and format of an information amendment.* An information amendment is required to bear prominent identification of its contents (e.g., "Information Amendment: Chemistry, Manufacturing, and Control", "Information Amendment: Pharmacology-Toxicology", "Information Amendment: Clinical"), and to contain the following:

(1) A statement of the nature and purpose of the amendment.

(2) An organized submission of the data in a format appropriate for scientific review.

(3) If the sponsor desires FDA to comment on an information amendment, a request for such comment.

(c) *When submitted.* Information amendments to the IND should be submitted as necessary but, to the extent feasible, not more than every 30 days.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 53 FR 1918, Jan. 25, 1988]

§ 312.32 IND safety reports.

(a) *Definitions.* The following definitions of terms apply to this section:

*Associated with the use of the drug* means that there is a reasonable possibility that the experience may have been caused by the drug.

*Serious adverse experience* means any experience that suggests a significant hazard, contraindication, side effect, or precaution. With respect to human clinical experience, a serious adverse drug experience includes any experience that is fatal or life-threatening, is permanently disabling, requires inpatient hospitalization, or is a congenital anomaly, cancer, or overdose. With respect to results obtained from tests in laboratory animals, a serious adverse drug experience includes any experience suggesting a significant risk for human subjects, including any finding of mutagenicity, teratogenicity, or carcinogenicity.

*Unexpected adverse experience* means any adverse experience that is not identified in nature, severity, or frequency in the current investigator brochure; or, if an investigator brochure is not required, that is not identified in nature, severity, or frequency in the risk information described in the general investigational plan or elsewhere in the current application, as amended.

(b) *Review of safety information.* The sponsor shall promptly review all information relevant to the safety of the drug obtained or otherwise received by the sponsor from any source, foreign or domestic, including information derived from clinical investigations, animal investigations, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers.

(c) *IND safety reports.* (1)(i) *Written reports.* The sponsor shall notify FDA and all participating investigators in a written IND safety report of any adverse experience associated with use of the drug that is both serious and unexpected. Such notification shall be made as soon as possible and in no event later than 10 working days after the sponsor's initial receipt of the information. Each written notification shall bear prominent identification of its contents, i.e., "IND Safety Report." Each written notification to FDA shall be transmitted to the FDA division of the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research which has responsibility for review of the IND.

(ii) In each written IND safety report, the sponsor shall identify all safety reports previously filed with the IND concerning a similar adverse experience, and shall analyze the significance of the adverse experience in light of the previouos, similar reports.

(2) *Telephone report.* The sponsor shall also notify FDA by telephone of any unexpected fatal or life-threatening experience associated with use of the drug in the clinical studies conducted under the IND no later than 3 working days after receipt of the information. Each telephone call to FDA shall be transmitted to the FDA division of the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research which has responsibility for review of the IND. For purposes of this section, life-threatening means that the patient was, in the view of the investigator, at *immediate* (emphasis added) risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more serious form, might have caused death. For example, drug-induced hepatitis that resolved without evidence of hepatic failure would not be considered life-threatening even though drug-induced hepatitis can be fatal.

(3) *Reporting format or frequency.* FDA may request a sponsor to submit IND safety reports in a format or at a frequency different than that required under this paragraph. The sponsor may also propose and adopt a different reporting format or frequency if the change is agreed to in advance by the director of the division in the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research which is responsible for review of the IND.





(4) A sponsor of a clinical study of a marketed drug is not required to make a safety report for any adverse experience associated with use of the drug that is not from the clinical study itself.

(d) *Followup.* (1) The sponsor shall promptly investigate all safety information received by it.

(2) Followup information to a safety report shall be submitted as soon as the relevant information is available.

(3) If the results of a sponsor's investigation show that an adverse experience not initially determined to be reportable under paragraph (c) of this section is so reportable, the sponsor shall report such experience in a safety report as soon as possible after the determination is made, but in no event longer than 10-working days.

(4) Results of a sponsor's investigation of other safety information shall be submitted, as appropriate, in an information amendment or annual report.

(e) *Disclaimer.* A safety report or other information submitted by a sponsor under this section (and any release by FDA of that report or information) does not necessarily reflect a conclusion by the sponsor or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse experience. A sponsor need not admit, and may deny, that the report or information submitted by the sponsor constitutes an admission that the drug caused or contributed to an adverse experience.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11579, Mar. 29, 1990]

§ 312.33 Annual reports.

A sponsor shall within 60 days of the anniversary date that the IND went into effect, submit a brief report of the progress of the investigation that includes:

(a) *Individual study information.* A brief summary of the status of each study in progress and each study completed during the previous year. The summary is required to include the following information for each study:

(1) The title of the study (with any appropriate study identifiers such as protocol number), its purpose, a brief statement identifying the patient population, and a statement as to whether the study is completed.

(2) The total number of subjects initially planned for inclusion in the study, the number entered into the study to date, the number whose participation in the study was completed as planned, and the number who dropped out of the study for any reason.

(3) If the study has been completed, or if interim results are known, a brief description of any available study results.

(b) *Summary information.* Information obtained during the previous year's clinical and nonclinical investigations, including:

(1) A narrative or tabular summary showing the most frequent and most serious adverse experiences by body system.

(2) A summary of all IND safety reports submitted during the past year.

(3) A list of subjects who died during participation in the investigation, with the cause of death for each subject.

(4) A list of subjects who dropped out during the course of the investigation in association with any adverse experience, whether or not thought to be drug related.

(5) A brief description of what, if anything, was obtained that is pertinent to an understanding of the drug's actions, including, for example, information about dose response, information from controlled trails, and information about bioavailability.

(6) A list of the preclinical studies (including animal studies) completed or in progress during the past year and a summary of the major preclinical findings.

(7) A summary of any significant manufacturing or microbiological changes made during the past year.

(c) A description of the general investigational plan for the coming year to replace that submitted 1 year earlier. The general investigational plan shall contain the information required under § 312.23(a)(3)(iv).

(d) If the investigator brochure has been revised, a description of the revision and a copy of the new brochure.

(e) A description of any significant Phase 1 protocol modifications made during the previous year and not previously reported to the IND in a protocol amendment.

(f) A brief summary of significant foreign marketing developments with the drug during the past year, such as approval of marketing in any country or withdrawal or suspension from marketing in any country.

(g) If desired by the sponsor, a log of any outstanding business with respect to the IND for which the sponsor requests or expects a reply, comment, or meeting.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910–0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

### § 312.34 Treatment use of an investigational new drug.

(a) *General.* A drug that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease condition in patients for whom no comparable or satisfactory alternative drug or other therapy is available. During the clinical investigation of the drug, it may be appropriate to use the drug in the treatment of patients not in the clinical trials, in accordance with a treatment protocol or treatment IND. The purpose of this section is to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible, before general marketing begins, and to obtain additional data on the drug's safety and effectiveness. In the case of a serious disease, a drug ordinarily may be made available for treatment use under this section during Phase 3 investigations or after all clinical trials have been completed; however, in appropriate circumstances, a drug may be made available for treatment use during Phase 2. In the case of an immediately life-threatening disease, a drug may be made available for treatment use under this section earlier than Phase 3, but ordinarily not earlier than Phase 2. For purposes of this section, the "treatment use" of a drug includes the use of a drug for diagnostic purposes.

(b) *Criteria.* (1) FDA shall permit an investigational drug to be used for a treatment use under a treatment protocol or treatment IND if:

(i) The drug is intended to treat a serious or immediately life-threatening disease;

(ii) There is no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;

(iii) The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and

(iv) The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence.

(2) *Serious disease.* For a drug intended to treat a serious disease, the Commissioner may deny a request for treatment use under a treatment protocol or treatment IND if there is insufficient evidence of safety and effectiveness to support such use.

(3) *Immediately life-threatening disease.* (i) For a drug intended to treat an immediately life-threatening disease, the Commissioner may deny a request for treatment use of an investigational drug under a treatment protocol or treatment IND if the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the drug:

(A) May be effective for its intended use in its intended patient population; or

(B) Would not expose the patients to whom the drug is to be administered to an unreasonable and significant additional risk of illness or injury.

(ii) For the purpose of this section, an "immediately life-threatening" disease means a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

(c) *Safeguards.* Treatment use of an investigational drug is conditioned on the sponsor and investigators complying with the safeguards of the IND process, including the regulations governing informed consent (21 CFR Part 50) and institutional review boards (21 CFR Part 56) and the applicable provisions of Part 312, including distribution of the drug through qualified experts, maintenance of adequate manufacturing facilities, and submission of IND safety reports.

(d) *Clinical hold.* FDA may place on clinical hold a proposed or ongoing treatment protocol or treatment IND in accordance with § 312.42.

[52 FR 19476, May 22, 1987]

### § 312.35 Submissions for treatment use.

(a) *Treatment protocol submitted by IND sponsor.* A sponsor of a clinical investigation of a drug who intends to sponsor a treatment use for the drug under § 312.34 shall submit to FDA a treatment protocol. A treatment use under a treatment protocol may begin 30 days after FDA receives the protocol or on earlier notification by FDA that the treatment use described in the protocol may begin.

(1) A treatment protocol is required to contain the following:

(i) The intended use of the drug.

(ii) An explanation of the rationale for use of the drug, including, as appropriate, either a list of what available regimens ordinarily should be tried before using the investigational drug or an explanation of why the use of the investigational drug is preferable to the use of available marketed treatments.

(iii) A brief description of the criteria for patient selection.

(iv) The method of administration of the drug and the dosages.

(v) A description of clinical procedures, laboratory tests, or other measures to monitor the effects of the drug and to minimize risk.

(2) A treatment protocol is to be supported by the following:

(i) Informational brochure for supplying to each treating physician.

(ii) The technical information that is relevant to safety and effectiveness of the drug for the intended treatment purpose. Information contained in the sponsor's IND may be incorporated by reference.

(iii) A commitment by the sponsor to assure compliance of all participating investigators with the informed consent requirements of 21 CFR Part 50.

(3) A licensed practioner who receives an investigational drug for treatment use under a treatment protocol is an "investigator" under the protocol and is responsible for meeting all applicable investigator responsibilities under this part and 21 CFR Parts 50 and 56.

(b) *Treatment IND submitted by licensed practitioner.* (1) If a licensed medical practitioner wants to obtain an investigational drug subject to a controlled clinical trial for a treatment use, the practitioner should first attempt to obtain the drug from the sponsor of the controlled trial under a treatment protocol. If the sponsor of the controlled clinical investigation of the drug will not establish a treatment protocol for the drug under paragraph (a) of this section, the licensed medical practitioner may seek to obtain the drug from the sponsor and submit a treatment IND to FDA requesting authorization to use the investigational drug for treatment use. A treatment use under a treatment IND may begin 30 days after FDA receives the IND or on earlier notification by FDA that the treatment use under the IND may begin. A treatment IND is required to contain the following:

(i) A cover sheet (Form FDA 1571) meeting § 312.23(g)(1).

(ii) Information (when not provided by the sponsor) on the drug's chemistry, manufacturing, and controls, and prior clinical and nonclinical experience with the drug submitted in accordance with § 312.23. A sponsor of a clinical investigation subject to an IND who supplies an investigational drug to a licensed medical practitioner for purposes of a separate treatment clinical investigation shall be deemed to authorize the incorporation-by-reference of the technical information contained in the sponsor's IND into the medical practitioner's treatment IND.

(iii) A statement of the steps taken by the practitioner to obtain the drug under a treatment protocol from the drug sponsor.

(iv) A treatment protocol containing the same information listed in paragraph (a)(1) of this section.

(v) A statement of the practitioner's qualifications to use the investigational drug for the intended treatment use.

(vi) The practitioner's statement of familiarity with information on the drug's safety and effectiveness derived from previous clinical and nonclinical experience with the drug.

(vii) Agreement to report to FDA safety information in accordance with § 312.32.

(2) A licensed practitioner who submits a treatment IND under this section is the sponsor-investigator for such IND and is responsible for meeting all applicable sponsor and investigator responsibilities under this part and 21 CFR Parts 50 and 56.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 19477, May 22, 1987]

### § 312.36 Emergency use of an investigational new drug.

Need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND in accordance with § 312.23 or § 312.34. In such a case, FDA may authorize shipment of the drug for a specified use in advance of submission of an IND. A request for such authorization may be transmitted to FDA by telephone or other rapid communication means. For investigational biological drugs, the request should be directed to the Division of Biological Investigational New Drugs (HFB-230), Center for Biologics Evaluation and Research, 8800 Rockville Pike, Bethesda, MD 20892, 301-443-4864. For all other investigational drugs, the request for authorization should be directed to the Document Management and Reporting Branch (HFD-53), Center for Drug Evaluation and Research, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4320. After normal working hours, eastern standard time, the request should be directed to the FDA Division of Emergency and Epidemiological Operations, 202-857-8400. Except in extraordinary circumstances, such authorization will be conditioned on the sponsor making an appropriate IND submission as soon as practicable after receiving the authorization.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11579, Mar. 29, 1990]

### § 312.38 Withdrawal of an IND.

(a) At any time a sponsor may withdraw an effective IND without prejudice.

(b) If an IND is withdrawn, FDA shall be so notified, all clinical investigations conducted under the IND shall be ended, all current investigators notified, and all stocks of the drug returned to the sponsor or otherwise disposed of at the request of the sponsor in accordance with § 312.59.

(c) If an IND is withdrawn because of a safety reason, the sponsor shall promptly so inform FDA, all participating investigators, and all reviewing Institutional Review Boards, together with the reasons for such withdrawal.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

## Subpart C—Administrative Actions

### § 312.40 General requirements for use of an investigational new drug in a clinical investigation.

(a) An investigational new drug may be used in a clinical investigation if the following conditions are met:

(1) The sponsor of the investigation submits an IND for the drug to FDA; the IND is in effect under paragraph (b) of this section; and the sponsor complies with all applicable requirements in this part and Parts 50 and 56 with respect to the conduct of the clinical investigations; and

(2) Each participating investigator conducts his or her investigation in compliance with the requirements of this part and Parts 50 and 56.

(b) An IND goes into effect:





(1) Thirty days after FDA receives the IND, unless FDA notifies the sponsor that the investigations described in the IND are subject to a clinical hold under § 312.42; or

(2) On earlier notification by FDA that the clinical investigations in the IND may begin. FDA will notify the sponsor in writing of the date it receives the IND.

(c) A sponsor may ship an investigational new drug to investigators named in the IND:

(1) Thirty days after FDA receives the IND; or

(2) On earlier FDA authorization to ship the drug.

(d) An investigator may not administer an investigational new drug to human subjects until the IND goes into effect under paragraph (b) of this section.

### § 312.41 Comment and advice on an IND.

(a) FDA may at any time during the course of the investigation communicate with the sponsor orally or in writing about deficiencies in the IND or about FDA's need for more data or information.

(b) On the sponsor's request, FDA will provide advice on specific matters relating to an IND. Examples of such advice may include advice on the adequacy of technical data to support an investigational plan, on the design of a clinical trial, and on whether proposed investigations are likely to produce the data and information that is needed to meet requirements for a marketing application.

(c) Unless the communication is accompanied by a clinical hold order under § 312.42, FDA communications with a sponsor under this section are solely advisory and do not require any modification in the planned or ongoing clinical investigations or response to the agency.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

### § 312.42 Clinical holds and requests for modification.

(a) *General.* A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. The clinical hold order may apply to one or more of the investigations covered by an IND. When a proposed study is placed on clinical hold, subjects may not be given the investigational drug. When an ongoing study is placed on clinical hold, no new subjects may be recruited to the study and placed on the investigational drug; patients already in the study should be taken off therapy involving the investigational drug unless specifically permitted by FDA in the interest of patient safety.

(b) *Grounds for imposition of clinical hold*—(1) *Clinical hold of a Phase 1 study under an IND.* FDA may place a proposed or ongoing Phase 1 investigation on clinical hold if it finds that:

(i) Human subjects are or would be exposed to an unreasonable and significant risk of illness or injury;

(ii) The clinical investigators named in the IND are not qualified by reason of their scientific training and experience to conduct the investigation described in the IND;

(iii) The investigator brochure is misleading, erroneous, or materially incomplete; or

(iv) The IND does not contain sufficient information required under § 312.23 to assess the risks to subjects of the proposed studies.

(2) *Clinical hold of a Phase 2 or 3 study under an IND.* FDA may place a proposed or ongoing Phase 2 or 3 investigation on clinical hold if it finds that:

(i) Any of the conditions in paragraph (b)(1)(i) through (iv) of this section apply; or

(ii) The plan or protocol for the investigation is clearly deficient in design to meet its stated objectives.

(3) Clinical hold of a treatment IND or treatment protocol.

(i) *Proposed use.* FDA may place a proposed treatment IND or treatment protocol on clinical hold if it is determined that:

(A) The pertinent criteria in § 312.34(b) for permitting the treatment use to begin are not satisfied; or

(B) The treatment protocol or treatment IND does not contain the information required under § 312.35 (a) or

(b) to make the specified determination under § 312.34(b).

(ii) *Ongoing use.* FDA may place an ongoing treatment protocol or treatment IND on clinical hold if it is determined that:

(A) There becomes available a comparable or satisfactory alternative drug or other therapy to treat that stage of the disease in the intended patient population for which the investigational drug is being used;

(B) The investigational drug is not under investigation in a controlled clinical trial under an IND in effect for the trial and not all controlled clinical trials necessary to support a marketing application have been completed, or a clinical study under the IND has been placed on clinical hold;

(C) The sponsor of the controlled clinical trial is not pursuing marketing approval with due diligence;

(D) If the treatment IND or treatment protocol is intended for a serious disease, there is insufficient evidence of safety and effectiveness to support such use; or

(E) If the treatment protocol or treatment IND was based on an immediately life-threatening disease, the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the drug:

(*1*) May be effective for its intended use in its intended population; or

(*2*) Would not expose the patients to whom the drug is to be administered to an unreasonable and significant additional risk of illness or injury.

(c) *Discussion of deficiency.* Whenever FDA concludes that a deficiency exists in a clinical investigation that may be grounds for the imposition of clinical hold FDA will, unless patients are exposed to immediate and serious risk, attempt to discuss and satisfactorily resolve the matter with the sponsor before issuing the clinical hold order.

(d) *Imposition of clinical hold.* The clinical hold order may be made by telephone or other means of rapid communication or in writing. The clinical hold order will identify the studies under the IND to which the hold applies, and will briefly explain the basis for the action. The clinical hold order will be made by or on behalf of the Division Director with responsibility for review of the IND. As soon as possible, and no more than 30 days after imposition of the clinical hold, the Division Director will provide the sponsor a written explanation of the basis for the hold.

(e) *Resumption of clinical investigations.* If, by the terms of the clinical hold order, resumption of the affected investigation is permitted without prior notification by FDA once a stated correction or modification is made, the investigation may proceed as soon as the correction or modification is made. In all other cases, an investigation may only resume after the Division Director (or the Director's designee) with responsibility for review of the IND has notified the sponsor that the investigation may proceed. In these cases resumption of the affected investigation(s) will be authorized when the sponsor corrects the deficiency(ies) previously cited or otherwise satisfied the agency that the investigation(s) can proceed. Resumption of a study may be authorized by telephone or other means of rapid communication.

(f) *Appeal.* If the sponsor disagrees with the reasons cited for the clinical hold, the sponsor may request reconsideration of the decision in accordance with § 312.48.

(g) *Conversion of IND on clinical hold to inactive status.* If all investigations covered by an IND remain on clinical hold for 1 year or more, the IND may be placed on inactive status by FDA under § 312.45.

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 19477, May 22, 1987]

### § 312.44 Termination.

(a) *General.* This section describes the procedures under which FDA may terminate an IND. If an IND is terminated, the sponsor shall end all clinical investigations conducted under the IND and recall or otherwise provide for the disposition of all unused supplies of the drug. A termination action may be based on deficiencies in the IND or in the conduct of an investigation under an IND. Except as provided in paragraph (d) of this section, a termination shall be preceded by a proposal to terminate by FDA and an opportunity for the sponsor to respond. FDA will, in general, only initiate an action under this section after first attempting to resolve differences informally or, when appropriate, through the clinical hold procedures described in § 312.42.

(b) *Grounds for termination*—(1) *Phase 1.* FDA may propose to terminate an IND during Phase 1 if it finds that:

(i) Human subjects would be exposed to an unreasonable and significant risk of illness or injury.

(ii) The IND does not contain sufficient information required under § 312.23 to assess the safety to subjects of the clinical investigations.

(iii) The methods, facilities, and controls used for the manufacturing, processing, and packing of the investigational drug are inadequate to establish and maintain appropriate standards of identity, strength, quality, and purity as needed for subject safety.

(iv) The clinical investigations are being conducted in a manner substantially different than that described in the protocols submitted in the IND.

(v) The drug is being promoted or distributed for commercial purposes not justified by the requirements of the investigation or permitted by § 312.7.

(vi) The IND, or any amendment or report to the IND, contains an untrue statement of a material fact or omits material information required by this part.

(vii) The sponsor fails promptly to investigate and inform the Food and Drug Administration and all investigators of serious and unexpected adverse experiences in accordance with § 312.32 or fails to make any other report required under this part.

(viii) The sponsor fails to submit an accurate annual report of the investigations in accordance with § 312.33.

(ix) The sponsor fails to comply with any other applicable requirement of this part, Part 50, or Part 56.

(x) The IND has remained on inactive status for 5 years or more.

(2) *Phase 2 or 3.* FDA may propose to terminate an IND during Phase 2 or Phase 3 if FDA finds that:

(i) Any of the conditions in paragraphs (b)(1) (i) through (x) of this section apply; or

(ii) The investigational plan or protocol(s) is not reasonable as a bona fide scientific plan to determine whether or not the drug is safe and effective for use; or

(iii) There is convincing evidence that the drug is not effective for the purpose for which it is being investigated.

(3) FDA may propose to terminate a treatment IND if it finds that:

(i) Any of the conditions in paragraphs (b)(1)(i) through (x) of this section apply; or

(ii) Any of the conditions in § 312.42(b)(3) apply.

(c) *Opportunity for sponsor response.* (1) If FDA proposes to terminate an IND, FDA will notify the sponsor in writing, and invite correction or explanation within a period of 30 days.

(2) On such notification, the sponsor may provide a written explanation or correction or may request a conference with FDA to provide the requested explanation or correction. If the sponsor does not respond to the notification within the allocated time, the IND shall be terminated.

(3) If the sponsor responds but FDA does not accept the explanation or correction submitted, FDA shall inform the sponsor in writing of the reason for the nonacceptance and provide the sponsor with an opportunity for a regulatory hearing before FDA under Part 16 on the question of whether the IND should be terminated. The sponsor's request for a regulatory hearing must be made within 10 days of the sponsor's receipt of FDA's notification of nonacceptance.

(d) *Immediate termination of IND.* Notwithstanding paragraphs (a) through (c) of this section, if at any time FDA concludes that continuation of the investigation presents an immediate and substantial danger to the health of individuals, the agency shall immediately, by written notice to the sponsor from the Director of the Center for Drug Evaluation and Research or the Director of the Center for Biologics Evaluation and Research, terminate the IND. An IND so termi-

nated is subject to reinstatement by the Director on the basis of additional submissions that eliminate such danger. If an IND is terminated under this paragraph, the agency will afford the sponsor an opportunity for a regulatory hearing under Part 16 on the question of whether the IND should be reinstated.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11579, Mar. 29, 1990]

§ 312.45 Inactive status.

(a) If no subjects are entered into clinical studies for a period of 2 years or more under an IND, or if all investigations under an IND remain on clinical hold for 1 year or more, the IND may be placed by FDA on inactive status. This action may be taken by FDA either on request of the sponsor or on FDA's own initiative. If FDA seeks to act on its own initiative under this section, it shall first notify the sponsor in writing of the proposed inactive status. Upon receipt of such notification, the sponsor shall have 30 days to respond as to why the IND should continue to remain active.

(b) If an IND is placed on inactive status, all investigators shall be so notified and all stocks of the drug shall be returned or otherwise disposed of in accordance with § 312.59.

(c) A sponsor is not required to submit annual reports to an IND on inactive status. An inactive IND is, however, still in effect for purposes of the public disclosure of data and information under § 312.130.

(d) A sponsor who intends to resume clinical investigation under an IND placed on inactive status shall submit a protocol amendment under § 312.30 containing the proposed general investigational plan for the coming year and appropriate protocols. If the protocol amendment relies on information previously submitted, the plan shall reference such information. Additional information supporting the proposed investigation, if any, shall be submitted in an information amendment. Notwithstanding the provisions of § 312.30, clinical investigations under an IND on inactive status may only resume (1) 30 days after FDA receives the protocol amendment, unless FDA notifies the sponsor that the investigations described in the amendment are subject to a clinical hold under § 312.42, or (2) on earlier notification by FDA that the clinical investigations described in the protocol amendment may begin.

(e) An IND that remains on inactive status for 5 years or more may be terminated under § 312.44.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

§ 312.47 Meetings.

(a) *General.* Meetings between a sponsor and the agency are frequently useful in resolving questions and issues raised during the course of a clinical investigation. FDA encourages such meetings to the extent that they aid in the evaluation of the drug and in the solution of scientific problems concerning the drug, to the extent that FDA's resources permit. The general principle underlying the conduct of such meetings is that there should be free, full, and open communication about any scientific or medical question that may arise during the clinical investigation. These meetings shall be conducted and documented in accordance with Part 10.

(b) *"End-of-Phase 2" meetings and meetings held before submission of a marketing application.* At specific times during the drug investigation process, meetings between FDA and a sponsor can be especially helpful in minimizing wasteful expenditures of time and money and thus in speeding the drug development and evaluation process. In particular, FDA has found that meetings at the end of Phase 2 of an investigation (end-of-Phase 2 meetings) are of considerable assistance in planning later studies and that meetings held near completion of Phase 3 and before submission of a marketing application ("pre-NDA" meetings) are helpful in developing methods of presentation and submission of data in the





marketing application that facilitate review and allow timely FDA response.

(1) *End-of-Phase 2 meetings*—(i) *Purpose.* The purpose of an end-of-Phase 2 meeting is to determine the safety of proceeding to Phase 3, to evaluate the Phase 3 plan and protocols, and to identify any additional information necessary to support a marketing application for the uses under investigation.

(ii) *Eligibility for meeting.* While the end-of-Phase 2 meeting is designed primarily for IND's involving new molecular entities or major new uses of marketed drugs, a sponsor of any IND may request and obtain an end-of-Phase 2 meeting.

(iii) *Timing.* To be most useful to the sponsor, end-of-Phase 2 meetings should be held before major commitments of effort and resources to specific Phase 3 tests are made. The scheduling of an end-of-Phase 2 meeting is not, however, intended to delay the transition of an investigation from Phase 2 to Phase 3.

(iv) *Advance information.* At least 1 month in advance of an end-of-Phase 2 meeting, the sponsor should submit background information on the sponsor's plan for Phase 3, including summaries of the Phase 1 and 2 investigations, the specific protocols for Phase 3 clinical studies, plans for any additional nonclinical studies, and, if available, tentative labeling for the drug. The recommended contents of such a submission are described more fully in FDA Staff Manual Guide 4850.7 that is publicly available under FDA's public information regulations in Part 20.

(v) *Conduct of meeting.* Arrangements for an end-of-Phase 2 meeting are to be made with the division in FDA's Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research which is responsible for review of the IND. The meeting will be scheduled by FDA at a time convenient to both FDA and the sponsor. Both the sponsor and FDA may bring consultants to the meeting. The meeting should be directed primarily at establishing agreement between FDA and the sponsor of the overall plan for Phase 3 and the objectives and design of particular studies. The adequacy of technical information to support Phase 3 studies and/or a marketing application may also be discussed. Agreements reached at the meeting on these matters will be recorded in minutes of the conference that will be taken by FDA in accordance with § 10.65 and provided to the sponsor. The minutes along with any other written material provided to the sponsor will serve as a permanent record of any agreements reached. Barring a significant scientific development that requires otherwise, studies conducted in accordance with the agreement shall be presumed to be sufficient in objective and design for the purpose of obtaining marketing approval for the drug.

(2) *"Pre-NDA" meetings.* FDA has found that delays associated with the initial review of a marketing application may be reduced by exchanges of information about a proposed marketing application. The primary purpose of this kind of exchange is to uncover any major unresolved problems, to identify those studies that the sponsor is relying on as adequate and well-controlled to establish the drug's effectiveness, to acquaint FDA reviewers with the general information to be submitted in the marketing application (including technical information), to discuss appropriate methods for statistical analysis of the data, and to discuss the best approach to the presentation and formatting of data in the marketing application. Arrangements for such a meeting are to be initiated by the sponsor with the division responsible for review of the IND. To permit FDA to provide the sponsor with the most useful advice on preparing a marketing application, the sponsor should submit to FDA's reviewing division at least 1 month in advance of the meeting the following information:

(i) A brief summary of the clinical studies to be submitted in the application.

(ii) A proposed format for organizing the submission, including methods for presenting the data.

(iii) Any other information for discussion at the meeting.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11580, Mar. 29, 1990]

### § 312.48 Dispute resolution.

(a) *General.* The Food and Drug Administration is committed to resolving differences between sponsors and FDA reviewing divisions with respect to requirements for IND's as quickly and amicably as possible through the cooperative exchange of information and views.

(b) *Administrative and procedural issues.* When administrative or procedural disputes arise, the sponsor should first attempt to resolve the matter with the division in FDA's Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research which is responsible for review of the IND, beginning with the consumer safety officer assigned to the application. If the dispute is not resolved, the sponsor may raise the matter with the person designated as ombudsman, whose function shall be to investigate what has happened and to facilitate a timely and equitable resolution. Appropriate issues to raise with the ombudsman include resolving difficulties in scheduling meetings and obtaining timely replies to inquiries. Further details on this procedure are contained in FDA Staff Manual Guide 4820.7 that is publicly available under FDA's public information regulations in Part 20.

(c) *Scientific and medical disputes.* (1) When scientific or medical disputes arise during the drug investigation process, sponsors should discuss the matter directly with the responsible reviewing officials. If necessary, sponsors may request a meeting with the appropriate reviewing officials and management representatives in order to seek a resolution. Requests for such meetings shall be directed to the director of the division in FDA's Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research which is responsible for review of the IND. FDA will make every attempt to grant requests for meetings that involve important issues and that can be scheduled at mutually convenient times.

(2) The "end-of-Phase 2" and "pre-NDA" meetings described in § 312.47(b) will also provide a timely forum for discussing and resolving scientific and medical issues on which the sponsor disagrees with the agency.

(3) In requesting a meeting designed to resolve a scientific or medical dispute, applicants may suggest that FDA seek the advice of outside experts, in which case FDA may, in its discretion, invite to the meeting one or more of its advisory committee members or other consultants, as designated by the agency. Applicants may rely on, and may bring to any meeting, their own consultants. For major scientific and medical policy issues not resolved by informal meetings, FDA may refer the matter to one of its standing advisory committees for its consideration and recommendations.

[52 FR 8831, Mar. 19, 1987, as amended at 55 FR 11580, Mar. 29, 1990]

## Subpart D—Responsibilities of Sponsors and Investigators

### § 312.50 General responsibilities of sponsors.

Sponsors are responsibile for selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND, maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. Additional specific responsibilities of sponsors are described elsewhere in this part.

### § 312.52 Transfer of obligations to a contract research organization.

(a) A sponsor may transfer responsibility for any or all of the obligations set forth in this part to a contract research organization. Any such transfer shall be described in writing. If not all





obligations are transferred, the writing is required to describe each of the obligations being assumed by the contract research organization. If all obligations are transferred, a general statement that all obligations have been transferred is acceptable. Any obligation not covered by the written description shall be deemed not to have been transferred.

(b) A contract research organization that assumes any obligation of a sponsor shall comply with the specific regulations in this chapter applicable to this obligation and shall be subject to the same regulatory action as a sponsor for failure to comply with any obligation assumed under these regulations. Thus, all references to "sponsor" in this part apply to a contract research organization to the extent that it assumes one or more obligations of the sponsor.

### § 312.53 Selecting investigators and monitors.

(a) *Selecting investigators.* A sponsor shall select only investigators qualified by training and experience as appropriate experts to investigate the drug.

(b) *Control of drug.* A sponsor shall ship investigational new drugs only to investigators participating in the investigation.

(c) *Obtaining information from the investigator.* Before permitting an investigator to begin participation in an investigation, the sponsor shall obtain the following:

(1) A signed investigator statement (Form FDA-1572) containing:

(i) The name and address of the investigator;

(ii) The name and code number, if any, of the protocol(s) in the IND identifying the study(ies) to be conducted by the investigator;

(iii) The name and address of any medical school, hospital, or other research facility where the clinical investigation(s) will be conducted;

(iv) The name and address of any clinical laboratory facilities to be used in the study;

(v) The name and address of the IRB that is responsible for review and approval of the study(ies);

(vi) A commitment by the investigator that he or she:

(*a*) Will conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, the rights, or welfare of subjects;

(*b*) Will comply with all requirements regarding the obligations of clinical investigators and all other pertinent requirements in this part;

(*c*) Will personally conduct or supervise the described investigation(s);

(*d*) Will inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent and institutional review board review and approval are met;

(*e*) Will report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with § 312.64;

(*f*) Has read and understands the information in the investigator's brochure, including the potential risks and side effects of the drug; and

(*g*) Will ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

(vii) A commitment by the investigator that, for an investigation subject to an institutional review requirement under Part 56, an IRB that complies with the requirements of that part will be responsible for the initial and continuing review and approval of the clinical investigation and that the investigator will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others, and will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to the human subjects.

(viii) A list of the names of the subinvestigators (e.g., research fellows, residents) who will be assisting the investigator in the conduct of the investigation(s).

(2) *Curriculum vitae.* A curriculum vitae or other statement of qualifications of the investigator showing the

education, training, and experience that qualifies the investigator as an expert in the clinical investigation of the drug for the use under investigation.

(3) *Clinical protocol.* (i) For Phase 1 investigations, a general outline of the planned investigation including the estimated duration of the study and the maximum number of subjects that will be involved.

(ii) For Phase 2 or 3 investigations, an outline of the study protocol including an approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; the clinical uses to be investigated; characteristics of subjects by age, sex, and condition; the kind of clinical observations and laboratory tests to be conducted; the estimated duration of the study; and copies or a description of case report forms to be used.

(d) *Selecting monitors.* A sponsor shall select a monitor qualified by training and experience to monitor the progress of the investigation.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

**§ 312.55 Informing investigators.**

(a) Before the investigation begins, a sponsor (other than a sponsor-investigator) shall give each participating clinical investigator an investigator brochure containing the information described in § 312.23(a)(5).

(b) The sponsor shall, as the overall investigation proceeds, keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug, particularly with respect to adverse effects and safe use. Such information may be distributed to investigators by means of periodically revised investigator brochures, reprints or published studies, reports or letters to clinical investigators, or other appropriate means. Important safety information is required to be relayed to investigators in accordance with § 312.32.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

**§ 312.56 Review of ongoing investigations.**

(a) The sponsor shall monitor the progress of all clinical investigations being conducted under its IND.

(b) A sponsor who discovers that an investigator is not complying with the signed agreement (Form FDA-1572), the general investigational plan, or the requirements of this part or other applicable parts shall promptly either secure compliance or discontinue shipments of the investigational new drug to the investigator and end the investigator's participation in the investigation. If the investigator's participation in the investigation is ended, the sponsor shall require that the investigator dispose of or return the investigational drug in accordance with the requirements of § 312.59 and shall notify FDA.

(c) The sponsor shall review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator. The sponsors shall make such reports to FDA regarding information relevant to the safety of the drug as are required under § 312.32. The sponsor shall make annual reports on the progress of the investigation in accordance with § 312.33.

(d) A sponsor who determines that its investigational drug presents an unreasonable and significant risk to subjects shall discontinue those investigations that present the risk, notify FDA, all institutional review boards, and all investigators who have at any time participated in the investigation of the discontinuance, assure the disposition of all stocks of the drug outstanding as required by § 312.59, and furnish FDA with a full report of the sponsor's actions. The sponsor shall discontinue the investigation as soon as possible, and in no event later than 5 working days after making the determination that the investigation should be discontinued. Upon request, FDA will confer with a sponsor on the need to discontinue an investigation.





(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

**§ 312.57 Recordkeeping and record retention.**

(a) A sponsor shall maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug. These records are required to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment.

(b) A sponsor shall retain the records and reports required by this part for 2 years after a marketing application is approved for the drug; or, if an application is not approved for the drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and FDA has been so notified.

(c) A sponsor shall retain reserve samples of any test article and reference standard used in a bioequivalence or bioavailability study and release the reserve samples to FDA upon request, in accordance with, and for the period specified in, § 320.32 of this chapter.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 47038, Nov. 8, 1990]

**§ 312.58 Inspection of sponsor's records and reports.**

(a) *FDA inspection.* A sponsor shall upon request from any properly authorized officer or employee of the Food and Drug Administration, at reasonable times, permit such officer or employee to have access to and copy and verify any records and reports relating to a clinical investigation conducted under this part. Upon written request by FDA, the sponsor shall submit the records or reports (or copies of them) to FDA. The sponsor shall discontinue shipments of the drug to any investigator who has failed to maintain or make available records or reports of the investigation as required by this part.

(b) *Controlled substances.* If an investigational new drug is a substance listed in any schedule of the Controlled Substances Act (21 U.S.C. 801; 21 CFR Part 1308), records concerning shipment, delivery, receipt, and disposition of the drug, which are required to be kept under this part or other applicable parts of this chapter shall, upon the request of a properly authorized employee of the Drug Enforcement Administration of the U.S. Department of Justice, be made available by the investigator or sponsor to whom the request is made, for inspection and copying. In addition, the sponsor shall assure that adequate precautions are taken, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

**§ 312.59 Disposition of unused supply of investigational drug.**

The sponsor shall assure the return of all unused supplies of the investigational drug from each individual investigator whose participation in the investigation is discontinued or terminated. The sponsor may authorize alternative disposition of unused supplies of the investigational drug provided this alternative disposition does not expose humans to risks from the drug. The sponsor shall maintain written records of any disposition of the drug in accordance with § 312.57.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

**§ 312.60 General responsibilities of investigators.**

An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation. An investigator



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shall, in accordance with the provisions of Part 50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in § 50.23. Additional specific responsibilities of clinical investigators are set forth in this part and in Parts 50 and 56.

### § 312.61 Control of the investigational drug.

An investigator shall administer the drug only to subjects under the investigator's personal supervision or under the supervision of a subinvestigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized under this part to receive it.

### § 312.62 Investigator recordkeeping and record retention.

(a) *Disposition of drug.* An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under § 312.59.

(b) *Case histories.* An investigator is required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent to the investigation on each individual treated with the investigational drug or employed as a control in the investigation.

(c) *Record retention.* An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

### § 312.64 Investigator reports.

(a) *Progress reports.* The investigator shall furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained. The sponsor is required under § 312.33 to submit annual reports to FDA on the progress of the clinical investigations.

(b) *Safety reports.* An investigator shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately.

(c) *Final report.* An investigator shall provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

### § 312.66 Assurance of IRB review.

An investigator shall assure that an IRB that complies with the requirements set forth in Part 56 will be responsible for the initial and continuing review and approval of the proposed clinical study. The investigator shall also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

### § 312.68 Inspection of investigator's records and reports.

An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee





to have access to, and copy and verify any records or reports made by the investigator pursuant to § 312.62. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

### § 312.69 Handling of controlled substances.

If the investigational drug is subject to the Controlled Substances Act, the investigator shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

### § 312.70 Disqualification of a clinical investigator.

(a) If FDA has information indicating that an investigator has repeatedly or deliberately failed to comply with the requirements of this part, Part 50, or Part 56, or has submitted to the sponsor false information in any required report, the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research will furnish the investigator written notice of the matter complained of and offer the investigator an opportunity to explain the matter in writing, or, at the option of the investigator, in an informal conference. If an explanation is offered but not accepted by the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research, the investigator will be given an opportunity for a regulatory hearing under Part 16 on the question of whether the investigator is entitled to receive investigational new drugs.

(b) After evaluating all available information, including any explanation presented by the investigator, if the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, Part 50, or Part 56, or has deliberately or repeatedly submitted false information to the sponsor in any required report, the Commissioner will notify the investigator and the sponsor of any investigation in which the investigator has been named as a participant that the investigator is not entitled to receive investigational drugs. The notification will provide a statement of basis for such determination.

(c) Each IND and each approved application submitted under Part 314 containing data reported by an investigator who has been determined to be ineligible to receive investigational drugs will be examined to determine whether the investigator has submitted unreliable data that are essential to the continuation of the investigation or essential to the approval of any marketing application.

(d) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor who shall have an opportunity for a regulatory hearing under Part 16. If a danger to the public health exists, however, the Commissioner shall terminate the IND immediately and notify the sponsor of the determination. In such case, the sponsor shall have an opportunity for a regulatory hearing before FDA under Part 16 on the question of whether the IND should be reinstated.

(e) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the continued approval of the drug product for which the data were submitted cannot be justified, the Commissioner will proceed to withdraw approval of the drug product in accordance with the applicable provisions of the act.

(f) An investigator who has been determined to be ineligible to receive investigational drugs may be reinstated as eligible when the Commissioner determines that the investigator has presented adequate assurances that the investigator will employ investigational drugs solely in compliance with the

provisions of this part and of Parts 50 and 56.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11580, Mar. 29, 1990]

## Subpart E—Drugs Intended to Treat Life Threatening and Severely-debilitating Illnesses

AUTHORITY: Secs. 501, 502, 503, 505, 506, 507, 701, 52 Stat. 1049-1053 as amended, 1055-1056 as amended, 55 Stat. 851, 59 Stat. 463 as amended (21 U.S.C. 351, 352, 353, 355, 356, 357, 371); sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262); 21 CFR 5.10, 5.11.

SOURCE: 53 FR 41523, Oct. 21, 1988, unless otherwise noted.

### § 312.80 Purpose.

The purpose of this section is to establish procedures designed to expedite the development, evaluation, and marketing of new therapies intended to treat persons with life-threatening and severely-debilitating illnesses, especially where no satisfactory alternative therapy exists. As stated § 314.105(c) of this chapter, while the statutory standards of safety and effectiveness apply to all drugs, the many kinds of drugs that are subject to them, and the wide range of uses for those drugs, demand flexibility in applying the standards. The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated. The procedure outlined in this section should be interpreted consistent with that purpose.

### § 312.81 Scope.

This section applies to new drug, antibiotic, and biological products that are being studied for their safety and effectiveness in treating life-threatening or severely-debilitating diseases.

(a) For purposes of this section, the term "life-threatening" means:

(1) Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted; and

(2) Diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival.

(b) For purposes of this section, the term "severely debilitating" means diseases or conditions that cause major irreversible morbidity.

(c) Sponsors are encouraged to consult with FDA on the applicability of these procedures to specific products.

### § 312.82 Early consultation.

For products intended to treat life-threatening or severely-debilitating illnesses, sponsors may request to meet with FDA-reviewing officials early in the drug development process to review and reach agreement on the design of necessary preclinical and clinical studies. Where appropriate, FDA will invite to such meetings one or more outside expert scientific consultants or advisory committee members. To the extent FDA resources permit, agency reviewing officials will honor requests for such meetings

(a) *Pre-investigational new drug (IND) meetings.* Prior to the submission of the initial IND, the sponsor may request a meeting with FDA-reviewing officials. The primary purpose of this meeting is to review and reach agreement on the design of animal studies needed to initiate human testing. The meeting may also provide an opportunity for discussing the scope and design of phase 1 testing, and the best approach for presentation and formatting of data in the IND.

(b) *End-of-phase 1 meetings.* When data from phase 1 clinical testing are available, the sponsor may again request a meeting with FDA-reviewing officials. The primary purpose of this meeting is to review and reach agreement on the design of phase 2 controlled clinical trials, with the goal that such testing will be adequate to provide sufficient data on the drug's safety and effectiveness to support a decision on its approvability for marketing. The procedures outlined in § 312.47(b)(1) with respect to end-of-phase 2 conferences, including documentation of agreements reached, would also be used for end-of-phase 1 meetings.





### § 312.83 Treatment protocols.

If the preliminary analysis of phase 2 test results appears promising, FDA may ask the sponsor to submit a treatment protocol to be reviewed under the procedures and criteria listed in §§ 312.34 and 312.35. Such a treatment protocol, if requested and granted, would normally remain in effect while the complete data necessary for a marketing application are being assembled by the sponsor and reviewed by FDA (unless grounds exist for clinical hold of ongoing protocols, as provided in § 312.42(b)(3)(ii)).

### § 312.84 Risk-benefit analysis in review of marketing applications for drugs to treat life-threatening and severely-debilitating illnesses.

(a) FDA's application of the statutory standards for marketing approval shall recognize the need for a medical risk-benefit judgment in making the final decision on approvability. As part of this evaluation, consistent with the statement of purpose in § 312.80, FDA will consider whether the benefits of the drug outweigh the known and potential risks of the drug and the need to answer remaining questions about risks and benefits of the drug, taking into consideration the severity of the disease and the absence of satisfactory alternative therapy.

(b) In making decisions on whether to grant marketing approval for products that have been the subject of an end-of-phase 1 meeting under § 312.82, FDA will usually seek the advice of outside expert scientific consultants or advisory committees. Upon the filing of such a marketing application under § 314.101 or Part 601 of this chapter, FDA will notify the members of the relevant standing advisory committee of the application's filing and its availability for review.

(c) If FDA concludes that the data presented are not sufficient for marketing approval, FDA will issue (for a drug) a not approvable letter pursuant to § 314.120 of this chapter, or (for a biologic) a deficiencies letter consistent with the biological product licensing procedures. Such letter, in describing the deficiencies in the application, will address why the results of the research design agreed to under § 312.82, or in subsequent meetings, have not provided sufficient evidence for marketing approval. Such letter will also describe any recommendations made by the advisory committee regarding the application.

(d) Marketing applications submitted under the procedures contained in this section will be subject to the requirements and procedures contained in Part 314 or Part 600 of this chapter, as well as those in this subpart.

### § 312.85 Phase 4 studies.

Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain postmarketing (phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time.

### § 312.86 Focused FDA regulatory research.

At the discretion of the agency, FDA may undertake focused regulatory research on critical rate-limiting aspects of the preclinical, chemical/manufacturing, and clinical phases of drug development and evaluation. When initiated, FDA will undertake such research efforts as a means for meeting a public health need in facilitating the development of therapies to treat life-threatening or severely debilitating illnesses.

§ 312.87 Active monitoring of conduct and evaluation of clinical trials.

For drugs covered under this section, the Commissioner and other agency officials will monitor the progress of the conduct and evaluation of clinical trials and be involved in facilitating their appropriate progress.

§ 312.88 Safeguards for patient safety.

All of the safeguards incorporated within Parts 50, 56, 312, 314, and 600 of this chapter designed to ensure the safety of clinical testing and the safety of products following marketing approval apply to drugs covered by this section. This includes the requirements for informed consent (Part 50 of this chapter) and institutional review boards (Part 56 of this chapter). These safeguards further include the review of animal studies prior to initial human testing (§ 312.23), and the monitoring of adverse drug experiences through the requirements of IND safety reports (§ 312.32), safety update reports during agency review of a marketing application (§ 314.50 of this chapter), and postmarketing adverse reaction reporting (§ 314.80 of this chapter).

## Subpart F—Miscellaneous

§ 312.110 Import and export requirements.

(a) *Imports.* An investigational new drug offered for import into the United States complies with the requirements of this part if it is subject to an IND that is in effect for it under § 312.40 and: (1) The consignee in the United States is the sponsor of the IND; (2) the consignee is a qualified investigator named in the IND; or (3) the consignee is the domestic agent of a foreign sponsor, is responsible for the control and distribution of the investigational drug, and the IND identifies the consignee and describes what, if any, actions the consignee will take with respect to the investigational drug.

(b) *Exports.* An investigational new drug intended for export from the United States complies with the requirements of this part as follows:

(1) If an IND is in effect for the drug under § 312.40 and each person who receives the drug is an investigator named in the application; or

(2) If FDA authorizes shipment of the drug for use in a clinical investigation. Authorization may be obtained as follows:

(i) Through submission to the International Affairs Staff (HFY-50), Associate Commissioner for Health Affairs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, of a written request from the person that seeks to export the drug. A request must provide adequate information about the drug to satisfy FDA that the drug is appropriate for the proposed investigational use in humans, that the drug will be used for investigational purposes only, and that the drug may be legally used by that consignee in the importing country for the proposed investigational use. The request shall specify the quantity of the drug to be shipped per shipment and the frequency of expected shipments. If FDA authorizes exportation under this paragraph, the agency shall concurrently notify the government of the importing country of such authorization.

(ii) Through submission to the International Affairs Staff (HFY-50), Associate Commissioner for Health Affairs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, of a formal request from an authorized official of the government of the country to which the drug is proposed to be shipped. A request must specify that the foreign government has adequate information about the drug and the proposed investigational use, that the drug will be used for investigational purposes only, and that the foreign government is satisfied that the drug may legally be used by the intended consignee in that country. Such a request shall specify the quantity of drug to be shipped per shipment and the frequency of expected shipments.

(iii) Authorization to export an investigational drug under paragraph (b)(2)(i) or (ii) of this section may be revoked by FDA if the agency finds that the conditions underlying its authorization are not longer met.

(3) This paragraph applies only where the drug is to be used for the purpose of clinical investigation.





(4) This paragraph does not apply to the export of an antibiotic drug product shipped in accordance with the provisions of section 801(d) of the act.

(5) This paragraph does not apply to the export of new drugs (including biological products) approved for export under section 802 of the act or section 351(h)(1)(A) of the Public Health Service Act.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987]

§ 312.120 Foreign clinical studies not conducted under an IND.

(a) *Introduction.* This section describes the criteria for acceptance by FDA of foreign clinical studies not conducted under an IND. In general, FDA accepts such studies provided they are well designed, well conducted, performed by qualified investigators, and conducted in accordance with ethical principles acceptable to the world community. Studies meeting these criteria may be utilized to support clinical investigations in the United States and/or marketing approval. Marketing approval of a new drug or antibiotic drug based solely on foreign clinical data is governed by § 314.106.

(b) *Data submissions.* A sponsor who wishes to rely on a foreign clinical study to support an IND or to support an application for marketing approval shall submit to FDA the following information:

(1) A description of the investigator's qualifications;

(2) A description of the research facilities;

(3) A detailed summary of the protocol and results of the study, and, should FDA request, case records maintained by the investigator or additional background data such as hospital or other institutional records;

(4) A description of the drug substance and drug product used in the study, including a description of components, formulation, specifications, and bioavailability of the specific drug product used in the clinical study, if available; and

(5) If the study is intended to support the effectiveness of a drug product, information showing that the study is adequate and well controlled under § 314.126.

(c) *Conformance with ethical principles.* (1) Foreign clinical research is required to have been conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" (see paragraph (c)(4) of this section) or the laws and regulations of the country in which the research was conducted, whichever represents the greater protection of the individual.

(2) For each foreign clinical study submitted under this section, the sponsor shall explain how the research conformed to the ethical principles contained in the "Declaration of Helsinki" or the foreign country's standards, whichever were used. If the foreign country's standards were used, the sponsor shall explain in detail how those standards differ from the "Declaration of Helsinki" and how they offer greater protection.

(3) When the research has been approved by an independent review committee, the sponsor shall submit to FDA documentation of such review and approval, including the names and qualifications of the members of the committee. In this regard, a "review committee" means a committee composed of scientists and, where practicable, individuals who are otherwise qualified (e.g., other health professionals or laymen). The investigator may not vote on any aspect of the review of his or her protocol by a review committee.

(4) The "Declaration of Helsinki" states as follows:

RECOMMENDATIONS GUIDING PHYSICIANS IN BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

*Introduction*

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of

weakening the physical and mental condition of the patient."

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.

In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

*I. Basic Principles*

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.

3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.

8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing.

10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.

11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.

Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

*II. Medical Research Combined with Professional Care (Clinical Research)*

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering.

2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

3. In any medical study, every patient—including those of a control group, if any—should be assured of the best proven diagnostic and therapeutic method.

4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.

5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (I, 2).

6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

*III. Non-Therapeutic Biomedical Research Involving Human Subjects, (Non-Clinical Biomedical Research)*

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.

2. The subjects should be volunteers—either healthy persons or patients for whom the experimental design is not related to the patient's illness.

3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.

4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910–0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 56 FR 22113, May 14, 1991]







**§ 312.130 Availability for public disclosure of data and information in an IND.**

(a) The existence of an investigational new drug application will not be disclosed by FDA unless it has previously been publicly disclosed or acknowledged.

(b) The availability for public disclosure of all data and information in an investigational new drug application for a new drug or antibiotic drug will be handled in accordance with the provisions established in § 314.430 for the confidentiality of data and information in applications submitted in Part 314. The availability for public disclosure of all data and information in an investigational new drug application for a biological product will be governed by the provisions of §§ 601.50 and 601.51.

(c) Notwithstanding the provisions of § 314.430, FDA shall disclose upon request to an individual to whom an investigational new drug has been given a copy of any IND safety report relating to the use in the individual.

[52 FR 8831, Mar. 19, 1987. Redesignated at 53 FR 41523, Oct. 21, 1988]

**§ 312.140 Address for correspondence.**

(a) Except as provided in paragraph (b) of this section, a sponsor shall send an initial IND submission to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, Park Bldg., Rm. 214, 12420 Parklawn Dr., Rockville, MD 20852. On receiving the IND, FDA will inform the sponsor which one of the divisions in the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research is responsible for the IND. Amendments, reports, and other correspondence relating to matters covered by the IND should be directed to the appropriate division. The outside wrapper of each submission shall state what is contained in the submission, for example, "IND Application", "Protocol Amendment", etc.

(b) Applications for the products listed below should be submitted to the Division of Biological Investigational New Drugs (HFB-230), Center for Biologics Evaluation and Research, Food and Drug Administration, 8800

Rockville Pike, Bethesda, MD 20892. (1) Products subject to the licensing provisions of the Public Health Service Act of July 1, 1944 (58 Stat. 682, as amended (42 U.S.C. 201 et seq.)) or subject to Part 600; (2) ingredients packaged together with containers intended for the collection, processing, or storage of blood or blood components; (3) urokinase products; (4) plasma volume expanders and hydroxyethyl starch for leukapheresis; and (5) coupled antibodies, i.e., products that consist of an antibody component coupled with a drug or radionuclide component in which both components provide a pharmacological effect but the biological component determines the site of action.

(c) All correspondence relating to biological products for human use which are also radioactive drugs shall be submitted to the Division of Oncology and Radiopharmaceutical Drug Products (HFD–150), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, except that applications for coupled antibodies shall be submitted in accordance with paragraph (b) of this section.

(d) All correspondence relating to export of an investigational drug under § 312.110(b)(2) shall be submitted to the International Affairs Staff (HFY–50), Office of Health Affairs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910–0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 55 FR 11580, Mar. 29, 1990]

§ 312.145 Guidelines.

(a) FDA has made available guidelines under § 10.90(b) to help persons to comply with certain requirements of this part.

(b) The Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research maintain lists of guidelines that apply to the Centers' regulations. The lists state how a person can obtain a copy of each guideline. A request for a copy of the lists should be directed to the CDER Executive Secretariat Staff (HFD–8), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, for drug products, and the Congressional, Consumer, and International Affairs Staff (HFB–142), Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892, for biological products.

[52 FR 8831, Mar. 19, 1987, as amended at 55 FR 11580, Mar. 29, 1990; 56 FR 3776, Jan. 31, 1991; 57 FR 10814, Mar. 31, 1992]

## Subpart G—Drugs for Investigational Use in Laboratory Research Animals or in Vitro Tests

### § 312.160 Drugs for investigational use in laboratory research animals or in vitro tests.

(a) *Authorization to ship.* (1)(i) A person may ship a drug intended solely for tests in vitro or in animals used only for laboratory research purposes if it is labeled as follows:

CAUTION: Contains a new drug for investigational use only in laboratory research animals, or for tests in vitro. Not for use in humans.

(ii) A person may ship a biological product for investigational in vitro diagnostic use that is listed in § 312.2(b)(2)(ii) if it is labeled as follows:

CAUTION: Contains a biological product for investigational in vitro diagnostic tests only.

(2) A person shipping a drug under paragraph (a) of this section shall use due diligence to assure that the consignee is regularly engaged in conducting such tests and that the shipment of the new drug will actually be used for tests in vitro or in animals used only for laboratory research.

(3) A person who ships a drug under paragraph (a) of this section shall maintain adequate records showing the name and post office address of the expert to whom the drug is shipped and the date, quantity, and batch or code mark of each shipment and delivery. Records of shipments under paragraph (a)(1)(i) of this section are to be maintained for a period of 2 years after the shipment. Records





and reports of data and shipments under paragraph (a)(1)(ii) of this section are to be maintained in accordance with § 312.57(b). The person who ships the drug shall upon request from any properly authorized officer or employee of the Food and Drug Administration, at reasonable times, permit such officer or employee to have access to and copy and verify records required to be maintained under this section.

(b) *Termination of authorization to ship.* FDA may terminate authorization to ship a drug under this section if it finds that:

(1) The sponsor of the investigation has failed to comply with any of the conditions for shipment established under this section; or

(2) The continuance of the investigation is unsafe or otherwise contrary to the public interest or the drug is used for purposes other than bona fide scientific investigation. FDA will notify the person shipping the drug of its finding and invite immediate correction. If correction is not immediately made, the person shall have an opportunity for a regulatory hearing before FDA pursuant to Part 16.

(c) *Disposition of unused drug.* The person who ships the drug under paragraph (a) of this section shall assure the return of all unused supplies of the drug from individual investigators whenever the investigation discontinues or the investigation is terminated. The person who ships the drug may authorize in writing alternative disposition of unused supplies of the drug provided this alternative disposition does not expose humans to risks from the drug, either directly or indirectly (e.g., through food-producing animals). The shipper shall maintain records of any alternative disposition.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910–0014)

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987. Redesignated at 53 FR 41523, Oct. 21, 1988]

# PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG OR AN ANTIBIOTIC DRUG

### Subpart A—General Provisions



### Subpart B—Applications



### Subpart C—FDA Action on Applications



### Subpart D—Hearing Procedures for New Drugs

AUTHORITY: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 701, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 371, 376).

SOURCE: 50 FR 7493, Feb. 22, 1985, unless otherwise noted.

## Subpart A—General Provisions

### § 314.1 Scope of this part.

(a) This part sets forth procedures and requirements for the submission to, and the review by, the Food and Drug Administration of applications and abbreviated applications, as well as amendments, supplements, and postmarketing reports to them, by persons seeking or holding approval from FDA of the following:

(1) An application under section 505 of the Federal Food, Drug, and Cosmetic Act to market a new drug.

(2) An application under section 507 of the Federal Food, Drug, and Cosmetic Act to market an antibiotic drug.

(b) This part does not apply to drug products subject to licensing by FDA under the Public Health Service Act (58 Stat. 632 as amended (42 U.S.C. 201 et seq.)) and subchapter F of chapter I of title 21 of the Code of Federal Regulations.

(c) References in this part to regulations in the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.

### § 314.2 Purpose.

The purpose of this part is to establish an efficient and thorough drug review process in order to: (a) Facilitate the approval of drugs shown to be safe and effective; and (b) ensure the disapproval of drugs not shown to be safe and effective. These regulations are also intended to establish an effective system for FDA's surveillance of marketed drugs. These regulations shall be construed in light of these objectives.

### § 314.3 Definitions.

(a) The definitions and interpretations contained in section 201 of the act apply to those terms when used in this part.

(b) The following definitions of terms apply to this part:

*Act* means the Federal Food, Drug, and Cosmetic Act (sections 201-901, 52 Stat. 1040 et seq., as amended (21 U.S.C. 301-392)).

*Applicant* means any person who submits an application or abbreviated application or an amendment or supplement to them under this part to obtain Food and Drug Administration approval of a new drug or an antibiotic drug and any person who owns an approved application.

*Application* means both the application described under § 314.50 and the abbreviated application under § 314.55, including all amendments and supplements.

*Approvable letter* means a written communication to an applicant from FDA stating that the agency will approve the application if specific additional information or material is submitted or specific conditions are met. An approvable letter does not constitute approval of any part of an application and does not permit marketing of the drug that is the subject of the application.

*Approval letter* means a written communication to an applicant from FDA approving an application. An approval letter permits marketing of the drug product that is the subject of the application.

*Drug product* means a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

*Drug substance* means an active ingredient that is intended to furnish

# Acronyms

| | |
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| APhA | American Pharmaceutical Association |
| CMHS | Center for Mental Health Services |
| CSAP | Center for Substance Abuse Prevention |
| CSAT | Center for Substance Abuse Treatment |
| DEA | Drug Enforcement Administration |
| DHHS | Department of Health and Human Services |
| EIR | Establishment Inspectional Report |
| FDA | Food and Drug Administration |
| HIV | Human Immunodeficiency Virus |
| IND | Investigational New Drug |
| IV | Intravenous |
| LAAM | Levo-alpha Acetylmethadol |
| MTIP | Methadone Treatment Improvement Project |
| NADDIS | Narcotics and Dangerous Drugs Information System |
| NASADAD | National Association of State Alcohol and Drug Abuse Directors |
| NIDA | National Institute on Drug Abuse |
| NIMH | National Institute of Mental Health |
| SAMHSA | Substance Abuse and Mental Health Services Administration |
| SAODAP | Special Action Office for Drug Abuse Prevention |
| SAPT | Substance Abuse Prevention and Treatment |
| SMA | State Methadone Authority |

# Bibliography


Bloom, E. "Drugs Used for the Treatment of Narcotic Addicts." Unpublished draft report for the Methadone Coordination Project Workgroup, Office of National Drug Control Policy, Washington, DC, September 1991.

*Federal Register* 54(40): 8972-8976, March 2, 1989.

Greenstein, R.A.; Fudala, P.J.; and O'Brien, C.P. Alternative pharmacotherapies for opiate addiction. In: Lowinson, J.H.; Ruiz,P.; and Millman, R.B., eds. *Substance Abuse: A Comprehensive Textbook.* Baltimore: Williams and Wilkins, 1992.

Joseph, H., and Appel, P. Methadone maintenance treatment: Historical perspectives and public issues. In: *State Methadone Maintenance Treatment Guidelines,* Rockville, MD: Center for Substance Abuse Treatment, U.S. Dept. of Health and Human Services, 1992.

Parrino, M. Methadone maintenance in the 1990's. Office for Treatment Improvement *Treatment Improvement Exchange Communiqué* Spring 1992:13, 23–24.

*Public Law 89-793* Chapter 314: Narcotic addicts. Nov. 8, 1966.

*Public Law 91-513:Comprehensive Drug Abuse Prevention and Control Act* Oct. 27, 1970.

*Public Law 94-281:Amendment to the Controlled Substances Act,* May 14, 1974.

Reuter, N. Regulating methadone treatment programs: The FDA perspective. Office for Treatment Improvement *Treatment Improvement Exchange Communiqué,* Spring 1992:17–18.

21 CFR 291.501, 291.505: *Drugs Used for Treatment of Narcotic Addicts.*

U.S. Congress. House. *Hearings Before the Special Subcommittee on Alcoholism and Narcotics of the Committee on Labor and Public Welfare, United States of America,* No.91–1:118–126, 147–149, 232–234, 237–241, September 18-19, 1969.

U.S. Congress. House. *Narcotic Addict Treatment Act of 1974 Report,* HR 93–884. March 7, 1974.

U.S. Congress. House. Committee on Ways and Means. *Comparison of Bills to Regulate Controlled Substances and to Amend the Narcotic and Drug Laws.* GPO 48-646. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., August 8, 1970.

Zweben, J.E., and Payte, J.T. Methadone maintenance in the treatment of opioid dependence: A current perspective. *The Western Journal of Medicine,* Special Issue on Addiction Medicine, 152(5): 588-599, 1990.


☆ U.S. GOVERNMENT PRINTING OFFICE:1994-301-049/13639

DHHS Publication No. (SMA) 94-2082
Substance Abuse and Mental Health Services Administration
Printed 1994

SAMHSA