

Drug Abuse Handbook

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PREFACE

It is my hope that this book will be used both by scientists and the policymakers who determine where the research dollars are spent. Anyone who takes the time to read more than a few pages of this Handbook will encounter quite a few surprises, some good and some bad. The good news is that during the last decade, a tremendous amount has been learned about abused drugs. The bad news is that progress has not been equally rapid on all fronts. Molecular biologists and neurochemists who, perhaps not coincidentally receive the lion's share of federal funding, have made breathtaking advances. They are tantalizingly close to characterizing the basic mechanisms of addiction. Progress has been somewhat less dramatic on other fronts.

Testing workers for drugs has become a huge, competitive business. Market forces have ensured that the necessary research was done. Regulated urine drug testing is now a reliable and reasonably well-understood process. Yet, desperately needed studies to test the efficacy (as opposed to the accuracy) of workplace drug testing programs are not on the horizon, and we still do not know with any certainty whether the enormous amount of money being spent really has an effect on worker absenteeism, accident rates, and productivity.

In areas where government and industry share common interests, there has been impressive progress. Researchers interested in impairment testing have received sufficient funding to finally place this discipline on firm scientific footing. But practical workplace applications for impairment testing are hampered by the paucity of data relating blood, hair, sweat, and saliva drug concentrations with other workplace performance measures.

The use of alternate testing matrices poses a daunting challenge. Until very recently, alternate approaches to workplace testing were not permitted. There was little government interest, and no potential market in sight. With no money to be made, industry leaders saw no reason to invest in new technologies. Now it appears that pressure from private industry has altered government perceptions, and changes may be imminent. But a great deal of science remains to be done. In particular, basic pharmacokinetic research is needed to describe the disposition of abused drugs in alternate specimens. Without such data, the utility of alternate specimens is limited, and reliable interpretation of test results is nearly impossible.

Farther away from university and government laboratories, at the bedside and at the autopsy table, the picture is not quite so rosy. SAMHSA supported the development of LAAM, the long acting methadone substitute, and funding has gone into improving methadone maintenance programs. But methadone clinics are not ivory towers, and controlled studies with non-compliant patients are fiendishly difficult. Politicians intent on being "tough on drugs" have created a regulatory climate where control of treatment has largely been taken away from physicians, and political considerations outweigh reasoned scientific judgment. The recent suggestion by National Drug Control Policy Director Barry McCaffrey that physicians be allowed to prescribe methadone, may mark an important shift in the way our leaders address these problems.

Even so, research into the medical management of drug users is not exactly a priority issue. One might suppose that given the very sophisticated techniques now available for therapeutic drug monitoring, the kinetics of abused drugs would be well characterized. There are several reasons why they have not. Discounting the fact that such projects have little commercial appeal, and seem not to be a priority for our government (even though most of the important research has been done at the federally funded Addiction Research Center), the greatest handicaps are ethical and political. Drug abusers take drugs in quantities that no Institutional

Review Board would ever approve and that doctors would refuse to administer. Whether or not the body metabolizes 50 mg of cocaine given intravenously the same way it manages 250 mg is, for the moment, at least, anyone's guess. However, the results of recent studies from the Addiction Research Center suggest that chronic oral dosing with cocaine may allow researchers to simulate the high doses used on the street.

Cocaine and heroin abuse claim the lives of more than 15,000 Americans every year, but no pathologist sits on the advisory board that passes on drug research grants, and there is no federal funding for pathology or for pathologists interested in drug abuse. The sorry state of the DAWN report (Drug Abuse Warning Network) offers a hint of the importance our government accords to the investigation of drug-related deaths; results for 1995 were finally released in May of 1997! Three-year-old epidemiologic data may be of some interest to historians, but it certainly is of little value to clinicians.

At least the epidemiologic studies get funded. Lack of federal support means that a great many promising leads are being passed up. There is mounting evidence that chronic drug abuse produces identifiable morphologic changes in the heart, brain, lungs, and liver. But there are no federal funds to support the studies needed to translate these preliminary observations into useful diagnostic tools.

Toxicologists studying postmortem materials have done no better than the pathologists. Technologic innovations in workplace testing and therapeutic drug monitoring now allow the routine measurement of nanogram quantities of drugs in tissue obtained at autopsy, but the interpretation of these measurements is not a straightforward process. Even though postmortem drug concentrations are frequently debated in court, research on the interpretation of postmortem drug levels consists of little more than a handful of case reports, published by a few dedicated researchers. During the last decade, more than 50,000 Americans have died using cocaine, but postmortem tissue levels have only been reported in a handful of cases.

Even if the tissue levels were better characterized, tolerance occurs. It is impossible to speak of "lethal" and "non-lethal" cocaine and morphine concentrations because tolerant users may be unaffected by levels that would be lethal in naive drug users. But, poorly informed physicians and attorneys continue to ignore these subtleties, just as they continue to ignore the wealth of scientific knowledge that has been accumulated on the effects of alcohol, both in the living and the dead. The same legal arguments are debated again and again, even though the science has been very well worked out.

Important research remains to be done, yet we have already learned a great deal. Unfortunately, that knowledge is not being shared effectively, not with the rest of the medical community, not with the courts, and certainly not with drug policy makers. If we can do a better job of educating, then sometime in the not too distant future, we may be able to obtain the support for the work that we know needs to be done. I hope this book helps in that process.

THE EDITOR

Dr. Karch received his bachelors degree from Brown University, did graduate work in cell biology and biophysics at Stanford, and attended Tulane Medical School. He studied neuropathology at the Barnard Baron Institute in London, and cardiac pathology at Stanford. During the 1970s, he was a Medical Advisor for Bechtel in Southeast Asia. He is an Assistant Medical Examiner in San Francisco, where he consults on cases of drug-related death. His textbook, *The Pathology of Drug Abuse*, is used around the world, and is generally considered the standard reference on the subject. He and his wife, Donna, live in Berkeley, California.

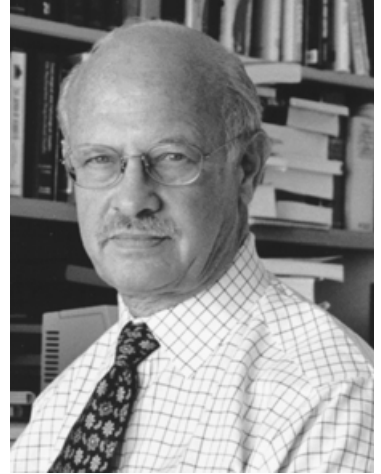


Photo courtesy of Brandon White, Berkeley, California

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DEDICATION

For RBT

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TABLE OF CONTENTS

- 1 **Criminalistics—Introduction to Controlled Substances** *Joseph P. Bono*
- 2 **Pathology of Drug Abuse** *Edited by Charles V. Wetli*
 - 2.1 **Preliminary Observations** *Charles V. Wetli*
 - 2.2 **Diseases of the Heart**
 - 2.2.1 **Techniques for Examination of the Heart** *Renu Virmani, Allen P. Burke, and Andrew Farb*
 - 2.2.2 **Myocardial Alterations in Drug Abusers** *Steven B. Karch*
 - 2.2.3 **Endocarditis** *Michael D. Bell*
 - 2.2.4 **Vascular Effects of Substance Abuse** *Frank D. Kolodgie, Allen Burke, Jagat Narula, Florabel G. Mullick, and Renu Virmani*
 - 2.3 **Lung Disease** *Michael D. Bell*
 - 2.4 **Disorders of the Central Nervous System** *Michael D. Bell*
 - 2.5 **Miscellaneous Complications** *Charles V. Wetli*
- 3 **Pharmacokinetics: Drug Absorption, Distribution, and Elimination** *Amanda J. Jenkins, and Edward J. Cone*
- 4 **Pharmacodynamics** *Edited by Stephen J. Heishman*
 - 4.1 **Effects of Abused Drugs on Human Performance: Laboratory Assessment** *Stephen J. Heishman*
 - 4.2 **Performance Measures of Behavioral Impairment in Applied Settings** *Thomas H. Kelly, Richard C. Taylor, Stephen J. Heishman, and Dennis J. Crouch*
 - 4.3 **Effects of Abused Drugs on Pupillary Size and the Light Reflex** *Wallace B. Pickworth, Reginald V. Fant, and Edward B. Bunker*
 - 4.4 **Evaluating Abuse Liability: Methods and Predictive Value** *Kenzie L. Preston, and Sharon L. Walsh*
- 5 **Alcohol** *Edited by Christopher S. Martin*
 - 5.1 **Measuring Acute Alcohol Impairment** *Christopher S. Martin*
 - 5.2 **Measuring Blood-Alcohol Concentration for Clinical and Forensic Purposes** *A. Wayne Jones and Derrick J. Pounder*
 - 5.3 **Measuring Alcohol Postmortem** *Derrick J. Pounder and A. Wayne Jones*
 - 5.4 **Biochemical Tests for Acute and Chronic Alcohol Ingestion** *Anders Helander and Alan Wayne Jones*
- 6 **Neurochemistry of Drug Abuse** *Edited by Deborah C. Mash and Julie K. Staley*
 - 6.1 **The Dopamine Transporter and Addiction** *John W. Boja and William M. Meil*
 - 6.2 **Neuropsychiatric Consequences of Chronic Cocaine Abuse** *Deborah C. Mash*
 - 6.3 **Neurochemical Adaptations and Cocaine Dependence** *Julie K. Staley*
 - 6.4 **The Neurobiology of Relapse** *David W. Self*

-
- 6.5 Serotonergic Dysfunction During Cocaine Withdrawal: Implications for Cocaine-Induced Depression *Michael H. Baumann and Richard B. Rothman*
 - 6.6 Neurochemistry of Psychedelic Drugs *J.C. Callaway and D.J. McKenna*
 - 7 Addiction Medicine *Edited by Kim Wolff*
 - 7.1 The Principles of Addiction Medicine *Duncan Raistrick*
 - 7.2 Substitute Prescribing *Kim Wolff*
 - 7.2.1.6 Buprenorphine Maintenance Prescribing *Douglas Fraser*
 - 7.3 Treatment of Withdrawal Syndromes *Joanna Banbery*
 - 7.4 Replacement Prescribing *Kim Wolff*
 - 7.4.1 Opiate Specific Prescribing *Douglas Fraser*
 - 7.5 Management of Comorbidity *Duncan Raistrick*
 - 7.6 Toxicologic Issues *Alastair W.M. Hay*
 - 8 Medical Complications of Drug Abuse *Edited by Neal L. Benowitz*
 - 8.1 Drug-Related Syndromes *Shoshana Zevin and Neal L. Benowitz*
 - 8.2 Emergency Management of Drug Abuse-Related Disorders *Brett A. Roth, Neal L. Benowitz, and Kent R. Olson*
 - 9 Sports *Edited by Jordi Segura*
 - 9.1 Introduction *Jordi Segura*
 - 9.2 Specific Agents *Rafael de la Torre*
 - 9.3 Anabolic Androgenic Steroids *Don H. Catlin*
 - 9.4 Detection of Exogenous Anabolic Androgenic Steroids *Wilhelm Schänzer*
 - 9.5 Growth Hormone Abuse in Elite Athletes *Ross C. Cuneo, Jennifer D. Wallace, and Peter Sönksen*
 - 9.6 Erythropoietin *Björn Ekblom*
 - 9.7 Summary of International Olympic Committee Regulations *Jordi Segura*
 - 10 Workplace Testing *Edited by Yale H. Caplan*
 - 10.1 Development and Scope of Regulated Testing *J. Michael Walsh*
 - 10.2 Laboratory Accreditation Programs
 - 10.2.1 An Overview of the Mandatory Guidelines for Federal Workplace Drug Testing Programs *Donna M. Bush*
 - 10.2.2 The College of American Pathologists Voluntary Laboratory Accreditation Program *John Baenziger*
 - 10.3 Analytical Considerations and Approaches for Drugs *Michael Peat and Alan E. Davis*
 - 10.4 Urine Specimen Suitability for Drug Testing *Ruth E. Winecker and Bruce A. Goldberger*
 - 10.5 The Role of the Medical Review Officer: Current Issues *Steven St. Clair*
 - 10.6 Alternative Drugs, Specimens, and Approaches for Non-Regulated Drug Testing *Dennis Crouch*
 - 10.7 Implementation of Alcohol Testing: General Considerations and Processes *Donna R. Smith*
 - 11 Alternative Testing Matrices *Marilyn A. Huestis and Edward J. Cone*
 - 12 Postmortem Toxicology *Edited by Wm. Lee Hearn*
 - 12.1 Introduction of Postmortem Toxicology *Wm. Lee Hearn and H. Chip Walls*
-

-
- 12.2 Specimen Selection, Collection, Preservation, and Security
Bradford R. Hepler and Daniel S. Isenschmid
 - 12.3 Common Methods in Postmortem Toxicology *Wm. Lee Hearn and
H. Chip Walls*
 - 12.4 Strategies for Postmortem Toxicology Investigation *Wm. Lee Hearn and
H. Chip Walls*
 - 12.5 Quality Assurance in Postmortem Toxicology *Wilmo Andollo*
 - 12.6 Interpretation of Postmortem Drug Levels *Graham R. Jones*

13 Drug Law

- 13.1 Current Legal Issues of Workplace Drug Testing *Theodore F. Shults*
- 13.2 DUI Defenses *Alan Wayne Jones and Barry Logan*
- 13.3 Fetal Rights *Stephen M. Mohaupt*

Appendices

- Ia Glossary of Terms in Forensic Toxicology *Chip Walls*
- Ib Common Abbreviations *Chip Walls*
- Ic References for Methods of Drug Quantitative Analysis
- II Sample Calculations *Barry K. Logan and Alan Wayne Jones*
- III Predicted Normal Heart Weight (g) as a Function of Body Height

CHAPTER 1

CRIMINALISTICS—INTRODUCTION TO CONTROLLED SUBSTANCES

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TABLE OF CONTENTS

- 1.1 *Definition and Scheduling of Controlled Substances*
- 1.2 *Scheduling of Controlled Substances*
- 1.3 *Controlled Substance Analogue Enforcement Act of 1986*
- 1.4 *Controlled Substances*
 - 1.4.1 *Heroin*
 - 1.4.1.1 *Heroin Sources by Region*
 - 1.4.1.2 *Isolation of Morphine and Heroin Production*
 - 1.4.2 *Cocaine*
 - 1.4.2.1 *Sources of Cocaine*
 - 1.4.2.2 *Historical Considerations*
 - 1.4.2.3 *Isolation and Purification*
 - 1.4.2.4 *Conversion to “Crack”*
 - 1.4.2.5 *Other Coca Alkaloids*
 - 1.4.2.6 *Cocaine Adulterants*
 - 1.4.3 *Marijuana*
 - 1.4.3.1 *History and Terminology*
 - 1.4.3.2 *Laboratory Analysis*
 - 1.4.4 *Peyote*
 - 1.4.5 *Psilocybin Mushrooms*
 - 1.4.6 *Lysergic Acid Diethylamide (LSD)*
 - 1.4.7 *Phencyclidine (PCP)*
 - 1.4.8 *Fentanyl*
 - 1.4.9 *Phenethylamines*
 - 1.4.10 *Methcathinone (CAT)*
 - 1.4.11 *Catha Edulis (KHAT)*
 - 1.4.12 *Anabolic Steroids*
 - 1.4.12.1 *Regulatory History*
 - 1.4.12.2 *Structure Activity Relationship*
 - 1.4.12.3 *Forensic Analysis*
- 1.5 *Legitimate Pharmaceutical Preparations*
 - 1.5.1 *Benzodiazepines*
 - 1.5.2 *Other Central Nervous System Depressants*

- 1.5.3 *Narcotic Analgesics*
- 1.5.4 *Central Nervous System Stimulants*
- 1.5.5 *Identifying Generic Products*
- 1.6 *Unique Identify Factors*
 - 1.6.1 *Packaging Logos*
 - 1.6.2 *Tablet Markings and Capsule Imprints*
 - 1.6.3 *Blotter Paper LSD*
- 1.7 *Analyzing Drugs in the Forensic Science Laboratory*
 - 1.7.1 *Screening Tests*
 - 1.7.1.1 *Physical Characteristics*
 - 1.7.1.2 *Color Tests*
 - 1.7.1.3 *Thin Layer Chromatography*
 - 1.7.2 *Confirmatory Chemical Tests*
 - 1.7.2.1 *Microcrystal Identifications*
 - 1.7.2.2 *Gas Chromatography*
 - 1.7.2.3 *High Performance Liquid Chromatography (HPLC)*
 - 1.7.2.4 *Capillary Electrophoresis (CE)*
 - 1.7.2.5 *Infrared Spectrophotometry (IR)*
 - 1.7.2.6 *Gas Chromatography/Mass Spectroscopy (GC/MS)*
 - 1.7.2.7 *Nuclear Magnetic Resonance (NMR) Spectroscopy*
 - 1.7.3 *Controlled Substances Examinations*
 - 1.7.3.1 *Identifying and Quantitating Controlled Substances*
 - 1.7.3.2 *Identifying Adulterants and Diluents*
 - 1.7.3.3 *Quantitating Controlled Substances*
 - 1.7.3.4 *Reference Standards*
- 1.8 *Comparative Analysis*
 - 1.8.1 *Determining Commonality of Source*
 - 1.8.2 *Comparing Heroin Exhibits*
 - 1.8.3 *Comparing Cocaine Exhibits*
- 1.9 *Clandestine Laboratories*
 - 1.9.1 *Safety Concerns*
 - 1.9.2 *Commonly Encountered Chemicals in the Clandestine Laboratory*
 - 1.9.3 *Tables of Controlled Substances*
 - 1.9.3.1 *Generalized List by Category of Physiological Effects and Medical Uses of Controlled Substances*
 - 1.9.3.2 *Listing of Controlled Substances by Schedule Number*

1.1 DEFINITION AND SCHEDULING OF CONTROLLED SUBSTANCES

A “controlled substance” is a drug or substance of which the use, sale, or distribution is regulated by the federal government or a state government entity. These controlled substances are listed specifically or by classification on the federal level in the Controlled Substances Act (CSA) or in Part 1308 of the Code of Federal Regulations. The purpose of the CSA is to minimize the quantity of useable substances available to those who are likely to abuse them. At the same time, the CSA provides for the legitimate medical, scientific, and industrial needs of these substances in the U.S.

1.2 SCHEDULING OF CONTROLLED SUBSTANCES

Eight factors are considered when determining whether or not to schedule a drug as a controlled substance:

1. Actual or relative potential for abuse.
2. Scientific evidence of pharmacological effect.
3. State of current scientific knowledge.
4. History of current pattern of abuse.
5. Scope, duration, and significance of abuse.
6. Risk to the public health.
7. Psychic or physiological dependence liability.
8. Immediate precursor.

The definition of potential for abuse is based upon an individual taking a drug of his own volition in sufficient amounts to cause a health hazard to himself or to others in the community. Data is then collected to evaluate three factors: (1) actual abuse of the drug; (2) the clandestine manufacture of the drug; (3) trafficking and diversion of the drug or its precursors from legitimate channels into clandestine operations. Pre-clinical abuse liability studies are then conducted on animals to evaluate physiological responses to the drug. At this point, clinical abuse liability studies can be conducted with human subjects, which evaluate preference studies and epidemiology.

Accumulating scientific evidence of a drug's pharmacological effects involves examining the scientific data concerning whether the drug elicits a stimulant, depressant, narcotic, or hallucinogenic response. A determination can then be made as to how closely the pharmacology of the drug resembles that of other drugs that are already controlled.

Evidence is also accumulated about the scientific data on the physical and chemical properties of the drug. This can include determining which salts and isomers are possible and which are available. There is also a concern for the ease of detection and identification using analytical chemistry. Since many controlled substances have the potential for clandestine synthesis, there is a requirement for evaluating precursors, possible synthetic routes, and theoretical yields in these syntheses. At this phase of the evaluation, medical uses are also evaluated.

The next three factors—(1) history and patterns of abuse; (2) scope, duration, and significance of abuse; and (3) risks to public health—all involve sociological and medical considerations. The results of these studies focus on data collection and population studies. Psychic and physiological dependence liability studies must be satisfied for a substance to be placed into Schedules II through V. This specific finding is not necessary to place a drug into Schedule I. A practical problem here is that it is not always easy to prove a development of dependence.

The last factor is one that can involve the forensic analyst. Under the law, an “immediate precursor” is defined as a substance that is an immediate chemical intermediary used or likely to be used in the manufacture of a specific controlled substance. Defining synthetic pathways in the clandestine production of illicit controlled substances requires knowledge possessed by the experienced analyst.

A controlled substance will be classified and named in one of five schedules. Schedule I includes drugs or other substances that have a high potential for abuse, no currently accepted use in the treatment of medical conditions, and little, if any, accepted safety criteria under the supervision of a medical professional. Use of these substances will almost always lead to abuse and dependence. Some of the more commonly encountered Schedule I controlled substances

are heroin, marijuana, lysergic acid diethylamide (LSD), 3,4-methylenedioxy-amphetamine (MDA), and psilocybin mushrooms.

Progressing from Schedule II to schedule V, abuse potential decreases. Schedule II controlled substances also include drugs or other substances that have a high potential for abuse, but also have some currently accepted, but severely restricted, medical uses. Abuse of Schedule II substances may lead to dependence which can be both physical and/or psychological. Because Schedule II controlled substances do have some recognized medical uses, they are usually available to health professionals in the form of legitimate pharmaceutical preparations. Cocaine hydrochloride is still used as a topical anesthetic in some surgical procedures. Methamphetamine, up until a few years ago, was used in the form of Desoxyn to treat hyperactivity in children. Raw opium is included in Schedule II. Amobarbital and secobarbital, which are used as central nervous system depressants are included, as is phencyclidine (PCP) which was used as a tranquilizer in veterinary pharmaceutical practices. In humans, PCP acts as a hallucinogen. Though many of the substances seized under Schedule II were not prepared by legitimate pharmaceutical entities, cocaine hydrochloride and methamphetamine are two examples of Schedule II drugs which, when confiscated as white to off-white powder or granules in plastic or glassine packets, have almost always been prepared on the illicit market for distribution. As one progresses from Schedules III through V, most legitimate pharmaceutical preparations will be encountered.

1.3 CONTROLLED SUBSTANCE ANALOGUE ENFORCEMENT ACT OF 1986

In recent years, the phenomenon of controlled substance analogues and homologues has presented a most serious challenge to the control of drug trafficking and successful prosecution of clandestine laboratory operators. These homologues and analogues are synthesized drugs that are chemically and pharmacologically similar to substances that are listed in the Controlled Substances Act, but which themselves are not specifically controlled by name. (The term “designer drug” is sometimes used to describe these substances.) The concept of synthesizing controlled substances analogues in an attempt to circumvent existing drug law was first noticed in the late 1960s. At about this time there were seizures of clandestine laboratories engaged in the production of analogues of controlled phenethylamines. In the 1970s variants of methaqualone and phencyclidine were being seized in clandestine laboratories. By the 1980s, Congress decided that the time had come to deal with this problem with a federal law enforcement initiative. The Controlled Substance Analogue Enforcement Act of 1986 amends the Comprehensive Drug Abuse Prevention and Control Act of 1970 by including the following section:

Section 203. A controlled substance analogue shall to the extent intended for human consumption, be treated, for the purposes of this title and title III as a controlled substance in schedule I.

The 99th Congress went on to define the meaning of the term “controlled substance analogue” as a substance:

- (i) the chemical structure of which is substantially similar to the chemical structure of a controlled substance in schedule I or II;
- (ii) which has a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II; or

(iii) with respect to a particular person, which person represents or intends to have a stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II.”

The Act goes on to exclude:

- (i) a controlled substance
- (ii) any substance for which there is an approved new drug application
- (iii) with respect to a particular person any substance, if an exemption is in effect for investigational use, for that person, under section 505...to the extent conduct with respect to such substance is pursuant to such exemption; or
- (iv) any substance to the extent not intended for human consumption before such an exemption takes effect with respect to that substance.

Treatment of exhibits falling under the purview of the federal court system is described in Public Law 91-513 or Part 1308 of the Code of Federal Regulations. Questions relating to controlled substance analogues and homologues can usually be answered by reference to the Controlled Substances Analogue and Enforcement Act of 1986.

1.4 CONTROLLED SUBSTANCES

1.4.1 HEROIN

Whenever one thinks about drugs of abuse and addiction, heroin is one of the most recognized drugs. Heroin is a synthetic drug, produced from the morphine contained in the sap of the opium poppy. The abuse of this particular controlled substance has been known for many years. The correct chemical nomenclature for heroin is O³, O⁶-diacetylmorphine. Heroin is synthesized from morphine in a relatively simple process. The first synthesis of diacetylmorphine reported in the literature was in 1875 by two English chemists, G.H. Beckett and C.P. Alder Wright.¹ In 1898 in Eberfeld, Germany, the Farbenfabriken vorm Friedrich Bayer and Company produced the drug commercially. An employee of the company, H. Dresser, named the morphine product “Heroin”.² There is no definitive documentation as to where the name “heroin” originated. However, it probably had its origin in the “heroic remedies” class of drugs of the day.

Heroin was used in place of codeine and morphine for patients suffering from lung diseases such as tuberculosis. Additionally, the Bayer Company advertised heroin as a cure for morphine addiction. The analgesic properties of the drug were very effective. However, the addictive properties were quite devastating. In 1924, Congress amended the Narcotic Drug Import and Export Act to prohibit the importation of opium for the manufacture of heroin. However, stockpiles were still available and could be legally prescribed by physicians. The 1925 International Opium Convention imposed drug controls that began to limit the supply of heroin from Europe. Shortly thereafter, the clandestine manufacture of heroin was reported in China. The supplies of opium in the Far East provided a ready source of morphine—the starting material for the synthesis. The medical use of heroin in the U.S. was not banned until July 19, 1956 with the passage of Public Law 728, which required all inventories to be surrendered to the federal government by November 19, 1956.

In the past 50 or so years, the source countries for opium used in clandestine heroin production have increased dramatically. Political and economic instability in many areas of the world account for much of the increased production of heroin. The opium that is used to produce the heroin that enters the U.S. today has four principal sources. Geographically all of these regions are characterized by a temperate climate with appropriate rainfall and proper soil conditions. However, there are differences in the quality of opium, the morphine content, and the number of harvests from each of these areas. Labor costs are minimal and the profit margins are extremely high for those in the upper echelons of heroin distribution networks.

1.4.1.1 Heroin Sources by Region

The “Golden Triangle” areas of Burma, China, and Laos are the three major source countries in this part of the world for the production of illicit opium. Of these three countries, 60 to 80% of the total world supply of heroin comes from Burma. Heroin destined for the U.S. transits a number of countries including Thailand, Hong Kong, Japan, Korea, the Philippines, Singapore, and Taiwan. Southeast Asian heroin is usually shipped to the U.S. in significant quantities by bulk cargo carriers. The techniques for hiding the heroin in the cargo are quite ingenious. The shipment of Southeast Asian (SEA) Heroin in relatively small quantities is also commonplace. Criminal organizations in Nigeria have been deeply involved in the small quantity smuggling of SEA heroin into the U.S. The “body carry” technique and ingestion are two of the better known methods of concealment by the Nigerians. SEA heroin is high quality and recognized by its white crystalline appearance. Though the cutting agents are numerous, caffeine and acetaminophen appear quite frequently.

Southwest Asia—Turkey, Iraq, Iran, Afghanistan, Pakistan, India, Lebanon, and the Newly Independent States of the former Soviet Union (NIS) are recognized as source countries in this part of the world. Trafficking of Southwest Asian heroin has been on the decline in the U.S. since the end of 1994. Southwest Asian heroin usage is more predominant in Europe than in the U.S. The Southwest Asian heroin that does arrive in the U.S. is normally transhipped through Europe, Africa, and the NIS. The political and economic conditions of the NIS and topography of the land make these countries ideal as transit countries for heroin smuggling. The rugged mountainous terrain and the absence of significant enforcement efforts enable traffickers to proceed unabated. Most Southwest Asian heroin trafficking groups in the originating countries, the transitting countries, and the U.S. are highly cohesive ethnic groups. These groups rely less on the bulk shipment and more on smaller quantity commercial cargo smuggling techniques. Southwest Asian heroin is characterized by its off-white to tan powdery appearance as compared to the white SEA heroin. The purity of Southwest Asian heroin is only slightly lower than that of SEA heroin. The cutting agents are many. Phenobarbital, caffeine, acetaminophen, and calcium carbonate appear quite frequently.

Central America—Mexico and Guatemala are the primary source countries for heroin in Central America. Mexico’s long border with the U.S. provides easy access for smuggling and distribution networks. Smuggling is usually small scale and often involves illegal immigrants and migrant workers crossing into the U.S. Heroin distribution in the U.S. is primarily the work of Mexican immigrants from the States of Durango, Michoacan, Nuevo Leon, and Sinaloa. Concealment in motor vehicles, public transportation, external body carries, and commercial package express are common. This heroin usually ranges from a dark brown powder to a black tar. The most commonly encountered adulterants are amorphous (formless and indeterminate) materials and sugars. The dark color of Mexican heroin is attributed to processing by-products. The purity of Mexican heroin varies greatly from seizure to seizure.

South America—Heroin production in this part of the world is a relatively new phenomenon. Cultivation of opium has been documented along the Andean mountain range within Colombia in the areas of Cauca, Huila, Tolima, and Santaner. There have been a number of

morphine base and heroin processing facilities seized in Colombia in the past few years. Smuggling of South American heroin into the U.S. increased dramatically in 1994 and 1995. The primary method of smuggling has been by Colombian couriers aboard commercial airliners using false-sided briefcases and luggage, hollowed out shoes, or by ingestion. Miami and New York are the primary ports of entry into the U.S. One advantage which the traffickers from South America have is the importation networks that are already in place for the distribution of cocaine into the U.S. Transshipment of this heroin through other South American countries and the Caribbean is also a common practice. South American heroin has many of the same physical characteristics of Southwest Asian heroin. However, the purity of South American heroin is higher with fewer adulterants than Southwest Asian heroin. Cocaine in small quantities is oftentimes encountered in South American heroin exhibits. In such cases, it is not always clear whether the cocaine is present as a contaminant introduced due to common packaging locations of cocaine and heroin, or whether it has been added as an adulterant.

1.4.1.2 Isolation of Morphine and Heroin Production

There are some very specific methods for producing heroin. However, all involve the same four steps: (1) The opium poppy (*Papaver Somniferum L.*) is cultivated; (2) the poppy head is scored and the opium latex is collected; (3) the morphine is isolated from the latex; and (4) the morphine is treated with an acetylating agent. Isolation of the morphine in Step 3 is accomplished using a rendition of one of the following five methods:

- 1. The Thiboumery and Mohr Process (TMP)**—This is the most well known of the reported methods for isolating morphine followed by the acetylation to heroin. Dried opium latex is dissolved in three times its weight of hot water. The solution is filtered hot which removes undissolved botanical substances. These undissolved botanicals are washed with hot water and filtered. This is done to ensure a maximized yield of morphine in the final product. The filtrate is reduced to half its volume by boiling off the water. The laboratory operator then adds to the filtrate a boiling solution of calcium hydroxide which forms the water soluble calcium morphinate. The precipitates, which include the insoluble alkaloids from the opium, and the insoluble materials from this step are filtered. These insolubles are then washed three more times with water and filtered. The resulting filtrate, which contains calcium morphinate still in solution, is then evaporated to a weight of approximately twice the weight of the original weight of the opium and then filtered. This results in a concentrated calcium morphinate solution which is heated to a boil. Ammonium chloride is then added to reduce the pH below 9.85. When this solution cools, morphine base precipitates and is collected by filtration. The morphine base is dissolved in a minimum volume of warm hydrochloric acid. When this solution cools the morphine hydrochloride precipitates. The precipitated morphine hydrochloride is then isolated by filtration.
- 2. The Robertson and Gregory Process (RGP)**—This method is similar to the Thiboumery and Mohr Process. The laboratory operator washes the opium with five to ten times its weight of cold water. The solution is then evaporated to a syrup which is then re-extracted with cold water and filtered. The filtrate is evaporated until the specific gravity of the solution is 1.075. The solution is boiled and calcium chloride is added. Cold water is added to the calcium morphinate solution which is then filtered. The solution is concentrated and the calcium morphinate then precipitates out of solution as the liquid evaporates. The calcium morphinate is then redissolved in water and filtered. To the filtrate is added ammonia which allows the

morphine base to precipitate. This morphine base can then be further treated to produce the pharmaceutical quality morphine.

The Thiboumery and Mohr Process and the Robertson and Gregory Process are used by commercial suppliers for the initial isolation of morphine from opium. In clandestine laboratories, the same methodologies and rudimentary steps are followed. However, since the operators are using “bucket chemistry”, there are modifications to hasten and shortcut the processes.

Three other methods can then be utilized to convert the relatively crude morphine base through purification processes to high quality morphine base or morphine hydrochloride crystals. Modifications of these purifications are used by clandestine laboratory operators.

- 3. The Barbier Purification**—The morphine base is dissolved in 80°C water. Tartaric acid is added until the solution becomes acidic to methyl orange. As the solution cools, morphine bitartrate precipitates, is filtered, washed with cold water, and dried. The morphine bitartrate is then dissolved in hot water and ammonia is added to pH 6. This results in a solution of morphine monotartrate. The laboratory operator then adds activated carbon black, sodium bisulfite, sodium acetate, and ammonium oxalate. This process results in a decolorization of the morphine. When this decolorization process is complete, ammonia is added to the solution which results in white crystals of morphine base. These purified morphine base crystals are then filtered and dried. This high quality morphine base is converted to morphine hydrochloride by adding 30% ethanolic HCl to a warm solution of morphine in ethanol. The morphine hydrochloride crystallizes from solution as the solution cools.
- 4. The Schwyzer Purification**—The acetone insoluble morphine base (from either the TMB or RGP) is washed in with acetone. The morphine base is then re-crystallized from hot ethyl alcohol.
- 5. The Heumann Purification**—The laboratory operator washes the morphine base (from either the TMB or RGP) with trichloroethylene, followed by a cold 40% ethanol wash. This is subsequently followed by an aqueous acetone wash.

The quality of the clandestine product is usually evaluated by the color and texture of the morphine from one of these processes. If the clandestine laboratory operator is producing morphine as his end product, with the intention of selling the morphine for conversion by a second laboratory, the morphine will usually be very pure. However, if he continues with the acetylation of the morphine to heroin, the “intermediate” morphine will frequently be relatively impure.

Heroin can be produced synthetically, but requires a 10-step process and extensive expertise in synthetic organic chemistry. The total synthesis of morphine has been reported by Gates and Tschudi in 1952 and by Elad and Ginsburg in 1954.^{3,4} A more recent synthesis was reported by Rice in 1980.⁵ All of these methods require considerable forensic expertise and result in low yield. There are also methods reported in the literature for converting codeine to morphine using an O-demethylation. The morphine can then be acetylated to heroin. One of these procedures is referred to as “homebake” and was described in the literature by Rapoport et al.⁶ This particular procedure has been reported only in New Zealand and Australia.

Acetylation of Morphine to Diacetylmorphine (Heroin)—This process involves placing dried morphine into a reaction vessel and adding excess acetic anhydride (Figure 1.4.1.2). Sometimes a co-solvent is also used. The mixture is heated to boiling and stirred for varying periods of time ranging from 30 min up to 3 or 4 h. The vessel and contents are cooled and diluted in cold water. A sodium carbonate solution is then added until precipitation of the

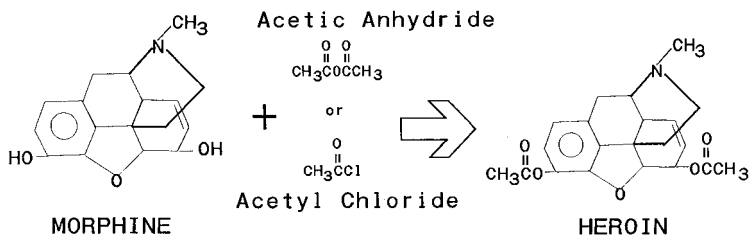


Figure 1.4.1.2 Clandestine laboratory synthesis of heroin

heroin base is complete and settles to the bottom of the reaction vessel. The heroin base is then either filtered and dried, or undergoes further processing to enhance the purity or to convert the base to heroin hydrochloride.

Processing By-Products and Degradation Products in Heroin—Pharmaceutical grade heroin has a purity of greater than 99.5%. Impurities include morphine, the O-3- and O-6-monoacetylmorphines, and other alkaloidal impurities and processing by-products. The impurities found in clandestinely produced heroin include but are certainly not limited to: the monoacetylmorphines, morphine, codeine, acetylcodeine, papaverine, noscapine, thebaine, meconine, thebaol, acetylthebaol, norlaudanisine, reticuline, and codamine. These impurities (from both quantitative and qualitative perspectives) are retained as the result of anomalies in processing methodologies.

REFERENCES

1. Anon. Heroin, *J. Chem. Soc. London*, 28: 315-318, 1875.
2. Anon. Heroin, *Arch. Gesam. Physiologie*, 72: 487, 1898.
3. Gates, M. and Tschudi, G., The synthesis of morphine, *J. Am. Chem. Soc.*, 74: 1109-1110, 1952.
4. Elad, E. and Ginsburg, D., The synthesis of morphine, *J. Am. Chem. Soc.*, 76: 312-313, 1954.
5. Rice, K.C., Synthetic opium alkaloids and derivatives. A short total synthesis of (+)-dihydrothebainone, (+)-dihydrocodinone, and (+)-nordihydrocodinone as an approach to the practical synthesis of morphine, codeine, and congeners, *J. Org. Chem.*, 45: 3135-3137, 1980.
6. Rapoport, H. and Bonner, R.M., Delta-7-desoxymorphine, *J. Am. Chem. Soc.*, 73:5485, 1951.

1.4.2 COCAINE

The social implications of cocaine abuse in the U.S. have been the subject of extensive media coverage during much of the 1980s and most of the 1990s. As a result, the general public has acquired some of the terminology associated with the cocaine usage. “Smoking crack” and “snorting coke” are terms that have become well understood in the American culture from elementary school through adulthood. However, there are facts associated with this drug which are not well understood by the general public. There are documented historical aspects associated with coca and cocaine abuse which go back 500 years. Recognizing some of these historical aspects enables the public to place today’s problem in perspective. Cocaine addiction has been with society for well over 100 years.

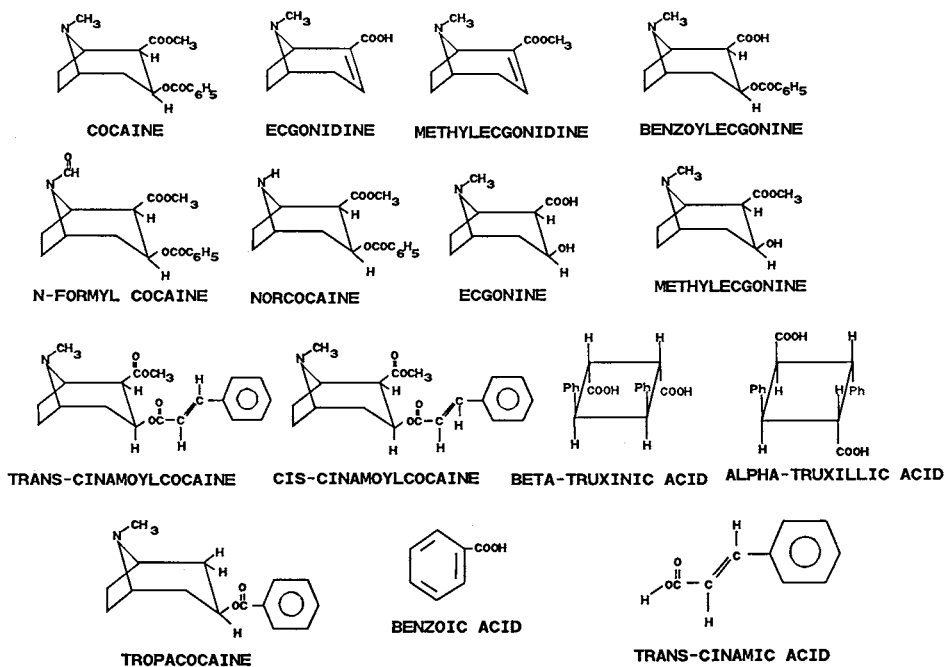


Figure 1.4.2.1

There are four areas of interest this section will address: (1) Where does cocaine come from? (2) How is cocaine isolated from the coca plant? (3) What does one take into the body from cocaine purchased on the street? (4) How does the chemist analyzing the drug identify and distinguish between the different forms of cocaine?

Cocaine is a Schedule II controlled substance. The wording in Title 21, Part 1308.12(b)(4) of the Code of Federal Regulations states:

Coca leaves (9040) and any salt, compound, derivative or preparation of coca leaves (including cocaine (9041) and ecgonine (9180) and their salts, isomers, derivatives and salts of isomers and derivatives), and any salt, compound, derivative, or preparation thereof which is chemically equivalent or identical with any of these substances, except that the substances shall not include decocanized coca leaves, or extractions of coca leaves, do not contain cocaine or ecgonine.

It is significant that the term “coca leaves” is the focal point of that part of the regulation controlling cocaine. The significance of this fact will become more apparent as this discussion progresses.

1.4.2.1 Sources of Cocaine

Cocaine is just one of the alkaloidal substances present in the coca leaf. Other molecules, some of them psychoactive (norcocaine being the most prominent) are shown in Figure 1.4.2.1 Cocaine is extracted from the leaves of the coca plant. The primary of source of cocaine imported into the U.S. is South America, but the coca plant also grows in the Far East in Ceylon, Java, and India. The plant is cultivated in South America on the eastern slopes of the Andes in Peru, and Bolivia. There are four varieties of coca plants — *Erythroxylon coca* var. *coca* (ECVC), *Erythroxylon coca* var. *ipadu*, *Erythroxylum novogranatense* var. *novogranatense*, and

Erythroxylum novogranatense var. *truxillense*.¹⁻³ ECVC is the variety that has been used for the manufacture of illicit cocaine. While cultivated in many countries of South America, Peru and Bolivia are the world's leading producers of the coca plant. Cocaine is present in the coca leaves from these countries at dry weight concentrations of from 0.1 to 1%. The average concentration of cocaine in the leaf is 0.7%. The coca shrub has a life expectancy of 50 years and can be harvested three or four times a year.

The method of isolating cocaine from the coca leaf does not require a high degree of technical expertise or experience. It requires no formal education or expensive scientific equipment or chemicals. In most instances the methodology is passed from one generation to the next.

1.4.2.2 Historical Considerations

Prior to the 1880s, the physiological properties of cocaine and the coca leaf were not readily distinguishable in the literature. During that year, H.H. Rusby and W.G. Mortimer made the distinction between the physiological properties of "isolated" cocaine and the coca leaf. Mortimer wrote,

...the properties of cocaine, remarkable as they are, lie in an altogether different direction from those of coca.¹

In 1884, two significant papers appeared in the literature. Sigmund Freud published the first of his five papers on the medicinal properties of cocaine.² A few months later, Karl Koller discovered the use of cocaine as local anesthetic.^{2A} In 1886, Sir Arthur Conan Doyle, an eye specialist who had studied at Vienna General Hospital, where Freud and Koller made their discoveries, made reference to Sherlock Holmes' use of cocaine in *The Sign of Four*.³ During the same year in Atlanta, Georgia, John Pemberton introduced to this country, caught up in the frenzy of alcohol prohibition, a beverage consisting of coca leaf extracts, African kola nuts, and a sweet carbonated syrup. The product was named "Coca-Cola"⁴ Pemberton received his inspiration from Angelo Mariani, a Corsican pharmacist working in Paris, who had been selling a coca leaf-Bordeaux wine tincture since the early 1860s. Mariani's product was the most popular tonic of its time, and was used by celebrities, poets, popes, and presidents.⁵ Patterns of coca consumption changed dramatically as society entered the 20th century. In the 19th century, cocaine was only available in the form of a botanical product or a botanical product in solution. When chemical houses, such as Merck, began to produce significant quantities of refined cocaine, episodes of toxicity became much more frequent, the views of the medical profession changed, and physicians lost much of their enthusiasm for the drug.

Until 1923, the primary source of cocaine was from the coca leaf. In that year, Richard Willstätter was able to synthesize a mixture of d-cocaine, l-cocaine, d-pseudococaine, and l-pseudococaine. This multi-step synthesis requires a high degree of technical expertise in organic chemistry and results in low yields.⁶ These financial and technical factors make the extraction of cocaine from the coca leaf the method by which most, if not all, of the cocaine is isolated for distribution on both the licit and illicit markets.

1.4.2.3 Isolation and Purification

The extraction and isolation of cocaine from the coca leaf is not difficult. There is more than one way to do it. South American producers improvise depending on the availability of chemicals. All of the known production techniques involve three primary steps: (1) extraction of crude coca paste from the coca leaf; (2) purification of coca paste to cocaine base; and (3) conversion of cocaine base to cocaine hydrochloride. The paste and base laboratories in South America are deeply entrenched and widespread with thousands of operations, whereas the

conversion laboratories are more sophisticated and centralized. They border on semi-industrial pilot-plant type laboratories involving a knowledge of chemistry and engineering.

The primary isolation method used until recently is a Solvent Extraction Technique. The essential methodology involves macerating a quantity of coca leaves with lime water, and then adding kerosene with stirring. After a while the kerosene is separated from the aqueous layer. A dilute sulfuric acid solution is added to the kerosene with stirring. This time the kerosene is separated from the aqueous layer and set aside. It is common to save the kerosene for another extraction of the leaves. The aqueous layer is retained and neutralized with limestone or some other alkaline substance. The material that precipitates after the addition of limestone is crude coca paste containing anywhere from 30 to 80% cocaine, with the remainder of the cocaine matrix composed primarily of other alkaloids, hydrolysis products, and basic inorganic salts used in the processing. This solid material is isolated by filtration for purification of the cocaine.

The coca paste is then dissolved in dilute sulfuric acid, and dilute potassium permanganate solution is added to oxidize the impurities. This solution is then filtered, and ammonium hydroxide is added to the filtrate to precipitate cocaine base. This "cocaine" is not ready for shipment to the U.S. The cocaine will first be converted to hydrochloride for easier packaging, handling, and shipment.

A second method of isolating cocaine from the leaf which is more predominant today is the Acid Extraction Technique. In this method, the cocaine leaves are placed directly in the maceration pit with enough sulfuric acid to cover the leaves. The pit is a hole dug into the ground and lined with heavy duty plastic. The leaves are macerated by workers who stomp in the sulfuric acid/coca leaf pit. This stomping leaches the cocaine base from the leaf and forms an aqueous solution of cocaine sulfate. This stomping can continue for a matter of hours to ensure maximum recovery of the cocaine.

After stomping is complete, the coca solution is poured through a coarse filter to remove the insolubles including the plant material. More sulfuric acid is added to the leaves and a second or even third extraction of the remaining cocaine will take place. Maximized recovery of cocaine is important to the laboratory operators. After the extractions and filterings are completed, an excess basic lime or carbonate solution is added to the acidic solution with stirring and neutralizing the excess acid and cocaine sulfate. A very crude coca paste forms. The addition of the base is monitored until the solution is basic to an ethanolic solution of phenolphthalein. The coca paste is then back-extracted with a small volume of kerosene. The solution sets until a separation of the layers occurs. The kerosene is then back-extracted this time with a dilute solution of sulfuric acid. Then, an inorganic base is added to precipitate the coca paste. This coca paste is essentially the same as that generated by the solvent extraction method. The advantage to this Acid Extraction Technique is that a minimal volume of organic solvent is required. And while it is more labor intensive, the cost of labor in Bolivia, the major producing country of coca paste, is very low when compared to the financial return.

The resultant cocaine base, produced by either technique, is dissolved in acetone, ether, or a mixture of both. A dilute solution of hydrochloric acid in acetone is then prepared. The two solutions are mixed and a precipitate of cocaine hydrochloride forms almost immediately and is allowed to settle to the bottom of the reaction vessel (usually an inexpensive bucket). The slurry will then be poured through clean bed sheets filtering the cocaine hydrochloride from the solvent. The sheets are then wrung dry to eliminate excess acetone, and the high quality cocaine hydrochloride is dried in microwave ovens, under heat lamps, or in the sunlight. It is then a simple matter to package the cocaine hydrochloride for shipment. One of the more common packaging forms encountered in laboratories analyzing seizures of illicit cocaine is the "one kilo brick". This is a brick-shaped package of cocaine wrapped in tape or plastic, sometimes labeled with a logo, with the contents weighing near 1 kg. Once the cocaine hydrochloride arrives in the U.S., drug wholesalers may add mannitol or inositol as diluents,

or procaine, benzocaine, lidocaine, or tetracaine as adulterants. This cocaine can then be sold on the underground market in the U.S. either in bulk or by repackaging into smaller containers.

1.4.2.4 Conversion to “Crack”

“Crack” is the term used on the street and even in some courtrooms to describe the form of cocaine base which has been converted from the cocaine hydrochloride and can be smoked in a pipe. This procedure of conversion from the acid to the base is usually carried out in the U.S. Cocaine base usually appears in the form of a rock-like material, and is sometimes sold in plastic packets, glass vials, or other suitable packaging. Cocaine hydrochloride is normally ingested by inhalation through a tube or straw, or by injection. Cocaine base is ingested by smoking in an improvised glass pipe. Ingestion in this manner results in the cocaine entering the blood stream through the lungs and rushes to the brain very quickly.

Cocaine hydrochloride is converted to cocaine base in one of two ways. The first method involves dissolving the cocaine hydrochloride in water and adding sodium bicarbonate or household ammonia. The water is then boiled for a short period until all of the precipitated cocaine base melts to an oil, and ice is added to the reaction vessel. This vessel will usually be a metal cooking pan or a deep glass bowl. As the water cools, chunks of cocaine base oil will solidify at the bottom of the cooking vessel. After all the cocaine base has formed, the water can be cooled and then poured off leaving the solid cocaine base which is easily removed from the collection vessel. The cocaine base can be cut with a knife or broken into “rocks” which can then be dried either under a heat lamp or in a microwave oven. It is not unusual when analyzing cocaine base produced from this method to identify sodium bicarbonate mixed with the rock-like material. This cocaine base sometimes has a high moisture content due to incomplete drying.

A second method of producing cocaine base from cocaine hydrochloride involves dissolving the salt (usually cocaine hydrochloride) in water. Sodium bicarbonate or household ammonia is added to the water and mixed well. Diethyl ether is then added to the solution and stirred. The mixture then separates into two layers with the ether layer on top of the aqueous layer. The ether is decanted leaving the water behind. The ether is then allowed to evaporate and high quality cocaine base remains. If any of the adulterants mentioned previously (excluding sugars, which are diluents) are mixed with the cocaine hydrochloride prior to conversion, then they will also be converted to the base and will be a part of the rock-like material that results from this process. The term “free base” is used to describe this form of cocaine. Cocaine base in this form is also smoked in a glass pipe. However, residual (and sometimes substantial) amounts of ether remaining in these samples from the extraction process make ignition in a glass pipe very dangerous.

1.4.2.5 Other Coca Alkaloids

In the process of examining cocaine samples in the laboratory, it is not uncommon to identify other alkaloids and manufacturing by-products with the cocaine. These other alkaloids are carried over from the coca leaf in the extraction of the cocaine. Many manufacturing by-products result from the hydrolysis of the parent alkaloids (benzoylecgonine from cocaine, or truxillic acid from truxilline). As a forensic chemist, it is important to recognize the sources of these alkaloids as one progresses through an analytical scheme.

The major alkaloidal “impurities” present in the coca leaf which are carried over in the cocaine extraction are the *cis*- and *trans*-cinnamoylcocaines and the truxillines. There are 11 isomeric truxillic and truxinic acids resulting from the hydrolysis of truxilline. Another naturally occurring minor alkaloid from the coca leaf is tropacocaine. The concentration of tropacocaine will rarely, if ever, exceed 1% of the cocaine concentration and is well below the concentrations

of the cis- and trans-cinnamoylcocaines and the truxillines. Two other alkaloids from the coca leaf which have been identified are cuscohygrine and hygrine. These two products are not found in cocaine, just in the leaf.

The second class of substances found in the analysis of cocaine samples is the result of degradation or hydrolysis. Ecgonine, benzoylecgonine, and methylecgonine found in cocaine samples will be the result of the hydrolysis of cocaine. It is important to recognize that some of these manufacturing by-products, such as ecgonine, can be detected by gas chromatography only if they are derivatized prior to injection. Methyl ecgonidine is a by-product of the hydrolysis of cocaine and is often times identified in the laboratory by gas chromatography/mass spectrometry. This artifact can also result from the thermal degradation of cocaine or the truxillines in the injection port of the GC. Benzoic acid is the other product identified when this decomposition occurs.

There are at least two substances that result directly from the permanganate oxidation of cocaine. N-formyl cocaine results from oxidation of the N-methyl group of cocaine to an N-formyl group. Norcocaine is a hydrolysis product resulting from a Schiff's base intermediate during the permanganate oxidation. There is also evidence that norcocaine can result from the N-demethylation of cocaine, a consequence of the peroxides in diethyl ether.

1.4.2.6 Cocaine Adulterants

The primary adulterants identified in cocaine samples are procaine and benzocaine. Lidocaine is also found with less regularity. These adulterants are found in both the cocaine base and cocaine hydrochloride submissions. The primary diluents are mannitol and inositol. Many other sugars have been found, but not nearly to the same extent. Cocaine hydrochloride concentrations will usually range from 20 to 99%. The moisture content of cocaine hydrochloride is usually minimal. Cocaine base concentrations will usually range from 30 to 99%. There will usually be some moisture in cocaine base ("crack") submissions from the water/sodium bicarbonate or water/ammonia methods. The concentration of cocaine base ("free base") from the ether/sodium bicarbonate or ether/ammonia methods will usually be higher and free of water.

The methods for identifying cocaine in the laboratory include but are not limited to: infrared spectrophotometry (IR), nuclear magnetic resonance spectroscopy (NMR), mass spectrometry (MS), and gas chromatography (GC). IR and NMR will enable the analyst to distinguish between cocaine hydrochloride and cocaine base. However, it is not possible to identify the form in which the cocaine is present utilizing this instrumentation.

CONCLUSION

The user of either cocaine base or cocaine hydrochloride not only ingests the cocaine, but also other alkaloids from the coca plant, processing by-products, organic and inorganic reagents used in processing, diluents, and adulterants. There is no realistic way in which a cocaine user can ensure the quality of the cocaine purchases on the street, and "innocent" recreational drug use may provide more danger than the user would knowingly risk.

REFERENCES

1. Rusby, H.H., Bliss, A.R., and Ballard, C.W., *The Properties and Uses of Drugs*, Blakiston's Son & Co., Philadelphia, 1930, 125, 386, 407.
2. Byck, R., Ed., *Cocaine Papers by Sigmund Freud*, Stonehill, New York, 1975.

- 2A. Becker, H.K., 261, 276, 283-6.
3. Musto, D., A study in cocaine: Sherlock Holmes and Sigmund Freud, *JAMA*, 204: 125, 1968.
4. Brecher, E. and the Editors of Consumer Reports, *Licit and Illicit Drugs*, Little, Brown and Co., Boston, 1972, 33-6, 270.
5. Mariani, A., Ed., Album Mariani, Les Figures Contemporaines. Contemporary Celebrities from the Album Mariani, etc., various publishers for Mariani & Co., 13 Vols., 1891-1913.
6. Willstätter, R., Wolfes, O., and Mader, H., Synthese des Natürlichen Cocains, *Justus Liebig's Annalen Der Chemie*, 434: 111-139, 1923.
7. Casale, J.F. and Klein, RFX, Illicit cocaine production, *Forensic Sci Rev*, 5: 96-107, 1993.

1.4.3 MARIJUANA

1.4.3.1 History and Terminology

Marijuana is a Schedule I controlled substance. In botanical terms, “marijuana” is defined as *Cannabis sativa L.* Legally, marijuana is defined as all parts of the plant, *Cannabis sativa L.* (and any of its varieties) whether growing or not, the seeds thereof, the resin extracted from any part of the plant, and every compound, manufacture, salt, derivative, mixture, or preparation of such plant; its seeds and resins. Such terms do not include the mature stalk of the plants, fibers produced from such plants, oils or cakes made from the pressed seeds of such plants, any other compound, manufacture, salt derivative, mixture or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil or cake, pressed seed, or the sterilized seed which is incapable of germination.¹ Pharmaceutical preparations that contained the resinous extracts of cannabis were available on the commercial market from the 1900s to 1937. These products were prescribed for their analgesic and sedative effects. In 1937 the Food and Drug Administration declared these products to be of little medical utility and they were removed from the market in 1937. Cannabis, in the forms of the plant material, hashish, and hashish oil, is the most abused illicit drug in the world.

Cannabis is cultivated in many areas of the world. Commercial *Cannabis sativa L.* is referred to as “hemp”. The plant is cultivated for cloth and rope from its fiber. A valuable drying oil used in art and a substitute for linseed oil is available from the seeds. Bird seed mixtures are also found to contain sterilized marijuana seeds. In the early days of the U.S., hemp was grown in the New England colonies. Its cultivation spread south into Pennsylvania and Virginia. From there it spread south and west most notably into Kentucky and Missouri. Its abundance in the early days of the country is still evident by the fact that it still grows wild in many fields and along many roadways. The plant is now indigenous to many areas, and adapts easily to most soil and moderate climatic conditions.

Marijuana is classified as a hallucinogenic substance. The primary active constituents in the plant are cannabiniol, cannabidiol, and the tetrahydrocannabinols, illustrated in Figure 1.4.3.1. The tetrahydrocannabinols (THCs) are the active components responsible for the hallucinogenic properties of marijuana. The THC of most interest is the Δ^9 -tetrahydrocannabinol. The other THCs of interest in marijuana are the Δ^1 cis- and trans- tetrahydrocannabinols, the Δ^6 cis- and trans- tetrahydrocannabinols, and the Δ^3 - and Δ^4 -tetrahydrocannabinols. The concentration varies dramatically from geographic area to geographic area, from field to field, and from sample to sample. This concentration range varies from less than 1% to as high as 30%. In recent hash oil exhibits, the highest official reported concentration of Δ^9 -THC is 43%.² Five other terms associated with marijuana are

Hashish: Resinous material removed from cannabis. Hashish is usually found in the form of a brown to black cake of resinous material. The material is ingested by smoking in pipes or by consuming in food.

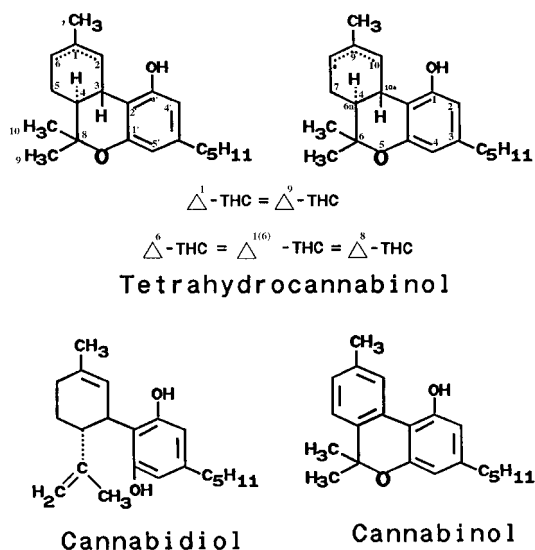


Figure 1.4.3.1 The primary active constituents in marijuana.

Hashish oil: Extract of the marijuana plant which has been heated to remove the extracting solvents. The material exists as a colorless to brown or black oil or tar-like substance.

Sinsemilla: The flowering tops of the unfertilized female cannabis plant. (There are no seeds on such a plant.) Sinsemilla is usually considered a “gourmet” marijuana because of its appearance and relatively high concentrations of the THC’s.

Thai sticks: Marijuana leaves tied around stems or narrow diameter bamboo splints. Thai sticks are considered a high quality product by the drug culture. The THC concentrations of the marijuana leaves on Thai sticks are higher than domestic marijuana. Unlike hashish and sinsemilla, seeds, and small pieces of stalks and stems are found in Thai sticks.

Brick or Kilo: Marijuana compressed into a brick-shaped package with leaves, stems, stalk, and seeds. The pressed marijuana is usually tightly wrapped in paper and tape. This is the form of marijuana encountered in most large scale seizures. These large scale seizure packages weigh approximately 1000 g (1 kg). This is the packaging form of choice for clandestine operators because of the ease of handling, packaging, shipping, and distribution.

1.4.3.2 Laboratory Analysis

The specificity of a marijuana analysis is still a widely discussed topic among those in the forensic and legal communities. In the course of the past 25 years, the consensus of opinion concerning the analysis of marijuana has remained fairly consistent. In those situations where plant material is encountered, the marijuana is first examined using a stereomicroscope. The presence of the bear claw cystolithic hairs and other histological features are noted using a compound microscope. The plant material is then examined chemically using Duquenois–Levine reagent in a modified Duenois Levine testing sequence. These two tests are considered to be conclusive within the realm of existing scientific certainty in establishing the presence of marijuana.^{3–5}

The Modified Duquenois–Levine test is conducted using Duquenois reagent, concentrated hydrochloric acid, and chloroform. The Duquenois reagent is prepared by dissolving 2 g of vanillin and 0.3 ml of acetaldehyde in 100 ml of ethanol. Small amounts (25 to 60 mg is usually sufficient) of suspected marijuana leaf is placed in a test tube and approximately 2 ml of Duquenois reagent is added. After 1 min, approximately 1 ml of concentrated hydrochloric acid is added. Small bubbles rise from the leaves in the liquid. These are carbon dioxide bubbles produced by the reaction of the hydrochloric acid with the calcium carbonate at the base of the cystolithic hair of the marijuana. A blue to blue-purple color forms very quickly in the solution. Approximately 1 ml of chloroform is then added to the Duquenois reagent/hydrochloric acid mixture. Because chloroform is not miscible with water, and because it is heavier than water, two liquid layers are visible in the tube—the Duquenois reagent/hydrochloric acid layer is on top, and the chloroform layer is on the bottom. After mixing with a vortex stirrer and on settling, the two layers are again clearly distinguishable. However, the chloroform layer has changed from clear to the blue to blue-purple color of the Duquenois reagent/hydrochloric acid mixture.

One variation in this testing process involve pouring off the Duquenois reagent sitting in the tube with the leaves before adding the hydrochloric acid. The remainder of the test is conducted using only the liquid. Another variation involves conducting the test in a porcelain spot plate. This works, although some analysts find the color change a bit more difficult to detect. A third variation involves extracting the cannabis resin with ether or some other solvent, separating the solvent from the leaves, allowing the solvent to evaporate, and conducting the Modified Duquenois–Levine test on the extract.

Marquis reagent is prepared by mixing 1 ml of formaldehyde solution with 9 ml of sulfuric acid. The test is done by placing a small amount of sample (1 to 5 mg) into the depression of a spot plate, adding one or two drops of reagent, and observing the color produced. This color will usually be indicative of the class of compounds, and the first color is usually the most important. A weak reponse may fade, and samples containing sugar will char on standing because of the sulfuric acid. Marquis reagent produces the following results:

1. Purple with opiates (heroin, codeine).
2. Orange turning to brown with amphetamine and methamphetamine.
3. Black with a dark purple halo with 3,4-methylenedioxyamphetamine (MDA) and 3,4- methylenedioxymethamphetamine (MDMA).
4. Pink with aspirin.
5. Yellow with diphenhydramine.

A thin-layer chromatographic (TLC) analysis, which detects a systematic pattern of colored bands, can then be employed as an additional test.^{6,7} Though it is not required, some analysts will run a gas chromatograph/mass spectrometer (GC/MS) analysis to identify the cannabinoids in the sample.

The solvent insoluble residue of hashish should be examined with the compound microscope. Cystolithic hairs, resin glands, and surface debris should be present. However, if most of the residue is composed of green leaf fragments, the material is pulverized marijuana or imitation hashish.

1.4.4 PEYOTE

Peyote is a cactus plant which grows in rocky soil in the wild. Historical records document use of the plant by Indians in northern Mexico from as far back as pre-Christian times, when it was used by the Chichimaec tribe in religious rites. The plant grows as small cylindrical-like

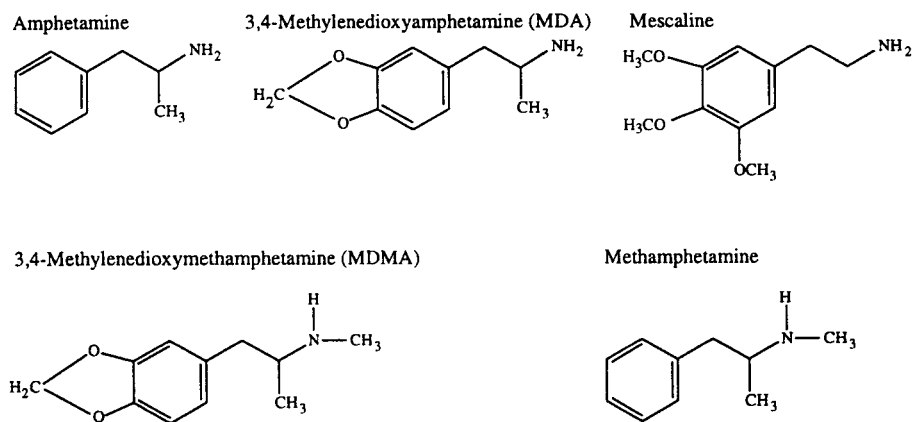


Figure 1.4.4 Chemical structure of mescaline.

“buttons”. The buttons were used to relieve fatigue and hunger, and to treat victims of disease. The peyote buttons were used in group settings to achieve a trance state in tribal dances.⁸

It was used by native Americans in ritualistic ceremonies. In the U.S., peyote was cited in 1891 by James Mooney of the Bureau of American Ethnology.⁹ Mooney talked about the use of peyote by the Kiowa Indians, the Comanche Indians, and the Mescalero Apache Indians, all in the southern part of the country. In 1918, he came to the aid of the Indians by incorporating the “Native American Church” in Oklahoma to ensure their rights in the use of peyote in religious ceremonies. Although several bills have been introduced over the years, the U.S. Congress has never passed a law prohibiting the Indians’ religious use of peyote. Both mescaline and peyote are listed as Schedule I controlled substances in the Comprehensive Drug Abuse Prevention and Control Act of 1970.

The principal alkaloid of peyote responsible for its hallucinogenic response is mescaline, a derivative of β -phenethylamine. Chemically, mescaline is 3,4,5-trimethoxyphenethylamine. As illustrated in [Figure 1.4.4](#), its structure is similar to the amphetamine group in general. Mescaline was first isolated from the peyote plant in 1894 by the German chemist A. Heffter.¹⁰ The first complete synthesis of mescaline was in 1919 by E. Späth.¹¹ The extent of abuse of illicit mescaline has not been accurately determined. The use of peyote buttons became popular in the 1950’s and again in the period from 1967 to 1970. These two periods showed a dramatic increase in experimentation with hallucinogens in general.

1.4.5 PSILOCYBIN MUSHROOMS

The naturally occurring indoles responsible for the hallucinogen properties in some species of mushrooms are psilocybin ([Figure 1.4.5](#)) and psilocin.¹² The use of hallucinogenic mushrooms dates back to the 16th century occurring during the coronation of Montezuma in 1502.⁸ In 1953, R. G. Wassen and V.P. Wason were credited with the rediscovery of the ritual of the Indian cultures of Mexico and Central America.¹³ They were able to obtain samples of these mushrooms. The identification of the mushrooms as the species *Psilocybe* is credited to the French mycologist, Roger Heim.¹⁴

Albert Hofmann (the discoverer of lysergic acid diethylamine) and his colleagues at Sandoz laboratories in Switzerland are credited with the isolation and identification of psilocybin (phosphorylated 4-hydroxydimethyltryptamine) and psilocin (4-hydroxydimethyltryptamine).¹⁵

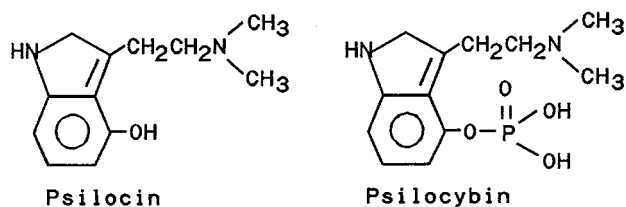


Figure 1.4.5 Chemical structure of psilocin and psilocybin.

Psilocybin was the major component in the mushrooms, and psilocin was found to be a minor component. However, psilocybin is very unstable and is readily metabolized to psilocin in the body. This phenomenon of phosphate cleavage from the psilocybin to form the psilocin occurs quite easily in the forensic science laboratory. This can be a concern in ensuring the specificity of identification.

The availability of the mushroom has existed worldwide wherever proper climactic conditions exist — that means plentiful rainfall. In the U.S., psilocybin mushrooms are reported to be plentiful in Florida, Hawaii,¹⁶ the Pacific Northwest, and Northern California.¹⁷ Mushrooms that are analyzed in the forensic science laboratory confirm the fact that the mushrooms spoil easily. The time factor between harvesting the mushrooms and the analysis proves to be the greatest detriment to successfully identifying the psilocybin or psilocin. Storage prior to shipment is best accomplished by drying the mushrooms. Entrepreneurs reportedly resort to storage of mushrooms in honey to preserve the psychedelic properties.¹⁸

Progressing through the analytical scheme of separating and isolating the psilocybin and psilocin from the mushroom matrix, cleavage of the phosphate occurs quite easily. Prior to beginning the analysis, drying the mushrooms in a desiccator with phosphorous pentoxide ensures a dry starting material. In many instances, the clean-up procedure involves an extraction process carried out through a series of chloroform washes from a basic extract and resolution of the components by TLC. The spots or, more probably, streaks are then scraped from the plate, separated by a back-extraction, and then analyzed by IR. Direct analysis by GC is very difficult because both psilocybin and psilocin are highly polar and not suitable for direct GC analysis. Derivatization followed by GC/MS is an option except in those instances where the mushrooms have been preserved in sugar.¹⁹ With the development and availability of HPLC, the identification and quantitation of psilocybin and psilocin in mushrooms are becoming more feasible for many forensic science laboratories.²⁰

REFERENCES

1. Section 102 (15), Public Law 91-513
2. ElSohly, M.A. and Ross, S.A., *Quarterly Report Potency Monitoring Project, Report #53, January 1, 1995 - March 31, 1995.*
3. Nakamura, G.R., Forensic aspects of cystolithic hairs of cannabis and other plants, *J. Assn. Offic. Analyt. Chem.*, 52: 5-16, 1969.
4. Thornton, J.I. and Nakamura, G.R., The identification of marijuana, *J. Forensic Sci. Soc.*, 24: 461-519, 1979.
5. Hughes, R.B. and Warner, V.J., A study of false positives in the chemical identification of marijuana, *J. Forensic Sci.*, 23: 304-310, 1978.
6. Hauber, D.J., Marijuana analysis with recording of botanical features present with and without the environmental pollutants of the Duquenois-Levine test, *J. Forensic Sci.*, 37:1656 -1661, 1992.

7. Hughes, R.B. and Kessler, R.R., Increased safety and specificity in the thin-layer chromatographic identification of marijuana," *J. Forensic Sci.*, 24: 842-846, 1979.
8. Report Series, National Clearinghouse for Drug Abuse Information, *Mescaline*, Series 15, No. 1, May 1973.
9. Mooney, J., The mesacal plant and ceremony, *Therapeutic Gazette*, 12: 7-11, 1896.
10. Heffter, A., Ein beitrage zur pharmakologischen Kenntniss der Cacteen, *Archiv. F. Exp Pathol. U. Pharmacol.*, 34, 65-86, 1894.
11. Spath, E., Uber die Anhalonium-Alkaloide, Anhalin und Mescaline, Monatshefte furh Chemie und verwandte Teile anderer Wissenschaften, 40, 1929, 1919.
12. Hofman, A., Heim, R., Brack, A., and Kobel, H., Psilocybin, ein psychotroper Wirkstoff aus dem mexikanischen rauschpitz Psilocybe mexicana Heim, *Experiencia*, 14:107-109, 1958.
13. Wasson, V.P. and Wasson, R.G., *Mushrooms, Russia, and History*. Pantheon Books, New York, 1957.
14. Heim, R., Genest, K., Hughes, D.W., and Belec, G., Botanical and chemical characterisation of a forensic mushroom specimen of the genus psilocybe, *Forensic Sci. Soc. J.*, 6: 192-201, 1966.
15. Hofmann, A., Chemical aspects of psilocybin, the psychotropic principle from the Mexican fungus, *Psilocybe mexicana Heim*, in Bradley, P.B., Deniker, P., and Radouco-Thomas, C., Eds. *Neuropsychopharmacology*. Elsevier, Amsterdam, 1959, pp. 446-448.
16. Pollock, S.H., A novel experience with Panaeolus: a case study from Hawaii, *J. Psychedelic Drugs*, 6: 85-90. 1974.
17. Weil, H., Mushroom hunting in Oregon, *J. Psychedelic Drugs*, 7: 89-102, 1975.
18. Pollock, S.H., Psilocybian Mycetismus With Special Reference to Panaeolus, *J. Psychedelic Drugs*, 8(1), 50.
19. Repke, D.B., Leslie, D.T., Mandell, D.M., and Kish, N.G., GLC-mass spectral analysis of psilocin and psilocybin, *J. Psychedelic Drugs*, 66: 743-744, 1977.
20. Thomas, B.M., Analysis of psilocybin and psilocin in mushroom extracts by reversed-phase high performance liquid chromatography, *J. Forensic Sci.*, 25: 779-785, 1980.

1.4.6 LYSERGIC ACID DIETHYLAMIDE (LSD)

LSD is an hallucinogenic substance produced from lysergic acid, a substance derived from the ergot fungus (*Clavica purpurea*) which grows on rye. It can also be derived from lysergic acid amide which is found in morning glory seeds.¹ LSD is also referred to as LSD-25 because it was the twenty-fifth in a series of compounds produced by Dr. Albert Hofmann in Basel, Switzerland. Hoffman was interested in the chemistry of ergot compounds, especially their effect on circulation. He was trying to produce compounds that might improve circulation without exhibiting the other toxic effects associated with ergot poisoning. One of the products he produced was Methergine™, which is still in use today. When LSD-25 was first tested on animals, in 1938, the results were disappointing. Five years later, in 1943, Hoffman decided to reevaluate LSD-25. The hallucinogenic experience that ensued when he accidentally ingested some of the compound led to the start of experimentation with "psychedelic" drugs.

LSD is the most potent hallucinogenic substance known to man. Dosages of LSD are measured in micrograms (one microgram equals one-one millionth of a gram). By comparison, dosage units of cocaine and heroin are measured in milligrams (one milligram equals one-one thousandth of a gram). LSD is available in the form of very small tablets ("microdots"), thin squares of gelatin ("window panes"), or impregnated on blotter paper ("blotter acid"). The most popular of these forms in the 1990s is blotter paper perforated into 1/4 inch squares. This paper is usually brightly colored with psychedelic designs or line drawing. There have been recent reports of LSD impregnated on sugar cubes.² These LSD-laced sugar cubes were commonplace in the 1970s. The precursor to LSD, Lysergic Acid, is a Schedule III controlled substance. LSD is classified as a Schedule I controlled substance. The synthetic route utilized for the clandestine manufacture of LSD is shown in [Figure 1.4.6](#).

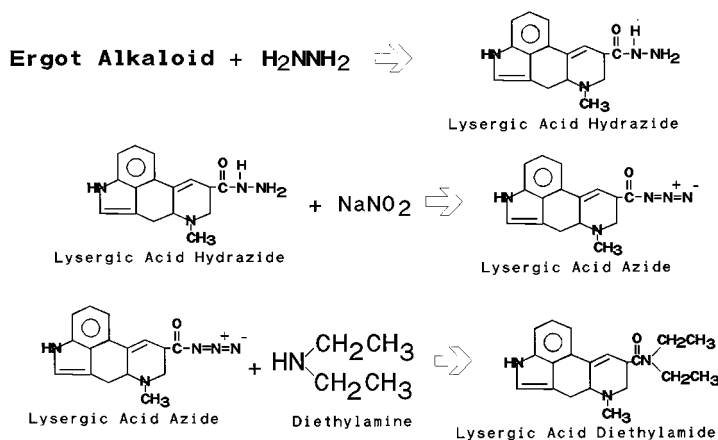


Figure 1.4.6 Synthetic route utilized for the clandestine manufacture of LSD.

1.4.7 PHENCYCLIDINE (PCP)

The chemical nomenclature of phencyclidine is phenylcyclohexylpiperidine. The term “PCP” is used most often when referring to this drug. The acronym PCP has two origins that are consistent. In the 1960s phencyclidine was trafficked as a peace pill (“PeaCePill”). PhenylCyclohexylPiperidine can also account for the PCP acronym.

PCP was first synthesized in 1926.³ It was developed as a human anesthetic in 1957, and found use in veterinary medicine as a powerful tranquilizer. In 1965 human use was discontinued because, as the anesthetic wore off confusional states and frightening hallucinations were common. Strangely, these side effects were viewed as desirable by those inclined to experiment with drugs. Today even the use of phencyclidine as a primate anesthetic has been all but discontinued. In 1978, the commercial manufacture of phencyclidine ceased and the drug was transferred from Schedule III to Schedule II of the Controlled Substances Act. Small amounts of PCP are manufactured for research purposes and as a drug standard.

The manufacture of PCP in clandestine laboratories is simple and inexpensive. Figure 1.4.7 shows three of the synthetic routes utilized for its illegal production. The first clandestinely produced PCP appeared in 1967 shortly after Parke Davis withdrew phencyclidine as a pharmaceutical.⁴ The clandestine laboratory production of PCP requires neither formal knowledge of chemistry nor a large inventory of laboratory equipment. The precursor chemicals produce phencyclidine when combined correctly using what is termed “bucket chemistry”. The opportunities for a contaminated product from a clandestine PCP are greatly enhanced because of the recognized simplicity of the chemical reactions in the production processes. The final product is often contaminated with starting materials, reaction intermediates, and by-products.⁵ Clandestine laboratory operators have been known to modify the manufacturing processes to obtain chemically related analogues capable of producing similar physiological responses. The most commonly encountered analogues are N-ethyl-1-phenylcyclohexylamine (PCE), 1-(1-phenylcyclohexyl)-pyrrolidine (PCPy), and 1-[1-(2-thienyl-cyclohexyl)]-piperidine (TCP).

In the 1960s, PCP was distributed as a white to off-white powder or crystalline material and ingested orally. In recent years, PCP has been encountered as the base and dissolved in diethyl ether. The liquid is then placed into small bottles which are recognized to hold

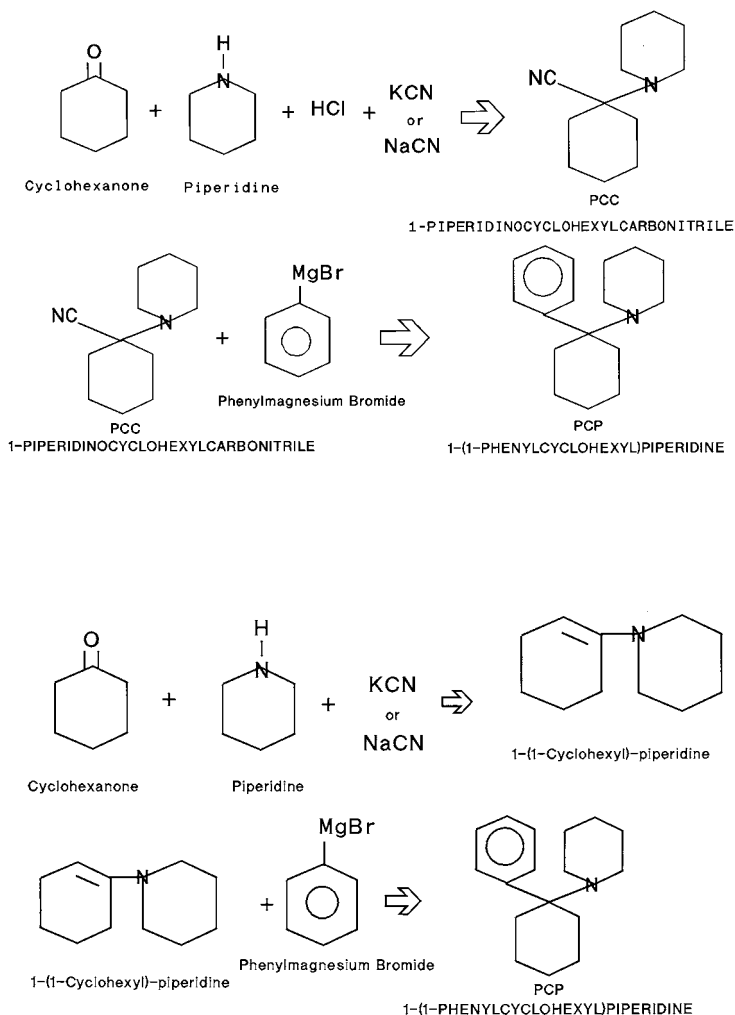


Figure 1.4.7 Synthetic routes utilized for illegal production of PCP.

commercial vanilla extract. This ether solution is then sprayed on leaves such as parsley and smoked. PCP is commonly encountered on long thin dark cigarettes (“Sherms”) which have been dipped in the PCP/ether solution.

1.4.8 FENTANYL

Fentanyl [the technical nomenclature is N-(1-phenethyl-4-piperidyl)propionanilide] is a synthetic narcotic analgesic approximately 50 to 100 times as potent as morphine.⁶ The drug had its origin in Belgium as a synthetic product of Janssen Pharmaceutica.⁷ In the 1960s in Europe and in the 1970s in the U.S., it was introduced for use as an anesthesia and for the relief of post-operative pain. Almost 70% of all surgical procedures in the U.S. use fentanyl for one of these purposes.⁸

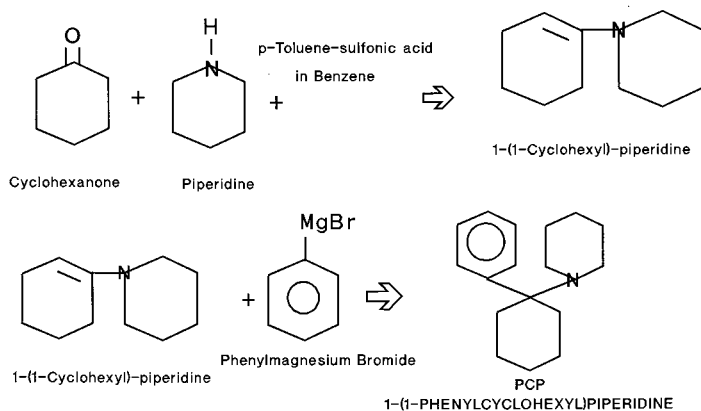


Figure 1.4.7 (continued) Synthetic routes utilized for illegal production of PCP.

Fentanyl has been called “synthetic heroin”. This is a misnomer. Victims of fentanyl overdoses were often heroin abusers with “tracks” and the typical paraphernalia. The fentanyls as a class of drugs are highly potent synthetic narcotic analgesics with all the properties of opiates and opinoids.⁹ However, the fentanyl molecule does not resemble heroin. Fentanyl is strictly a synthetic product while the morphine used in heroin production is derived from the opium poppy.

Beginning in the late 1970s with -methylfentanyl,¹⁰ nine homologues and one analogue (excluding enantiomers) of fentanyl appeared in the illicit marketplace.¹¹ The degrees of potency vary among the fentanyl homologues and analogues. The potencies of the fentanyl derivatives are much higher than those of the parent compound. But the high potencies cited above explain why even dilute exhibits result in the deaths of users who believe they are dealing with heroin. Another name used by addicts when referring to Fentanyl and its derivatives is “China White”. This term was first used to describe substances seized and later identified as alpha-methylfentanyl in 1981.¹²

There are many fentanyl homologues and analogues. Because of the size and complexity of fentanyl derivatives, the interpretation of IR, MS, and NMR spectral data prove very valuable in elucidating specific structural information required for the identification of the material.¹³

Several synthetic routes are possible. As shown in [Figure 1.4.8.1a](#) and [1.4.8.1 b](#), one of the methods requires that fentanyl precursor, N-(1-phenethyl)-4-piperidinyl) aniline, be produced first. Alternatively, fentanyl can be produced by reacting phenethylamine and methylacrylate to produce the phenethylamine diester (see [Figure 1.4.8.2](#))

1.4.9 PHENETHYLAMINES

The class of compounds with the largest number of individual compounds on the illicit drug market is the **Phenethylamines**. This class of compounds consists of a series of compounds having a phenethylamine skeleton. Phenethylamines are easily modified chemically by adding or changing substituents at various positions on the molecule. Phenethylamines fall into one of two categories in terms of physiological effects — these compounds are either stimulants or

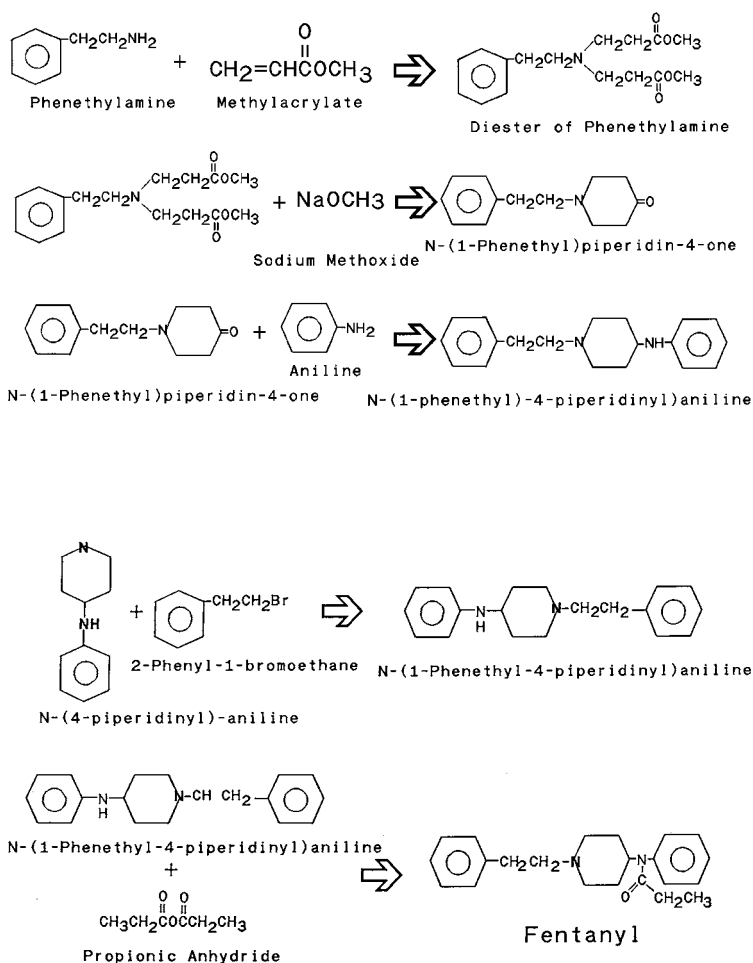


Figure 1.4.8.1 (a) Clandestine laboratory synthesis of fentanyl precursor. (b) Clandestine laboratory synthesis of fentanyl.

hallucinogens. Phenethylamines are suitable for clandestine laboratory production. The parent compound in the phenethylamine series is amphetamine, a central nervous system stimulant (CNS). With this molecule, the modifications begin by adding a methyl group to the nitrogen on the side chain. The resulting structure is the most popular clandestinely produced controlled substance in the U.S. in 1995 — methamphetamine (Figure 1.4.9).

Like amphetamine, methamphetamine is also a CNS stimulant. It is easily produced in clandestine laboratories using two basic synthetic routes. The traditional route used by “meth cooks” began with phenyl-2-propanone; however, when bulk sales were limited by law, most clandestine chemists began using ephedrine as a precursor (Figure 1.4.9.2), although, as illustrated in Figure 1.4.9.2, some now synthesize their own supply of phenyl-2-propanone, and still other routes are possible (Figure 1.4.9.3). New legislation has now limited bulk

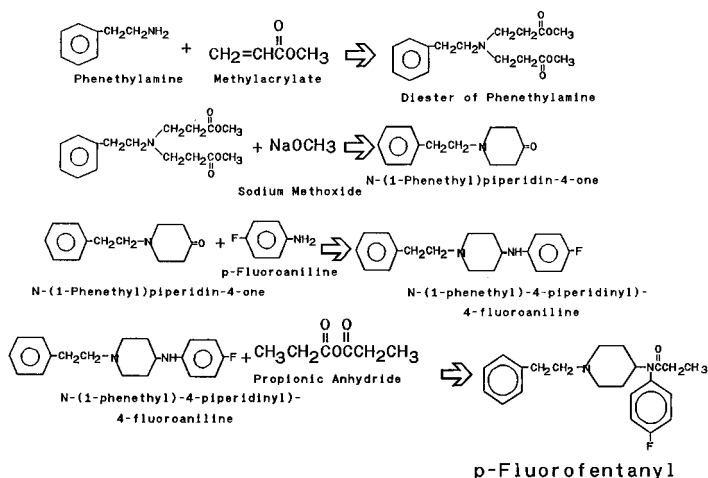


Figure 1.4.8.2 Clandestine laboratory synthesis of p-fluorofentanyl.

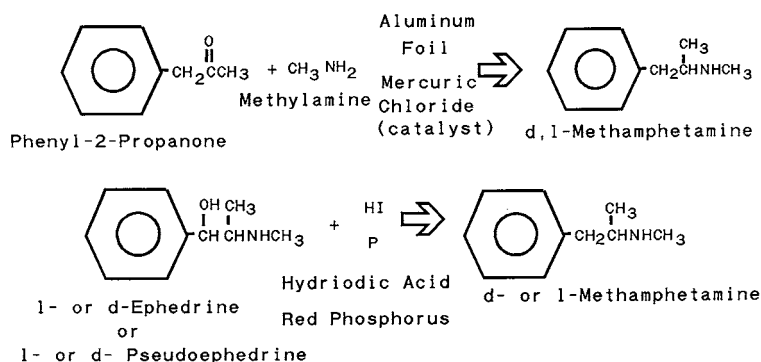


Figure 1.4.9 Clandestine laboratory synthesis of methamphetamine.

purchases of ephedrine in the U.S., though not in neighboring countries. And the chemical structure is such that further molecular synthetic modifications are easily accomplished resulting in a number of homologues and analogues. Few of the synthetic modifications of phenethylamines by clandestine laboratory “chemists” are novel. Most have been documented either in the scientific literature or in underground scientific literature. And the Internet now provides answers to anyone tenacious enough to search for a simple method to synthesize any analogue or homologue of a phenethylamine.

The parent compound of a second set of phenethylamine homologues and analogues (Figure 1.4.9.4) is 3,4-methylenedioxyamphetamine (MDA). This compound was first reported in the literature in 1910.¹⁴ In the mid-1980s, the N-methyl analogue of MDA came into

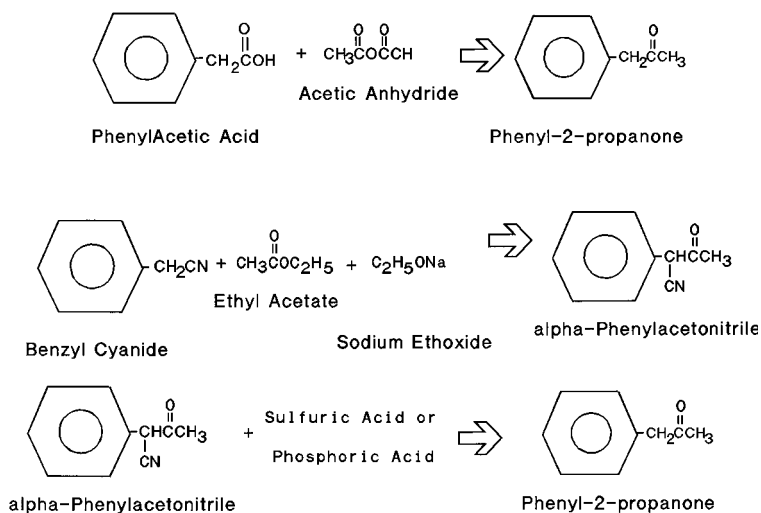


Figure 1.4.9.2 Clandestine laboratory synthesis of phenyl-2-propanone (p-2-p).

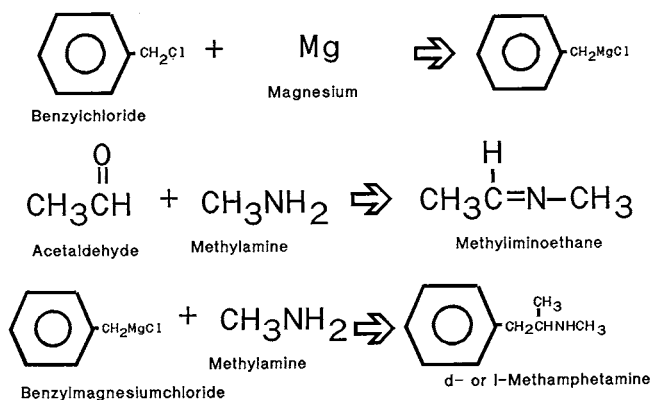


Figure 1.4.9.3 Clandestine laboratory synthesis of methamphetamine.

vogue and was known then and is still referred to as “Ecstasy”. The synthesis of 3,4-methylenedioxyamphetamine (MDMA) follows the same synthetic protocols as the less complicated phenethylamines. The clandestine laboratory operator or research chemist selectively adds one N-methyl group, an N,N-dimethyl group, an N-ethyl group, an N-propyl, an N-isopropyl group, and so on. In 1985 the N-hydroxy MDA derivative was reported.¹⁵ This

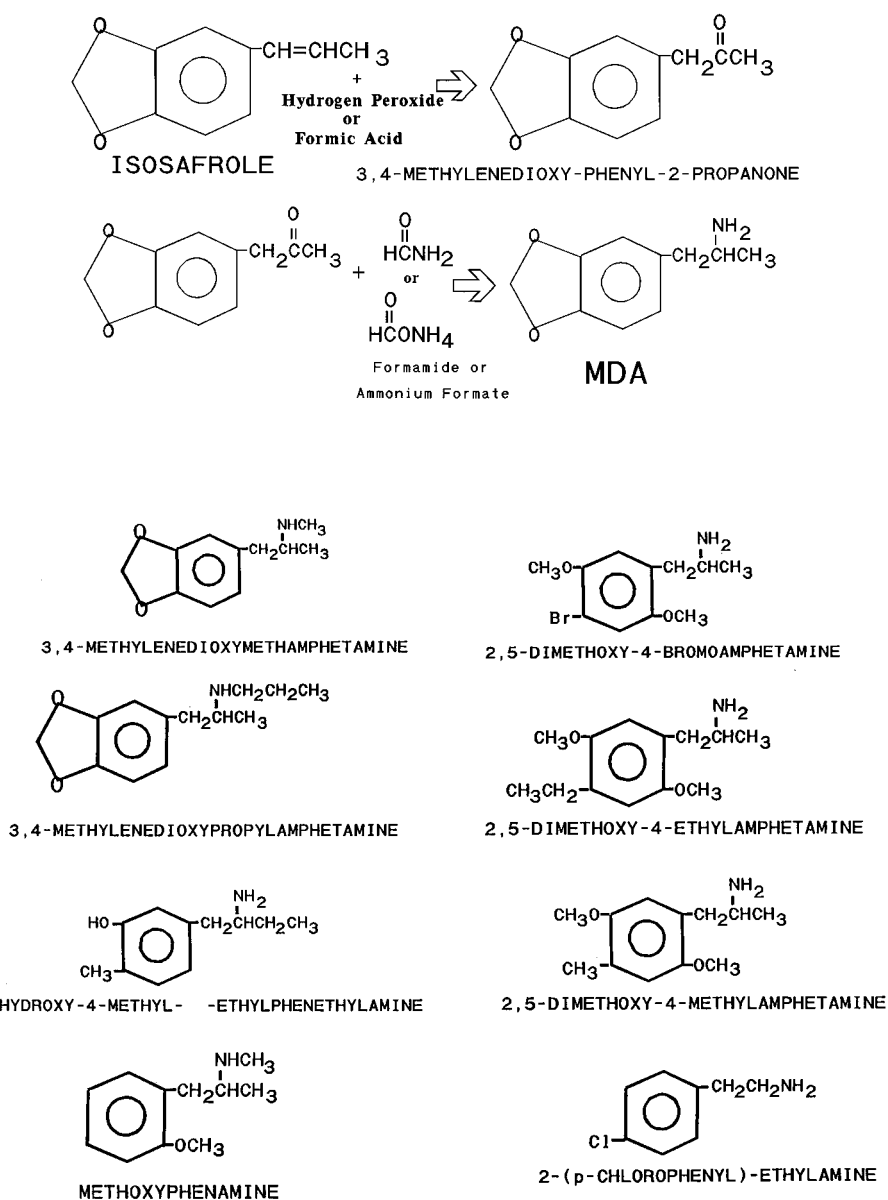


Figure 1.4.9.4 Clandestine laboratory synthesis of 3,4-methylenedioxyamphetamine (MDA).

was significant because here the modification involved the addition of a hydroxyl group as opposed to an alkyl substitution on the nitrogen. Clandestine laboratory synthesis of MDA and MDMA are shown in Figures 1.4.9.4 and 1.4.9.5

The identification of the phenethylamines in the laboratory requires great care because of the chemical and molecular similarities of the exhibits. IR combined with MS and NMR

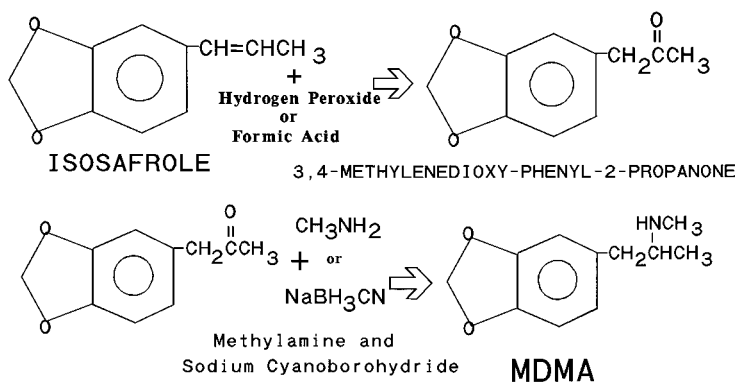


Figure 1.4.9.5 Clandestine laboratory synthesis of 3,4-methylenedioxyamphetamine (MDMA)

spectrometry provide the most specificity in the identifications of phenethylamines in the forensic science laboratory.^{15, 16} From a legal perspective, the laboratory identification of the phenethylamine is Part 1 in the forensic process. If prosecution is an option and the phenethylamine in question is not specified as a controlled substance under Public Law 91-513¹⁷ or Part 1308 of the Code of Federal Regulations, another legal option is available.

In 1986, the U.S. Congress realized that the legal system was at a standstill in attempting to prosecute clandestine laboratory operators involved in molecular modification of phenethylamines and other homologues and analogues of controlled substances. The attempted closing of this loophole was the passage of the Controlled Substances Analogue and Enforcement Act of 1986.¹⁸

1.4.10 METHCATHINONE (CAT)

Methcathinone is a structural analogue of methamphetamine and cathinone (Figure 1.4.10.1 and 1.4.10.2). It is potent and it, along with the parent compound, are easily manufactured. They are sold in the U.S. under the name CAT. It is distributed as a white to off-white chunky powdered material and is sold in the hydrochloride salt form. Outside of the U.S., methcathinone is known as ephedrone and is a significant drug of abuse in Russia and some of the Baltic States.¹⁹

Methcathinone was permanently placed in Schedule I of the Controlled Substances Act in October 1993. Prior to its scheduling, two federal cases were effectly prosecuted in Ann Arbor and Marquette, Michigan, utilizing the analogue provision of the Controlled Substances Analogue and Enforcement Act of 1986.

1.4.11 CATHA EDULIS (KHAT)

Khat consists of the young leaves and tender shoots of the *Catha Edulis* plant that is chewed for its stimulant properties.²⁰ *Catha edulis*, a species of the plant family Celastraceae, grows in eastern Africa and southern Arabia. Its effects are similar to the effects of amphetamine. The active ingredients in Khat are cathinone [(-)-a-aminopropiophenone], a Schedule I controlled substance which is quite unstable, and cathine [(+)-norpseudoephedrine] a Schedule IV

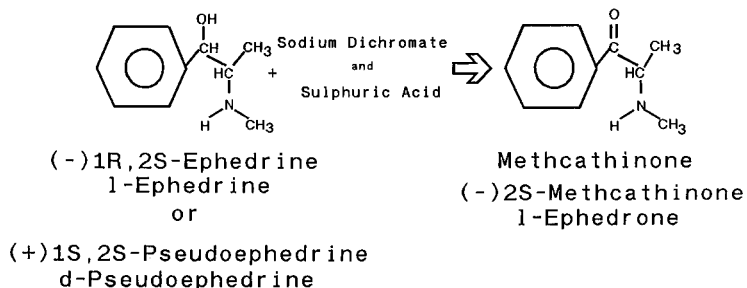


Figure 1.4.10.1 Clandestine laboratory synthesis of methcathinone.

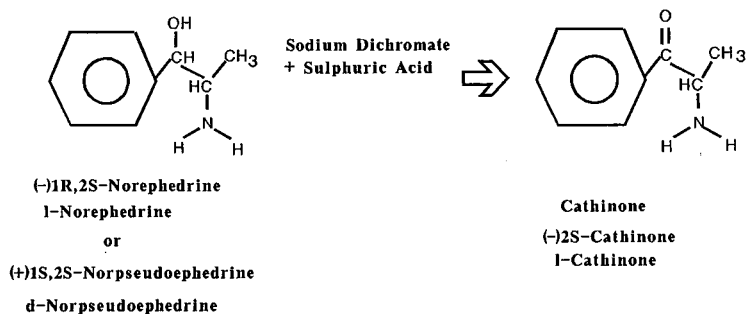


Figure 1.4.10.2 Clandestine laboratory synthesis of cathinone.

controlled substance. The identification of cathinone in the laboratory presents problems because of time and storage requirements to minimize degradation.²¹ Some of the decomposition or transformation products of *Catha edulis* are norpseudoephedrine, norephedrine, 3,6-dimethyl-2,5-diphenylpyrazine, and 1-phenyl-1,2-propanedione.²²

REFERENCES

1. *Drugs of Abuse*, U.S. Department of Justice, Drug Enforcement Administration, 1989, p. 49.
2. Kilmer, S.D., The isolation and identification of lysergic acid diethylamide (LSD) from sugar cubes and a liquid substrate, *J. Forensic Sci.*, 39: 860-862, 1994.
3. Feldman, H.W., Agar, M.H., and Beschner, G.M., Eds., *Angel Dust, An Ethnographic Study of PCP Users*, 1979, p.8.
4. Henderson, G.L., Designer drugs: Past history and future prospects, *J. Forensic Sci.*, 33: 569-575, 1988.

5. Angelos, S.A., Raney, J.K., Skoronski, G.T., and Wagenhofer, R.J., The Identification of Unreacted Precursors, Impurities, and By-Products in Clandestinely Produced Phencyclidine Preparations, *J. Forensic Sci.*, 35: 1297-1302, 1990.
6. Smialek, J.E., Levine, B., Chin, L., Wu, S.C., and Jenkins, A.J., A fentanyl epidemic in Maryland 1992, *J. Forensic Sci.*, 3:159-164, 1994.
7. Janssen, P.A.J., U.S. Patent 316400, 1965.
8. Henderson, G.L., The fentanyls, *American Association for Clinical Chemistry in-Service Training and Continuing Education*, 12(2), 5-17, Aug. 1990.
9. Henderson, *Designer*, p. 570.
10. Riley, R.N. and Bagley, J.R., *J. Med. Chem.*, 22:1167-1171.
11. Cooper, D., Jacob, M., and Allen, A., Identification of Fentanyl Derivatives, *J. Forensic Sci.*, 31: 511-528, 1986.
12. Kram, T.C., Cooper, D.A., and Allen, Behind the identification of China White," *Analytical Chem*, 53:1379-1386, 1981.
13. Cooper, *Identification*, p. 513.
14. Mannich, C. and Jacobsohn, W., Hydroxyphenylalkylamines and Dihydroxyphenylalkylamines, *Berichte*, 43:189-197, 1910.
15. Dal Cason, T.A., The characterization of some 3,4-methylenedioxyphenyl- isopropylamine (MDA) analogues, *J. Forensic Sci.*, 34:928-961, 1989.
16. Bost, R.O., 3,4-methylenedioxymethamphetamine (MDMA) and other amphetamine derivatives, *J. Forensic Sci.*, 33:576-587, 1988.
17. Comprehensive drug abuse prevention and control act of 1970, Public Law 91-513, 91st Congress, 27 Oct. 1970.
18. Controlled substance analogue and enforcement act of 1986, Public Law 99-570, Title I, Subtitle E, 99th Congress, 27 Oct. 1986.
19. Zhingel, K.Y., Dovensky, W., Crossman, A., and Allen, A., Ephedrone: 2- methylamino-1-phenylpropan-1-one (jell), *J. Forensic Sci.*, 36: 915-920, 1991.
20. Cath edulis (khat): Some Introductory Remarks," *Bulletin on Narcotics*, 32:1-3, 1980.
21. Lee, M.M., The identification of cathinone in khat (Catha edulis): A time study, *J. Forensic Sci.*, 40:116-121, 1995.
22. Szendrei, K., The chemistry of khat, *Bull. Narcotics*, 32, 5-34, 1980.

1.4.12 ANABOLIC STEROIDS

1.4.12.1 Regulatory History

In recent years anabolic steroid abuse has become a significant problem in the U.S. There are two physiological responses associated with anabolic steroids: **androgenic activity** induces the development of male secondary sex characteristics; **anabolic activity** promotes the growth of various tissues including muscle and blood cells. The male sex hormone testosterone is the prototype anabolic steroid. Individuals abuse these drugs in an attempt to improve athletic performance or body appearance. The more common agents are shown in [Figure 1.4.12.1](#).

Black market availability of anabolic steroids has provided athletes and bodybuilders with a readily available supply of these drugs. Both human and veterinary steroid preparations are found in the steroid black market. Anabolic steroid preparations are formulated as tablets, capsules, and oil- and water-based injectable preparations. There is also a thriving black market for preparations that are either counterfeits of legitimate steroid preparations, or are simply bogus.

Control of Steroids

In 1990, the U.S. Congress passed the Anabolic Steroid Control Act. This act placed anabolic steroids, along with their salts, esters, and isomers, as a class of drugs, into Schedule III of the

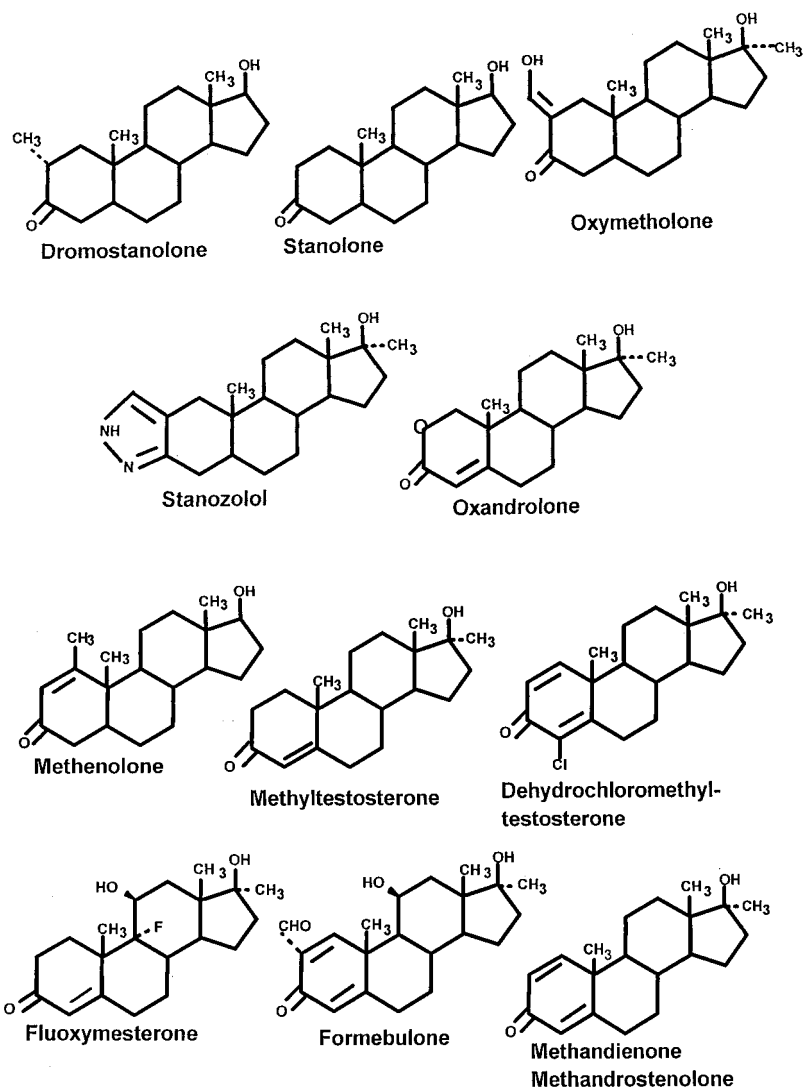


Figure 1.4.12.1 Common agents.

Federal Controlled Substances Act (CSA). This law provided 27 names of steroids that were specifically defined under the CSA as anabolic steroids. This list, which is provided in the *Federal Code of Regulations* is reproduced below.

- | | |
|------------------------------------|------------------------|
| 1. Boldenone | 10. Mesterolone |
| 2. Chlorotestosterone | 11. Methandienone |
| 3. Clostebol | 12. Methandranone |
| 4. Dehydrochloromethyltestosterone | 13. Methandriol |
| 5. Dihydrotestosterone | 14. Methandrostenolone |
| 6. Drostanolone | 15. Methenolone |
| 7. Ethylestrenol | 16. Methyltestosterone |
| 8. Fluoxymesterone | 17. Mibolerone |
| 9. Formebolone | 18. Nandrolone |

- | | |
|---------------------|------------------|
| 19. Norethandrolone | 23. Stanolone |
| 20. Oxandrolone | 24. Stanozolol |
| 21. Oxymesterone | 25. Testolactone |
| 22. Oxymetholone | 26. Testosterone |
| 27. Trenbolone | |

Unfortunately, the list contains three sets of duplicate names (chlorotestosterone and Clostebol; dihydrotestosterone and stanolone; and methandrostenolone and methandienone) as well as one name (methandranone) for a drug that did not exist. So, the actual number of different steroids specifically defined under the law as anabolic steroids is 23, not 27. Realizing that the list of 23 substances would not be all inclusive, Congress went on to define within the law the term “anabolic steroid” to mean “any drug or hormonal substance, chemically or pharmacologically related to testosterone (other than estrogens, progestins, and corticosteroids) and that promote muscle growth”.

The scheduling of anabolic steroids has necessitated forensic laboratories to analyze exhibits containing steroids. In those cases involving the detection of one or more of the 23 steroids specifically defined as anabolic steroids under the law, questions of legality are not likely to arise. However, when a steroid is identified that is not specifically defined under the law, it becomes necessary to further examine the substance to determine if it qualifies as an anabolic steroid under the definition of such a substance under the CSA. The forensic chemist must positively identify the steroid and convey to the pharmacologist the entire structure of the steroid. It then becomes the responsibility of the pharmacologist to determine the pharmacological activity, including effects on muscle growth, of the identified steroid.

1.4.12.2 Structure Activity Relationship

The pharmacology of the identified steroid may be evaluated in at least two ways. The first, and most important way, is to examine the scientific, medical, and patent literature for data on the pharmacological effects of the steroid. Over the years, numerous steroids have been examined in animal and/or human studies for anabolic/androgenic activity. It is possible that the identified steroid will be among that group of steroids. The second method is to evaluate possible pharmacological activity using **structure-activity relationships**. Such analysis is based on the assumption of a relationship between the structure of the steroid and its pharmacological effects. Small alterations of chemical structure may either enhance, diminish, eliminate, or have no effect on the pharmacological activity of the steroid. The structure-activity relationships of androgens and anabolic steroids have been reviewed extensively.^{1,2}

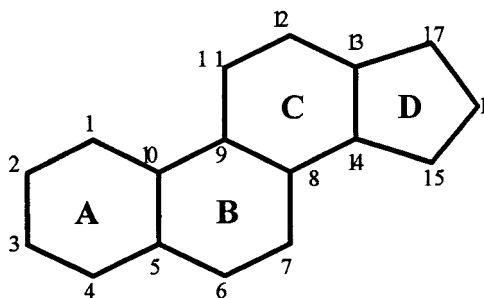


Figure 1.4.12.2 Cyclopentanoperhydrophenanthrene.

Extensive studies of the structure-activity relationships of anabolic/androgenic steroids have demonstrated that the following structural attributes are necessary for maximal androgenic and anabolic effects: rings A and B must be in the *trans* configuration;³ hydroxy function at C17 must be in the β conformational state;^{5,6} and high electron density must be present in the area of C₂ and C₃.⁷ The presence of a keto or hydroxyl group at position 3 in the A-ring usually enhances androgenic and anabolic activity, but it is not absolutely necessary for these effects.⁷ A few examples of structural alterations that enhance anabolic activity include: removal of the C-19 methyl group;⁸ methyl groups at the 2a and 7a positions;^{9,10} a fluorine at the 9a position; or a chlorine at the 4a position.^{10,11} To make it easier to visualize where these modifications are made in the ring structure, a numbered steroid skeletal ring structure, namely the cyclopentanoperhydrophenanthrene ring, is shown in [Figure 1.4.12.2](#).

It is essential to understand that structure-activity analysis can only predict whether or not a steroid is likely to produce androgenic/anabolic effects. It then becomes necessary to examine the steroid in the laboratory to determine whether the prediction is, in fact, true. It is also important to note that numerous studies performed over the years and designed to separate androgenic activity from anabolic activity have failed to obtain such a separation of pharmacological effect. That is, steroids found to possess androgenic activity also have anabolic activity and vice versa. An examination of the scientific and medical literature reveals that there are, indeed, additional steroids that are not specifically listed in the law but which do, based upon available data, probably produce androgenic/anabolic effects. A listing of some of these steroids is provided below.

Androisoaxazole	Mestanolone
Bolandiol	Methyltrienolone
Bolasterone	Norbolethone
Bolenol	Norclostebol
Flurazebol	Oxabolone Cypionate
Mebolazine	Quinbolone
Mesabolone	Stenbolone

1.4.12.3 Forensic Analysis

For the forensic chemist, when a steroid is tentatively identified, an additional problem arises, namely obtaining an analytical standard. Many products found in the illicit U.S. market are commercially available only outside of the U.S. Locating and making contact with a foreign distributor is one problem. Requesting and then receiving a legitimate standard is another problem. The expense incurred in obtaining these standards can be quite high. Once the standard has been received, authentication then enters the analytical process. If a primary standard is unavailable, an optimized analytical process presents a real problem. Fortunately, most steroids received by forensic science laboratories are labeled directly or have labeled packaging. So a manufacturer can be identified, and there is a starting point for the chemist in confirming the material as a particular steroid.

There are no known color tests, crystal tests, or TLC methods which are specific to anabolic steroids. Screening can be accomplished by GLC or HPLC. GLC sometimes presents a problem because of thermal decomposition in the injection port thereby resulting in several peaks. The steroid will not always be the largest peak. On-column injection will usually solve this problem. However, oil-base steroids rapidly foul or degrade GC columns. Samples in oils can be extracted with methanol/water 9:1 prior to injection onto a GC. Retention times for some anabolic steroids are quite long and nearly triple or quadruple that of heroin. Recognizing that several anabolic steroids are readily oxidized in polar, protic solvents vs. halogenated

hydrocarbons, screening and analysis must be accomplished as soon as possible after isolation and dilution.

GC/MS does provide definitive spectra; however, different MS systems may provide differences in the spectra for the same steroid. These differences can be traced to the quality of the MS source and the injection liner, thermal decomposition products, and induced hydration reactions related to high source temperatures set by the MS. C^{13} NMR is the most rigorous identification technique. The limitation here is the need for pure samples and high sample concentrations. Identification by infrared alone can result in problems due to polymorphism. This can be minimized by ensuring that the sample and standard are recrystallized from the same solvent.

Ideally, all anabolic steroids should be identified using two analytical methodologies which yield the same conclusions. The collection of a library of analytical data on different anabolic steroids is essential for the subsequent identification of steroids sent to the laboratory. An ability to interpret mass spectral data will be important in making an identification in so far as determining a molecular formula. Interpreting NMR data will be important in determining how substituents are attached to the parent steroid ring structure.

It should be noted that selected steroids, such as testosterone, nandrolone, methenolone, boldenone, methandriol, and trenbolone, will often be encountered by the laboratory, not as the parent drug, but instead as an ester. The type of ester will be dependent upon the particular steroid. For example, nandrolone is primarily found as a decanoate, laurate, or phenpropionate ester. Testosterone, although it is found as a parent drug, is actually most commonly encountered as the propionate, enanthate, cypionate, decanoate, isocaproate, or undecanoate esters. Less commonly encountered testosterone esters include the acetate, valerate, and undecylenate esters. Methenolone is almost always found in either the acetate or enanthate esterified form.

Upon reaching the forensic science laboratory, steroid preparations will be handled differently depending on the way each preparation is formulated. Tablets can be handled by finely grinding and extracting with chloroform or methanol. Aqueous suspensions can be handled by dilution/solution with methanol for HPLC screening or by extraction with chloroform for GC screening. Oils require a more specialized extraction which is outlined below:

1. 1 ml of oil is mixed with 10 mls of methanol/water 9:1 and the mixture is allowed to sit overnight at 0°C.
2. Methanol water mixture is removed by evaporating to dryness under a stream of nitrogen at 60°C.
3. The resulting solid is subjected directly to an IR analysis or taken up in an appropriate solvent for MS or NMR analysis.
4. Exhibits containing mixtures of anabolic steroids require semi-prep scale HPLC for rigorous isolation and identification.
5. Isocratic or gradient HPLC is recommended for quantitation of anabolic steroids.

What steroids have been the most predominate in the United States in the past few years? From January 1990 to October 1994, the following steroids or their esters have been identified by DEA laboratories.

This list provides an objective evaluation of what this chemist has encountered in the not too distant past. The data on these particular steroids should form the basis of a reference collection for comparison with future submissions.

Steroids or esters of a steroid	Numbers of	
	Cases	Exhibits
Testosterone	260	882
Nandrolone	140	244
Methenolone	99	189
Methandrostenolone	76	158
Oxymetholone	67	103
Stanozolol	61	115
Fluoxymesterone	54	7
Methyltestosterone	48	75
Boldenone	24	28
Mesterolone	21	22
Oxandrolone	16	21
Trenbolone	13	20
Methandriol	10	8
Drostanolone	6	7
Mibolerone	4	7
Stanolone	2	2
Testolactone	1	1

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REFERENCES

1. Counsell, R.E. and Klimstra, P.D., Androgens and anabolic agents, in *Medicinal Chemistry* 3rd ed., Burger, A., Ed., Wiley-Interscience, New York, 1970, 923.
2. Vida, J.A., *Androgens and Anabolic Agents: Chemistry and Pharmacology*, Academic Press, United Kingdom, 1969.
3. Huggins, C., Jensen, E.V., and Cleveland, A.S., Chemical structure of steroids in relation to promotion of growth of the vagina and uterus of the hypophysectomized rat, *J. Exp. Med.*, 100, 225-246, 1954.
4. Gabbard, R.B. and Segaloff, A., Facile preparation of 17 beta-hydroxy-5 beta-androstan-3-one and its 17 alpha-methyl derivative, *J. Organic Chem.*, 27, 655, 1962.
5. Kochakian, C.D. Recent progress in hormonal research, 1, 177, 1948.
6. Kochakian, C.D., *Am. J. Physiol.*, 160, 53, 1950.
7. Bowers, A., Cross, A.D., Edwards, J.A., Carpio, H., Calzada, M.C., and Denot, E., *J. Med. Chem.*, 6, 156, 1963.
8. Hershberger L.G., Shipley, E.G., and Meyer, R.K., *Proc. Soc. Experiment. Biol. Med.*, 83, 175, 1953.
9. Counsell, R.E., Kimstra, P.D., and Colton, F.B., Anabolic agents, derivatives of 5 alpha-androst-1-ene, *J. Organic Chem.*, 27, 248, 1962.
10. Sala G. and Baldratti, G., *Proc. Soc. Experiment. Biol. Med.*, 95, 22, 1957.
11. Backle, R.M., *Brit. Med. J.*, 1, 1378, 1959.

1.5 LEGITIMATE PHARMACEUTICAL PREPARATIONS

The Controlled Substances Act (CSA) of 1970 created a closed system for the production and distribution of legitimately manufactured controlled substances. The CSA includes contingencies to regulate the domestic commerce, importation, and exportation of these pharmaceutical preparations. Even with all of the controls that are in place, legitimate pharmaceuticals intended to help those in need are diverted onto the illegitimate market. Most of the diversion of these pharmaceuticals occurs at the retail rather than the wholesale level.

The analysis of pharmaceutical preparations in the forensic science laboratory is one of the most straightforward types of analysis. These samples are usually recognizable by their labels which usually include the manufacturers' logo and name. There are some samples that even have the name of the product inscribed on the tablet or capsule. In those instances where the manufacturer's logo is not recognized, the *Physician's Desk Reference* (PDR) is a readily available source of information which includes photographs and descriptions of the product along with information of the formulation. Another source of this information is the *Logo Index for Tablets and Capsules*.¹ This particular text lists data including inscriptions on most known products including generics. After the tablet or capsule has been tentatively identified in a reference text, it is the responsibility of the forensic chemist to conduct a series of analyses to verify the presence of a controlled substance. This verification process will usually consist of many of the same analytical processes utilized in the analysis and evaluation of any controlled substance.

1.5.1 BENZODIAZEPINES

The benzodiazepines form one of the largest classes of abused pharmaceuticals. These products are sedative/hypnotics, tranquilizers, and anti-anxiety drugs and they produce a calming effect and are often prescribed as tranquilizers. The drugs in this class are numerous and are included under Schedule IV control because while they do have a potential for abuse, there are recognized medical benefits that are both physiological and psychological. The most frequently diverted and abused benzodiazepines are alprazolam (Xanax[®]) and diazepam (Valium[®]). Other frequently abused benzodiazepines are lorazepam (Ativan[®]), triazolam (Halcion[®]), chlordiazepoxide (Librium[®]), flurazepam (Dalmane[®]), and temazepam (Restoril[®]). Another phenomenon that has been noted for several years is the abuse of legitimate pharmaceuticals in conjunction with illicit controlled substances. Clonazepam (Klonopin[®]) is just such a product. It is an anxiety reducer that is used in combination with methadone and heroin.

There has been a recent influx of flunitrazepam (Rohypnol[®]) into the Gulf Coast and other areas of the U.S. This product is a benzodiazepine manufactured principally in Colombia, Mexico, and Switzerland. It is also manufactured in lesser amounts in Argentina, Brazil, Peru, Uruguay, and Venezuela. It is neither manufactured nor marketed legally in the U.S. This is a powerful drug reported to be 7 to 10 times more potent than diazepam.

1.5.2 OTHER CENTRAL NERVOUS SYSTEM DEPRESSANTS

The oldest of the synthetic sleep inducing drugs dates back to 1862. Chloral hydrate is marketed as a soft gelatinous capsule under the name Noctec[®], and controlled under Schedule V. Its popularity declined after the introduction of barbiturates. Barbiturates are the drugs prescribed most frequently to induce sedation. Roughly 15 derivatives of barbituric acid are currently in use to calm nervous conditions. In larger doses they are used to induce sleep.

The actions of barbiturates fall into four categories. Some of the ultrashort acting barbiturates are hexobarbital (Sombulex[®]), methohexital (Brevital[®]), thiamylal (Surital[®]), and thio-

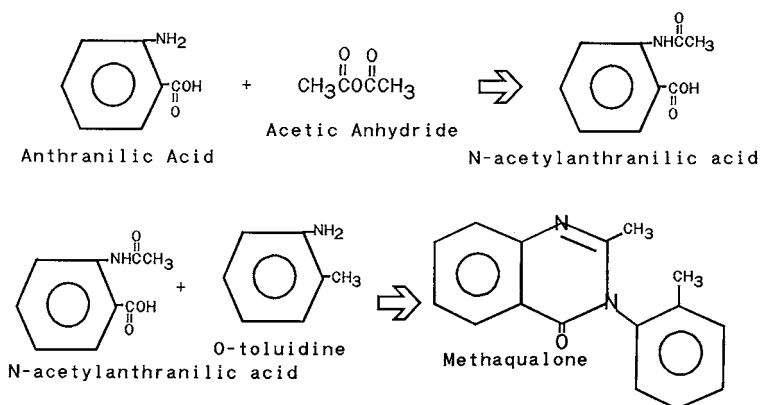


Figure 1.5.2 Clandestine laboratory synthesis of methaqualone.

pental (Pentothal®). Short-acting and intermediate-acting barbiturates include pentobarbital (Nembutal®), secobarbital (Seconal®), and amobarbital (Amytal®). These three drugs have been among the most abused barbituric acid derivatives. Also included in these categories but not as abused are butobarbital (Butisol®), talbutal (Lotusate®), and aprobarbital (Alurate®). The last category is the long-acting barbiturates. These drugs are used medicinally as sedatives, hypnotics, and anticonvulsants. The group includes phenobarbital (Luminal®), mephobarbital or methylphenobarbital (Mebaral®), and metharbital (Gemonil®).

Three other CNS depressants that have been marketed as legitimate pharmaceutical preparations and have a history of abuse include glutethimide (Doriden®), methaqualone (Quaalude®, Parest®, Mequin®, Optimil®, Somnafac®, Sopor®, and Mandrax®), and meprobamate (Miltown®, Equanil®, and SK-Bamate®). The route for the clandestine synthesis of methaqualone is shown in Figure 1.5.2.

1.5.3 NARCOTIC ANALGESICS

When one thinks of opium-like compounds, morphine and heroin immediately come to mind. However, there is another subset of this class of compounds which includes pharmaceutical preparations used to relieve pain and are purchased legitimately or illegitimately from a pharmacy with a prescription. Frequently used pharmaceutical opiates include oxycodone (Percodan®), hydromorphone (Dilaudid®), hydrocodone (Tussionex® and Vicodin®), pentazocine (Talwin®), and codeine combinations such as Tylenol® with Codeine and Empirin® with Codeine. All of these compounds are addictive.

Along with Tylenol® with Codeine and Empirin® with Codeine, which are Schedule III controlled substances, codeine is also available in combination with another controlled substance (butalbital) and sold under the trade name of Fiorinal® with Codeine. It is available with acetaminophen in Phenaphen®. Codeine is available in liquid preparations under the manufacturers' names Cosanyl®, Robitussin A-C®, Cheracol®, Cerase®, and Pediacof®. Because of the amounts of codeine in these preparations, they are controlled under Schedule V. There are also pharmaceutical codeine tablets which contain no drug other than codeine and are controlled under Schedule II.

While the compounds listed above are considered opiates, there is another class of compounds also classified as narcotic, but with synthetic origins. Meperidine (Demerol®) is one of the most widely used analgesics for the relief of pain. Methadone (Amidone® and Dolophine®) is another of these synthetic narcotics. It was synthesized during World War II by German scientists because of a morphine shortage. Although it is chemically unlike morphine or heroin, it produces many of the same effects and is often used to treat narcotic addictions.

Dextropropoxyphene is one of those drugs which falls into one of two controlled substance schedules. When marketed in dosage form under the trade names Darvon®, Darvocet®, Dolene®, or Propacet®, dextropropoxyphene is a Schedule IV controlled substance. However, when marketed in bulk non-dosage forms, dextropropoxyphene is a Schedule II controlled substance. The significance here is that the penalties for possession of a Schedule II controlled substance are usually much greater than for possession of a Schedule IV controlled substance.

1.5.4 CENTRAL NERVOUS SYSTEM STIMULANTS

Amphetamine (Benzedrine® and Biphphetamine®), dextroamphetamine (Dexedrine®), and methamphetamine (Desoxyn®) are three of the best known CNS stimulants and were prescribed for many years to treat narcolepsy. At one time, these drugs were sold over the counter without a prescription. For many years these drugs were sold as appetite suppressants. Their availability in the form of prescription drugs has all but been eliminated except under the close scrutiny of a physician. However, the clandestine laboratory production of methamphetamine in the forms of a powder or granular material has been one of the major problems facing law enforcement personnel in the past 20 or so years in the U.S.

Phenmetrazine (Preludin®) and methylphenidate (Ritalin®) are two other CNS stimulants which have patterns of abuse similar to the amphetamine and methamphetamine products. In recent years, a number of pharmaceutical products have appeared on the market as appetite suppressants and as replacements for the amphetamines. These anorectic drugs include benzphetamine (Didrex®), chlorphentermine (Pre-Sate®), clortermine (Voramil®), diethylpropion (Tenuate® and Tepanil®), fenfluramine (Pondimin®), mazindol (Sanorex® and Mazanor®), phendimetrazine (Plegine®, Bacarate®, Melifat®, Statobex®, and Tanorex®), and phentermine (Ionamin®, Fastin®, and Adipex-P®).

1.5.5 IDENTIFYING GENERIC PRODUCTS

There are a number of generic products on the market which are legitimate pharmaceutical preparations. These products will usually contain the active ingredient of the brand name product, but at the same time have a different formulation in the way of diluents and binders. These products are cataloged in various publications. When these products are encountered in the forensic science laboratory, the analyst will usually make a preliminary identification using one of the many publications listing the tablet or capsule's description and the code number that appears in the face of the product. This "preliminary" identification affords a starting point in the analytical process. The analyst will then proceed using the standard chemical techniques and instrumental methods to make an independent identification.

REFERENCE

1. Franzosa, E.S. and Harper W.W., *The Logo Index for Tablets and Capsules*, 3rd ed., GPO, 1995, 392-2401.

1.6 UNIQUE IDENTIFY FACTORS

1.6.1 PACKAGING LOGOS

There are unique factors associated with controlled substance examinations which involve packaging. Heroin and cocaine are usually imported into the U.S. clandestinely packaged. Sometimes this packaging takes the form of legitimate household or commercial products which have been hollowed out or have natural crevices into which drugs can be stored for shipment. These kinds of packages will usually be transported via commercial carriers to distributors who will reclaim the drugs and repackage them for street distribution. Sometimes drugs are shipped via human beings who store packages in body cavities, or swallow small packages in order to clear customs checks at points of entry. In these cases, it is not unusual for the packaging to break while in the body of the person transporting the drug. This usually results in severe injury or death.

Another common way of transporting controlled substances is to package the controlled substance in brick-size, 1 kg, packages for shipment to the U.S. This is often the case with shipments of heroin, cocaine, and marijuana, and the packages are usually wrapped in paper or tape. Sometimes a logo, serving as a type of trademark for the illicit distributor, will be affixed. Logos can take the form of any number of designs. They are applied using a stamping or printing device. Some commonly encountered designs include, but are not limited to, animals, symbols from Greek mythology, replications of brand name product logos, replications of the names of political figures, cartoon characters, and numbers.

When a number of these logos are encountered, examinations can be conducted to determine whether two logos have a common source. If the examiner determines that two logos are the same, and were produced using the same printing or stamping device, then the two packages must have originated from the same source. This kind of information is especially useful in tracking distribution networks.

Glassine envelopes measuring approximately 1 in. × 2 in. are commonly used to distribute heroin “on the street” directly to the primary user. More often than not, these glassine envelopes have rubber stamped images affixed. These rubber stamped images take many forms. Cartoon characters or words with social implications are common. The examiner can determine whether these rubber stamped images have a commonality of source and use this information to track distribution patterns of heroin within a geographical area.

1.6.2 TABLET MARKINGS AND CAPSULE IMPRINTS

Counterfeit tablets and capsules, which closely resemble tablets and capsules of legitimate pharmaceutical companies, are readily available on the clandestine market. They generally contain controlled substances that have been formulated in such a way as to mimic legitimate pharmaceutical preparations.¹ They are designed to be sold either on the clandestine or the legitimate market. These counterfeits sometimes are expertly prepared and closely resemble the pharmaceutical products that they are designed to represent. At other times, they are poorly made, inadequate representations of the products they are purported to represent.

The examiner in these types of cases will evaluate the suspected tablets or capsules by examining both the class and individual characteristics of the products. Legitimate products are usually prepared with few significant flaws on tablet or capsule surfaces. The lettering or numbering will be symmetrical in every way. The tablet surfaces will have minimal chips or gouges and will usually be symmetrical. The homogeneity of the tablet will be of the highest

quality. Counterfeits will usually have tableting flaws. These flaws can take the forms of imperfect lettering or numbering, rough surfaces, or inconsistencies in the tablet formulation. This can result in different hardening characteristics of the tablet. Legitimate capsules will be highly symmetrical. The lettering or numbering will usually line up on both halves of the capsule.^{2,3}

In recent years, methamphetamine and amphetamine tablets and capsules, crafted to mimic Dexedrine® and Benzedrine®, have been encountered with some frequency. These two products were distributed and used quite extensively on the legitimate market up until the 1970s. And while they are still available commercially with a prescription, they have been controlled under Schedule II since 1972 and their legal distribution and useage in the medical community has become fairly limited. Counterfeit barbiturate, methaqualone, and benzodiazepine tablets, sometimes from documented clandestine source laboratories from 20 years ago, have been encountered in recent seizures. Counterfeit Quaalude®, Mandrax®, and Valium® tablets are examples of legitimate trademark products that have been the favorites of clandestine laboratory operators. The “look-alike” market was especially lucrative in the 1970s and 1980s and became a \$50,000,000 a year industry.^{4,5}

A unique problem, encountered with regularity up until 1975, involved the refilling of capsules. Legitimate capsules were diverted from legitimate manufacturing sources. The capsules were then emptied of their contents and refilled with some innocuous material, such as starch or baking soda, and sold. The original filling usually containing a controlled substance was then diverted for sale on the illicit market. These capsules can usually be identified by imperfections in their surface characteristics. There may be small indentations on the gelatinous surface of the capsule and fingerprints indicating excessive handling. The seal holding both halves of the capsule together will not be tight. And there will usually be traces of powder around the seal of the capsule. Refilling capsules by hand or by improvised mechanical devices is not easy and usually results in these visible powder residues. A more common problem today is the refilling of over-the-counter capsules with heroin for distribution at the retail level.

A similar problem that is encountered with some frequency in the forensic science laboratory is the pre-packaged syringe from a hospital which is labeled and supposed to contain an analgesic such as meperidine. Patients complains they are receiving no relief from the injection they have been given. The syringes are then sent to the laboratory for analysis. Not infrequently, they are found to contain water, substituted for the active drug by an addicted doctor or nurse.

Legitimate tablets and capsules from reputable manufacturers are formulated with specific diluents, binders, and lubricants. Stearic acid and palmitic acid are examples of materials frequently used to hold the tablets together. Using microscopy and microchemical techniques, an examiner can determine whether a tablet or capsule is legitimate by examining the chemical composition. By evaluating the diluents, binders, lubricants, and active chemical components both qualitatively and quantitatively, the examiner can determine whether the tablet or capsule is legitimate or a counterfeit. Counterfeits take three forms—sometimes a counterfeit will actually contain the controlled substance which the legitimate product would contain; it will contain another controlled substance which has been substituted for the labeled product; at other times, it may contain only fillers, binders, and some non-controlled medicinal product.

The most commonly counterfeited tablets are diazepam tablets which look very much like legitimate commercially prepared Valium® tablets. Counterfeit Mandrax® and Quaalude®, which were produced legitimately in the 1980s and contained methaqualone or diazepam, are still available on the illicit market in the 1990s. Counterfeit anabolic steroid tablets are the newest illicit products to hit the market. They are usually manufactured to look like products manufactured in Europe. Sometimes they actually contain an anabolic steroid (which may or may not be the product as labeled), and sometimes they contain innocuous materials such as cooking oils which look very much like injectable steroids.

Clandestinely manufactured controlled substances are often-times encountered. These products are usually in the form of tablets that are prepared using punch presses. These presses usually consist of tableting dies into which powder is placed and high pressure applied forming a molded tablet. When tablets from different seizures are examined, the class and individual characteristics can be compared to determine source commonality. Since many of these clandestine punch presses have more than one set of dies, successful matches become more problematic. There are salient differences in the individual characteristics of tablets from the same punch press operation where different sets of tableting dies are configured on multi-punch machines to simultaneously produce tablets. The examiner must demonstrate skill and patience in determining which set of dies from a punch press was responsible for a particular set of tablets. The punch presses dies will always have surface imperfections which are transferred to the tablets and can be used to determine source commonality. In recent years, these clandestine tableting operations have been involved in the production of 3,4-methylenedioxymethamphetamine (MDMA) and 3,4-methylenedioxyethamphetamine (MDEA) tablets.

1.6.3 BLOTTER PAPER LSD

LSD has been available for years in the forms of small tablets (microdots), small gelatinous squares, clear plastic-like squares (window panes), powders or crystals, liquid, or in capsules. The most commonly encountered form of LSD available today is impregnated blotter paper. This LSD medium is prepared by dissolving the clandestinely produced LSD powder in an alcohol solution, and then spraying or soaking the paper with the solution. The alcohol solution used most frequently is EverClear®, a commercial ethyl alcohol product available in liquor stores. This LSD-impregnated paper is referred to as “blotter acid”. It is usually distributed on sheets of paper perforated into 1/4 in. × 1/4 in. squares. These sheets of paper range in size to hold from 1 square up to 1000 squares. These sheets of blotter paper can be plain white or single colored with no design imprints. More often than not, there will be a brightly colored design on the paper. The design can be simple such as a black and white circle, or it can be extremely intricate. One such design was brightly colored and with a detailed depiction of the crucifixion of Jesus Christ. The design can cover each and every individual square of a 1000-perforated square sheet of paper, or one design can cover the entire sheet of blotter paper where each 1/4 in. × 1/4 in. perforation square makes up 1/1000 of the total design.

By examining the intricate designs on LSD blotter paper from different seizures, it is possible to determine whether there is a common source. Depending on the printing process and the quality of the image, the examiner may be able to characterize an exhibit as having originated from the image transfer process and a specific printing device. This ability to determine source commonality is most valuable in determining the origins of LSD exhibits seized from different parts of the world.

The processes described above are most valuable in linking seizures to a particular source. Investigators who are skillful and fortunate enough to seize printing or tableting devices even without the actual controlled substances can have their efforts rewarded by terminating a controlled substance production operation. A qualified scientific examiner has the opportunity to use these devices as standards and to search reference collections of tablets, capsules, LSD blotter paper designs, or heroin or cocaine packaging logos to determine possible associations to past seizures. When this happens, the opportunity to eliminate another source of illicit drug distribution becomes a possibility.

REFERENCES

1. Franzosa, E.S., Solid dosage forms: 1975-1983, *J. Forensic Sci.*, 30:1194-1205, 1985.
2. Eisenberg, W.V. and Tillson, A.H., Identification of counterfeit drugs, particularly barbiturates and amphetamines by microscopic, chemical, and instrumental techniques, *J. Forensic Sci.*, 11 529-551, 1966.
3. Tillson, A.H. and Johnson, D.W., Identification of drug and capsule evidence as to source, *J. Forensic Sci.*, 19: 873-883, 1974.
4. Crockett, J. and Franzosa, E., Illicit solid dosage forms: Drug trafficking in the United States, presented at the 6th Interpol Forensic Sciences Symposium in 1980.
5. Crockett, J. and Sapienza, F., Illicit solid dosage forms: Drug trafficking in the United States, presented at the 10th Interpol Forensic Sciences Symposium in 1983.

1.7 ANALYZING DRUGS IN THE FORENSIC SCIENCE LABORATORY

1.7.1 SCREENING TESTS

No other topic related to the identification of controlled substances causes as much controversy as testing specificity. Forensic science laboratories conduct two different categories of tests. Tests in the first category are called “screening tests”. They include a series of tests used to make a preliminary determination of whether a particular drug or class of drugs is present. It must be emphasized that screening tests are not used to positively identify any drug. At best, screening tests can only be used to determine the possibility that members of a particular class of drug may be present. Some say that screening tests can result in “false positives”, meaning that either the test indicates the possible presence of a controlled substance when none is present or that the test indicates the possible presence of one controlled substance when a different controlled substance is present. That should not be a problem, so long as it is understood that screening tests have very little if any specificity, and that a false positive test will only lead to more testing, not a false conclusion. The identification of any drug by a chemical analysis is a systematic process involving a progression from less specific methods to more specific methods. The most specific methods involve instrumental analyses. Properly trained scientists should know when a false positive is possible, and how to take steps to narrow the focus of the testing. The more tests used, the fewer the chances for error.

False negative screening tests also occur. Very weak or diluted samples containing controlled substances may yield a negative screening test. An example of this situation would be a 1% heroin sample cut with a brown powder. Testing this sample with Marquis Reagent, which contains sulfuric acid and formaldehyde, may result in a charring of the brown powder and subsequent masking of the bleeding purple color characteristic of an opium alkaloid. Weak or old reagents may also yield false negatives. Examiner fallibility or inexperience in discerning colors may also result in false negatives. The possibility of a false negative leads many examiners to conduct a series of screening tests or, when warranted, to progress directly to more narrowly focused screening tests.

Specificity is the key to the forensic identification of controlled substances. There is no one method that will work as a specific test for any and all exhibits at any and all times. The choice of which specific method one utilizes must be determined by the type of controlled substance, the concentration of the controlled substance in the sample, the nature of the diluents and adulterants, the available instrumentation, and the experience of the examiner. There is an ongoing debate as to whether one can achieve this scientific certainty by combining a series of non-specific tests. This will be discussed later in this section.

1.7.1.1 Physical Characteristics

Occasionally an experienced forensic analyst can just look at an exhibit in a drug case and determine the probable nature of the substance. However, “probable natures” are not enough for an identification, and most examiners will usually conduct more than one test before reporting the presence of a controlled substance. The morphology of botanical substances such as marijuana and the peyote cactus are familiar enough to many laboratory analysts. Marijuana is one of those controlled substances which is examined with such frequency in the laboratory that a preliminary identification is probable based on the morphology of the botanical substance, gross physical appearance, texture, and odor. However, even after a microscopic examination of the cystolithic hairs using a microscope, the modified Duquenois–Levine test is usually run to corroborate the identification. The peyote cactus with its button-like appearance is also unique. In a like manner, the identification of the opium poppy requires a confirmation of the morphine; and the identification of the psilocybin mushroom requires an identification of the psilocybin or the psilocin.

The physical characteristics of these four agronomic substances might enable an expert witness with a background in plant taxonomy and botany to make an identification based solely on these characteristics. The forensic analyst relies on the physical characteristics and corroborating chemical examinations to identify these materials as controlled substances.

1.7.1.2 Color Tests

The color test is usually the first chemical examination examiners conduct after a package suspected of containing controlled substances is opened and weighed. Small amounts of the unknown material are placed in depressions in a porcelain spot plate or a disposable plastic or glass spot plate. Chemical reagents are then added to the depressions and the results noted: color changes, the way in which the color changes take place (flashing or bleeding), the rate at which the color changes take place, and the intensity of the final colors. The most common color reagents are the Marquis reagent for opium alkaloids, amphetamines, and phenethylamines such as MDA or MDMA; cobalt thiocyanate reagent for cocaine and phencyclidine (PCP); Dille-Koppanyi reagent for barbiturates; Duquenois reagent for marijuana; and Ehrlich’s reagent for LSD. A more complete listing of these tests is available in the literature.¹ Many of these tests are multi-step and multi-component.

These color tests are designed as a starting place for the examiner in deciding how to proceed as the pyramid of focus narrows in forming a conclusion. Adulterants and diluents can also cause color changes and are sometimes said to be responsible for “false positives.” The resulting color changes are not really false. They simply reflect the presence of a substance which is not the primary focus of the analytical scheme. Problems of “false negatives” and “false positives” are usually recognized very early in the analytical scheme, and they are resolved logically and rationally.

1.7.1.3 Thin Layer Chromatography

Thin-layer chromatography (TLC) is a separation technique. The method utilizes a glass plate which is usually coated evenly with a thin layer adsorbant. The most commonly used adsorbant is silica gel. A small amount of the sample is put into solution with a chemical solvent. A capillary pipet is then used to place a small amount of the liquid onto the TLC plate approximately 2 cm from the bottom of the plate. A second capillary pipet containing a small amount of a known controlled substance in solution is used to place a second spot on the plate usually next to, but not overlapping, the first spot.

The plate is then placed into a tank containing a solvent system which rises about 1 cm from the bottom of the tank. Through capillary action, the solvent will migrate up the plate, and the components of the unknown will usually separate as the solvent migrates. The

separated components can usually be visualized using longwave or shortwave ultraviolet light, a chemical spray, or some combination of both. The distance each sample migrates is then divided by the distance the solvent in the tank migrates up the plate (known as the R_f value). The result is then compared to published values that have been established for pure samples of the abused drugs. If one of the components of the unknown migrates the same distance up the plate as the known, the examiner has another piece of corroborating information. If the unknown does not contain a component that migrates the same distance as the known, there are many explanations. Perhaps the known and unknown are not the same. Perhaps there is a component in the unknown solution which is binding the chemical of interest to the silica gel. The explanations for matches are numerous. The explanations for non-matches are just as numerous.

The literature is replete with values for drug/solvent migration ratios. However, these values can be affected by many factors, including the storage conditions of the TLC plates and solvent temperature. It is not uncommon for the R_f values in the laboratory to differ from those in the literature. The importance of a TLC analysis lies in its ability to separate components in a mixture. A match is another piece of corroborating information. A non-match can usually be explained.

Using TLC to identify marijuana, hashish, or hash oil is a much more complicated process than using it to identify other controlled substances.² The TLC analysis of cannabis exhibits results in a series of bands on the thin-layer plate. Depending on the solvent system, the number of bands can range from at least three to at least six bands.³ Each band will have a specific color and lie at a specified place on the plate corresponding to the known cannabinoids in a standard marijuana, hashish, or THC sample.⁴ The key point here is that this type of identification involves a specific chromatographic pattern as opposed to one spot where a known is compared directly with an unknown. Even with the increased specificity of a TLC analysis in the examination of cannabis or a cannabis derivative, a modified Duquenois–Levine test is suggested.

1.7.2 CONFIRMATORY CHEMICAL TESTS

1.7.2.1 Microcrystal Identifications

Microcrystal tests are conducted using a polarized light microscope and chemical reagents. These microscopic examinations are not screening tests. The analyst will usually place a small amount of the sample on a microscope slide and add a chemical reagent and note the formation of a specific crystal formation. These crystals are formed from specified reagents. There should be very little subjectivity in evaluating a microcrystal test.⁵ Either the crystal forms or it does not form. If the appropriate crystal forms in the presence of the reagent, the drug is present. If the crystal does not form and the drug is present, the problem is usually one in which the drug concentration is too dilute, or the reagent has outlived its shelf life.

One disadvantage of microcrystal tests is the absence of a hard copy of what the analyst sees. Unless a photograph is taken of the crystal formation, the examiner cannot present for review documentation of what he saw under the microscope. Microcrystal tests are an excellent way of evaluating the relative concentration of a drug in a sample to determine the kind of extraction technique for separation and further confirmation.

1.7.2.2 Gas Chromatography

Gas chromatography (GC) has been a standard operating procedure in forensic science laboratories for the past three decades. In this technique, a gaseous mobile phase is passed through a column containing a liquid coated, stationary solid, support phase. The most common form of GC uses a capillary column of a very fine diameter for separating the

component of a mixture. The sample is usually put into solution using an organic solvent such as methanol. The liquid is then introduced into the injection port of the gas chromatograph using a fine needle syringe capable of delivering microliter quantities of the solution. The amount injected depends on the concentration of the sample. One microliter (one-one hundredth of a milliliter) of 1 mg of solute per 1 ml of solvent is a typical injection amount. The sample is vaporized in the heated injection port, and with the aid of a carrier gas travels through the long capillary column where the different components are separated. There are many different kinds of capillary columns with different internal coatings, lengths (which can vary from one foot up to tens of meters), and diameters (measured in micrometers). This separation is determined by the polarity and molecular size of each component. Each component exits the column onto a detector. A flame ionization detector (FID) is the most common detector used in most laboratories. Other types of less frequently encountered detectors include the nitrogen phosphorous detector and the electron capture detector.

As each component elutes from the column through the FID, a signal is generated which results in a "peak" on a recording device. The recorder is used to document the resulting data. This recorder is usually a part of a data station that not only generates a representation of the chromatogram on a monitor, but also controls instrument parameters and ensures the consistency of the analysis. The peaks of interest are evaluated by their retention times (RT's) and by the areas under the peaks. The retention time data can be used either as confirmation of the probable identity of the substance generating the peak, or the data can be evaluated as screening information to determine the possible presence of a controlled substance. This RT data is compared to the retention time of a known standard injected onto the same column in the same instrument at the same temperature and rate flow conditions. The RTs of the known and the unknown should be almost the same within a very narrow window. The area under the peak can be used to quantitatively determine the relative concentration of the substance.

There are some disadvantages of GC. Retention times are not absolute and usually fall within a narrow window. Other compounds may fall within this same RT window. One way to overcome this problem is to analyze the same sample using a second capillary column with a different internal coating and to note its retention time as compared to the known standard. The values should be the same within a narrow RT window. A second disadvantage of GC is that some samples degrade in the injection liner at high temperatures and must be evaluated by using a derivatizing agent. This derivatizing agent is added to the drug and forms a molecular complex. The molecule complex remains intact as it passes from the injection port, through the column, and onto the detector.

GC by itself is a very powerful tool for the forensic analyst. Its most useful application today remains one in which it is interfaced with a mass spectrometer (mass selective detector) which serves as a detector and separate instrumental identification method unto itself. Gas chromatography/mass spectrometry will be discussed later in this section.

1.7.2.3 High Performance Liquid Chromatography (HPLC)

This chromatographic technique is also a separation technique, but with a bit more selectivity than GC. In HPLC, the mobile phase is a liquid and the stationary phase is a solid support or a liquid-coated solid support. In GC, a carrier gas is used to carry the sample through the chromatography column. In HPLC, a high pressure pump is used to carry the solvent containing the compound of interest through the column. Separation results from selective interactions between the stationary phase and the liquid mobile phase.⁶ Unlike GC, the mobile phase plays a major role in the separation. HPLC can be used for the direct analysis of a wide spectrum of compounds and is not dependent on solute volatility or polarity. The operator need not worry about chemical changes in the molecule which can occur in GC due to thermal degradation.

HPLC chromatograms are evaluated based on retention time and area under the peak of interest. Retention time is not an absolute value, but a time within a narrowly defined window. The five basic parts of the liquid chromatograph include the solvent reservoir, the pump, the sample injection system, the column, and the detector. A recorder is used to document the resulting data. This recorder is usually a part of a data station which controls instrument parameters and ensures the consistency of the analysis. The most common detectors are the ultraviolet/visible detector (UV/VIS), the fluorescence detector, the electrochemical detector, the refractive index detector, and the mass spectrometer. The UV/VIS detector is the most widely used device, and it is dependent on the solute's ability to absorb ultraviolet or visible light. The variable wavelength detector allows the analyst to select any wavelength in the ultraviolet or visible range. The diode array or rapid scan detector is also used which allows a rapid scan of the entire UV spectrum to identify the components eluting from the column.

Because the components elute from the UV detector in solution, they do not undergo degradation or destruction. This one very useful characteristic of HPLC affords the analyst the option of collecting fractions of the eluent for further analysis. This is not possible in GC because the eluent is destroyed by the FID.

1.7.2.4 Capillary Electrophoresis (CE)

Capillary electrophoresis is a technique that separates components on the basis of charge-to-mass ratios under the influence of an electrical field. It uses high voltage for fast separations and high efficiencies. Osmotic flow is the main driving force in CE, especially at higher pH values, and results primarily from the interaction of positive ions in solution with the silanol groups on the capillary in the presence of an applied field. Narrow bore capillary columns of uncoated fused silica are used for heat dissipation during the separation process. The detector is normally an ultraviolet detector.

Micellar electrokinetic capillary chromatography (MECC) is a form of CE which allows for the separation of cations, neutral solutes, and anions.

CE has several advantages over HPLC and GC. The method can be used with ionic and neutral solutes which present problems in GC. There is a higher efficiency, resolving power, and speed of analysis compared to HPLC. From a cost perspective, CE requires much less solvent than HPLC, and the CE capillary column is much less expensive than the HPLC or GC capillary columns. Two disadvantages of CE are the limited sensitivity for UV detection (30 to 100 times less than that of HPLC); and fraction collection is troublesome because of mechanical problems and small sample size. This technique uses a micelle as a run buffer additive to give separations that are both electrophoretic and chromatographic.

One of the advantages of MECC is the ability to separate racemic mixtures of compounds into the d- and l-isomers. This is an ability that is extremely valuable when identifying compounds where one isomer is controlled (dextropropoxyphene) and the other isomer is not controlled (levopropoxyphene). This is usually accomplished by adding cyclodextrins to the run buffer.

1.7.2.5 Infrared Spectrophotometry (IR)

Infrared spectrophotometry is one of the most specific instrumental methods for the identification of a controlled substance. A pure drug as a thin film on a KBr salt plate, or as crystals mounted in a KBr matrix are placed into the sample compartment of the infrared spectrophotometer. A source of electromagnetic radiation in the form of light from a Nernst glower passes light through the sample. The instrument, through a mechanical means, splits the beam into a reference beam and an incident beam. The reference beam passes unobstructed through a monochromator to a photometer; the incident beam passes through the mounted sample through the same monochromator to the photometer. The reference beam passes 100%

unobstructed to the photometer. The incident beam passing through the sample has some of its energy absorbed by the sample. This energy is absorbed at different wave lengths across the infrared spectrum from 4000 cm^{-1} down to 250 cm^{-1} . The amount of relative absorption and where on this spectrum the absorption takes place is dependent upon the molecular structure and, more specifically, the functional groups of the drug. Different functional groups and molecular interactions brought on by symmetrical and asymmetrical molecular stretching vibrations and in-plane and out-of-plane bending vibrations result in a number of peaks and valleys on the IR chart. The resultant spectrum is usually formed on an x/y coordinate axes. The wavelength (μ) or wave number (cm^{-1}) where the absorption occurs is depicted on the x-axis, and a measure of the amount of light absorbed by the sample, but usually referenced by transmittance units from 0 to 100%, is depicted on the y-axis

The infrared spectrum of a suspected drug results in a specific pattern that can be used to positively determine the identity of the substance. For most controlled substances, the resulting spectrum consists of 20 to 70 peaks. These peaks form a pattern that is unique to the chemical structure of the drug. This pattern can then be compared with a reference IR spectrum of a primary drug standard. If the analyst determines that the two spectra match within the limits of scientific certainty, an identification is possible. It is rarely, if ever, possible to overlay the reference spectra with the spectra of the unknown and have a "perfect match". The analyst is looking for a match in the patterns. Any shifts in peak intensity or wave number must be evaluated in conjunction with the pattern. Small shifts of 1 or 2 cm^{-1} and minor intensity variations of individual peaks are expected. However, major variations must be evaluated on a case by case basis. Some authors refer to IR as a "fingerprint" identification method. This implies an ability to overlay two spectra and obtain a perfect match in every way. This degree of perfection is rarely, if ever, possible.

Another factor that must be considered is that when two spectra are being compared peak-by-peak as opposed to pattern-by-pattern, they ideally should be from the same instrument and collected at about the same time. Comparing a literature reference spectrum with an unknown for a pattern match is acceptable. Comparing the same literature reference spectrum wave number by wave number, absolute transmittance value by absolute transmittance value will probably result in minor differences.

IR does have limitations. In order to obtain an acceptable spectrum, the sample must be very clean and dry. For forensic exhibits, this usually means that most samples must go through extraction processes to remove impurities. In the past, sample size was a problem. However, because of advances in Fourier transform IR technology and the interfacing of an IR spectrophotometer with a microscope, evaluating microgram quantities of a sample results in excellent spectra which are conclusive for the identification of a controlled substance. IR has very definite limitations in its ability to quantitate controlled substances, and differentiating some isomers of controlled substances can pose problems.

1.7.2.6 Gas Chromatography/Mass Spectroscopy (GC/MS)

Gas chromatography/mass spectrometry is by far the most popular method of identifying controlled substances in the forensic science laboratory. In this method, a gas chromatograph is interfaced with a mass selective detector (MSD). The sample undergoing an examination is placed into solution with a solvent such as methanol. A very small injection volume of 1 or 2 μl is injected into the GC injection port. It then travels through the column where the different components of the sample are separated. The separated components can then be directed into the ionization chamber of MSD where they are bombarded by an electron beam. In electron impact gas chromatography/mass spectrometry (EI MS), high energy electrons impact the separated component molecules. The resulting spectrum of each component is typically complex with a large number of mass fragments. These fragments are represented as peaks of

varying intensity that provide the basis for comparison with a primary reference standard. The components are then ionized and positively charged. This ionization also results in a fission, or fragmentation process. The molecular fragments traverse into a magnetic field where they are separated according to their masses. In this magnetic field, larger mass fragments are less affected by the magnetic field, and smaller fragments are more affected and undergo a deflection. Upon exiting the magnetic field, these fragments impact a detector losing the charge generated by the beam of electrons impacting the sample. The result of this fragmentation process is a pattern unique for the substance that is being analyzed.

The resulting mass spectrum consists of an x/y coordinate axis. The numerical value on the x-axis represents the mass number determined by the number of neutrons and protons in the nucleus. It is usually the molecular weight of a specific fragment. The largest magnitude peak on the x-axis will often be the **molecular ion** and will represent the molecular weight of the unfragmented compound. There will usually be a very small peak to the right of the molecular ion which represents the molecular weight plus 1. The y-axis represents the relative abundance of each peak comprising the mass spectrum. The tallest peak on the y-axis is the **base peak** and represents that part of the molecule which is the most stable and undergoes the least amount of fragmentation. The base peak is assigned a relative abundance value of 100. The other peaks in the resulting spectrum are assigned relative values along the y-axis.

The numerical values on the x- and y-axis are calculated and assigned by the data station which is interfaced with the mass spectrometer. The accuracy of these numbers is predicated on the fact that the instrument has been properly tuned. This tuning process can be compared to checking the channel tuning on a television set. This might be accomplished by opening a television guide to determine what programs are scheduled at a particular hour. The television is then turned on and the program for each channel checked. If the programs cited in the television magazine appear on corresponding channels at the proper times, the television has been proven to be properly tuned. The tuning of a mass analyzer presents an analogous situation.

The tuning process of a mass analyzer involves a procedure in which a chemical of a known molecular weight and fragmentation pattern is analyzed and the resulting data evaluated. This process includes verifying instrument parameters and the resulting spectrum. If the response of the tuning process falls within specified limits, the mass spectrometer is deemed operationally reliable, and the resulting data can be considered reliable. One such chemical used to tune mass spectrometers is perfluorotributylamine (PFTBA).

Fragmentation patterns of controlled substances are typically unique. Once a fragmentation pattern has been obtained, the forensic analyst should be able to explain the major peaks of the spectrum and relate them to the molecular structure. If properly evaluated, mass spectral data can usually be used to form a conclusion as to the identity of a controlled substance.

GC/MS has many advantages in the analysis of controlled substances. The sample being analyzed need not be pure. Multi-component samples are separated and each soluble organic component can be individually identified. The analyst must be aware of isomeric compounds that have very similar chemical structures and similar fragmentation patterns. These kinds of situations can usually be handled by noting the GC retention time data to discriminate between similar compounds. Possible coelution of compounds from the capillary GC column and thermal degradation as noted in the gas chromatography section of this chapter should also be recognized. GC/MS does not allow the forensic analyst to directly identify the salt form of the drug. This task can be accomplished by considering the solubility properties of the drug being analyzed. In using this knowledge and performing extractions prior to injection onto the GC column, the salt form can be determined indirectly.

When all methods of instrumental analysis of controlled substances are considered, GC/MS is recognized in most instances as one of the efficient analytical techniques. If the analyst

is cognizant of maintaining instrument reliability standards and the guidelines of mass spectral interpretation, GC/MS affords one of the highest degrees of specificity in the identification of controlled substances.

1.7.2.7 Nuclear Magnetic Resonance (NMR) Spectroscopy

Nuclear magnetic resonance spectroscopy is one of the most powerful instrumental techniques available to the forensic chemist. In those laboratories fortunate enough to have NMR technology, extensive capabilities exist. Data interpretation of NMR spectra requires a high degree of expertise. This instrumental technique allows the analyst to detect paramagnetic atoms. (^1H , ^2H , ^{13}C , ^{15}N , ^{17}O , ^{31}P , ^{11}B , and ^{19}F are examples.) Most forensic applications of NMR focus on ^1H and ^{13}C . The resonant frequency of hydrogen (^1H) in the current high field magnets ranges from 200 to 750 MHz. This instrument generates a high magnetic field more than capable of damaging encrypted data on the back of a credit card. The NMR is a very expensive instrument requiring a high degree of specialized expertise to maintain and interpret the resulting data. The NMR is the one instrument which affords the analyst the ability to determine both the molecular structure and the three-dimensional orientation of some individual atoms of the molecule. This means that structural isomers can be determined directly. However, the extent of this kind of information is usually required only by research scientists in those instances where no other information is available from other instrumental methods, or where no primary analytical standard is available to confirm the presence of a controlled substance.

The major component of the NMR spectrometer is a high field superconducting magnet. The sample is dissolved in a deuterated solvent and then transferred to a long cylindrical glass tube usually measuring 5 mm in diameter. The tube is placed into the NMR probe located near the center of the magnetic field. In proton NMR, the magnetic field causes the hydrogen atoms on the molecule to orient in a particular direction. In order to obtain high-resolution spectra, the field produced by the magnet must be homogenous over the entire area of the sample in the probe. The resonance frequencies for all protons in a molecule may be different. These frequencies are dependent upon the molecular environment of the nucleus. This correlation between resonance frequencies and molecular environment enables the analyst to make judgments regarding the structure of the drug that he is analyzing.

The NMR spectrum is traced on a two-dimensional x/y coordinate axes. By evaluating an NMR proton spectrum, an analyst can determine an important factor that facilitates the identification of the compound — the area under each peak indicates the number of nuclei that are undergoing a transition and the number of protons that are present.

There are other types of examinations that are possible with high field NMR. A carbon-13 (^{13}C) evaluation enables an analyst to determine the number of carbons and their relative positioning in the molecule. ^{13}C is an isotope of the more abundant ^{12}C . About 1% of naturally occurring carbon is ^{13}C . There are two additional NMR “2D experiments” which are very valuable to the forensic analyst. Correlation spectroscopy (COSY) measures proton to proton ($^1\text{H} - ^1\text{H}$) interactions; and nuclear overhauser effect spectroscopy (NOESY) measures the interaction of protons which are close to one another, but not necessarily on adjoining atoms. Carbon 13, COSY, and NOESY spectra are all much more difficult to interpret and require specialized knowledge.

In the forensic analysis of controlled substances, most molecules are comprised of carbon and hydrogen. Proton NMR provided a unique spectral pattern which can be used to identify a controlled substance. This pattern also enables the analyst to distinguish between the basic and a salt form of the drug. NMR cannot distinguish halogenated salt forms. For instance, it cannot distinguish between heroin hydrochloride and heroin hydrobromide. But it can distinguish between a heroin salt and heroin base.

REFERENCES

1. Johns, S.H., Wist, A.A., and Najam, A.R., Spot tests: A color chart reference for forensic chemists, *J. Forensic Sci.*, 24: 631-649.
2. Hughes, R.B. and Kessler, R.R., Increased safety and specificity in the ythin-layer chromatographic identification of marijuana, *J. Forensic Sci.*, 24: 842-846.
3. Baggi, T.R., 3-methylbenzthiazolinone-2-hydrazone (MBTH) as a new visualization reagent in the detection of cannabinoids on thin-layer chromatography, *J. Forensic Sci.*, 25: 691-694.
4. Parker, K.D., Wright, J, A., Halpern, A.F., and Hine, C.H., Preliminary report on the separation and quantitative detemination of cannabis constituents present in plant material and when added to urine by thin-layer and gas chromatography, *Bull. Narc.*, 20: 9-14.
5. Fulton, C.C., *Modern Microcrystal Tests for Drugs*, John Wiley & Sons, New York, 1969.
6. Lurie, I. S. and Witmer, J.D., *High Performance Liquid Chromatography*, Marcel Decker, New York, 1983.

1.7.3 CONTROLLED SUBSTANCES EXAMINATIONS

Every examination made by a forensic chemist has a potential legal ramification or consequence. Forensic chemists must be prepared to depart from the familiar natural science setting of the laboratory and to enter the confrontational setting of the courtroom and be able to communicate with a prosecuting attorney, a defense attorney, a judge, 12 jurors, and on occasion, the press. The forensic chemist must be able to explain the significance of complicated analytical procedures to individuals with little or no scientific training. If the forensic analyst is to have any credibility on the witness stand, he must be able to describe what he has done in terminology understood by those individuals with whom he is communicating.

1.7.3.1 Identifying and Quantitating Controlled Substances

Whenever a controlled substance is identified, the possibility exists that an individual could be imprisoned or suffer some other legal consequence as a result. There is, therefore, an absolute, uncompromised requirement for certainty in the identification of controlled substances. Prior to 1960, the results of microscopic crystal tests, color screening tests, and TLC were considered definitive. From the 1960s through the mid-1970s, ultraviolet spectrophotometry and GC gained acceptance. It is interesting in 1997 to look back 20 years and contemplate the absolute faith placed in a retention time on a gas chromatogram, or upon the ultraviolet absorption maxima in acidic or basic solutions. In some instances these numerical values were measured with a ruler!

From 1975 through 1985 there were major advances in IR and MS. During those years “specificity”, as we understand the term today, was, for the first time, actually attainable in most cases. As the technology continually evolved, with increased Fourier transform peak resolution in IR and NMR, and multi-component separations improved with capillary column gas chromatography, specificity also increased.

In the mid-1980s the advent of “designer drugs” (properly referred to as “controlled substance analogues”) resurrected the problem of specificity. In attempts at circumventing existing controlled substance laws, clandestine laboratory chemists began to alter chemical structures of controlled drugs by increasingly sophisticated syntheses. By replacing a methyl group with an ethyl group, or by using a five-membered ring instead of a six-membered ring in a synthesis, these clandestine laboratory chemists developed what at the time were non-controlled analogues. The Controlled Substance Analogue and Enforcement Act of 1986 was passed by Congress, largely as a response to this problem. This particular piece of legislation also reinforced the responsibility of the chemist to accurately discriminate between controlled substances and endless lists of possible analogues.

A direct consequence of the new law's passage was the development of analytical procedures in Fourier Transform Infrared Spectrophotometry (FTIR), Fourier Transform Nuclear Magnetic Resonance Spectroscopy (FTNMR), Gas Chromatography/Fourier Transform Infrared Spectroscopy (GC/FTIR), and CE. These instrumental methods have made their way into the forensic science laboratory and now provide the increased specificity required by the courts.

Controlled substances sold on the street are usually mixed with adulterants and diluents in a crude and mostly unspecified manner. In some laboratories, the analysts are required to identify and quantitate both the controlled substance and the adulterant drugs and diluent materials. Color tests, thin layer chromatography, and microcrystal tests of the pre-1960s vintage are still used for screening. These testing procedures were valid then and are still valid today, but today additional instrumental techniques are utilized to make the absolute identification and quantitation.

After the analysis has been completed, it must be documented. The final report must be clear, concise, and accurate, with all conclusions substantiated by analytical data. The data may be in the form of notations on paper in the analyst's writing, or on chromatograms, spectra, or other instrumental printouts. Dates must be checked, and the documented description of the exhibit(s) must be consistent with the actual exhibit. Each time a report is signed, the analyst places his reputation and credibility before the scrutiny of the court and his peers. Discovering a "mistake" after the report has been submitted to the courts is not good.

Cocaine can exist as either the hydrochloride (HCl) salt or as the base. Pursuant to federal law, there are sentencing guidelines based on the identification of cocaine as either the base or as the salt form (usually HCl). Cocaine can be adulterated with benzocaine, procaine, lidocaine, or any combination of these non-controlled drugs, and further diluted with mannitol, lactose, or other processing sugars. A variety of instrumental techniques can be used to distinguish cocaine HCl from cocaine base. FTIR spectrophotometry is commonly available and used in many laboratories. The IR spectra of cocaine HCl and cocaine base are quite different and easily distinguished. The IR spectrum of a cocaine HCl sample mixed with an adulterant presents a problem. The same sample analyzed by GC/FTIR presents the chemist with a total response chromatogram showing all peaks in a mixture. The resulting IR spectrum and mass spectrum are identifiable. However, in this technique, cocaine HCl and cocaine base cannot be distinguished. At this point, NMR can provide a solution to distinguishing the two forms of cocaine and identifying the adulterants.

The solubility properties of controlled substances can be used to separate different forms of controlled substances. For instance, cocaine base is soluble in diethyl ether, cocaine HCl is insoluble. Therefore, if an analyst is analyzing a material which is believed to be cocaine in a questionable form, he can try placing the material into solution with diethyl ether, separate the ether from the insolubles, evaporate the diethyl ether, and analyze the resulting powder by GC/MS. The resulting cocaine spectrum would indicate the presence of cocaine base because cocaine HCl would not have gone into solution.

Methamphetamine is produced in clandestine laboratories from the reaction of ephedrine with hydriodic acid and red phosphorus, or from the reaction of phenyl-2-propanone (P-2-P) with methylamine. Methamphetamine samples submitted to the forensic science laboratory usually contain precursors from the synthesis, by-products for side reactions, and adulterants such as nicotinamide which has been added by the clandestine laboratory operator. As is true of the mass spectrum of some other phenethylamines, the mass spectrum of methamphetamine may not provide enough specificity for positive identification. The most accurate way to identify many phenethylamines is with IR. However, NMR is at least as specific as FTIR, and it also allows for an identification in the presence of diluents. Unfortunately, NMR is not available in many laboratories. Nicotinamide is one of the more commonly encountered

adulterants with methamphetamine and can easily be distinguished from isonicotinamide by NMR spectroscopy.

The IR spectrum of methamphetamine hydrochloride in a potassium chloride salt matrix is very specific, and GC/FTIR is excellent at separating the components of a methamphetamine sample. However, this method requires great care in selecting the optimized temperature and flow parameters, and column selection.

GC/MS is the method most often used for identifying heroin. The mass spectrum of heroin is very specific. Heroin is relatively simple to separate, and identification of the degradation products and the by-products of the heroin synthesis, from morphine and acetic anhydride, is relatively straightforward. Because morphine is derived from opium, many of the by-products from the opium processing are carried over to the final heroin product. Acetylcodeine and acetylmorphine are clearly identified from the corresponding mass spectra. The GC/FTIR also provides excellent spectra for making identifications of heroin, its by-products, degradation products, and precursors. The chloroform insoluble diluents from heroin samples can also be identified in a potassium bromide matrix by FTIR. These materials will usually consist of sugars such as mannitol and inositol. When the heroin has been isolated from diluents and adulterants, FTIR and NMR can be utilized to confirm the salt form of the heroin.

Phencyclidine, more properly identified as phenylcyclohexylpiperidine (PCP), is usually submitted to the laboratory as an exhibit of PCP base in diethyl ether, a powder, or sprayed or coated on marijuana. The analysis of PCP is relatively direct by GC/MS. The resulting mass spectrum is specific. The GC/FTIR spectrum of PCP is not as specific when one compares this spectrum with that of PCP analogues and precursors such as phenylcyclohexyl carbonitrile (PCC) and phenylcyclohexyl pyrrolidine (PCPy). FTIR spectrophotometry of the solid in a potassium bromide matrix is very specific. A word of caution is in order for anyone handling PCP. PCP is a substance that is believed to be easily absorbed through the skin of the analyst. Minimum handling is recommended.

1.7.3.2 Identifying Adulterants and Diluents

The terms adulterants and diluents are sometimes used in the context of illicitly distributed controlled substances. Adulterants are chemicals added to illicit drugs which, in and of themselves, can affect some sort of a physiological response. This response can range from very mild to quite severe. Diluents are chemicals added to controlled substances which are used more as fillers than to elicit a physiological response. They can be added to affect the color and composition for the sake of satisfying the user. Adulterants and diluents are usually added to the controlled substance mixture by those involved in illicit distribution. There is a third class of materials that is found in controlled substance mixtures. This class includes by-products. These by-products can be processing by-products, or they can exist as naturally occurring by-products found in botanical substances such as the coca leaf or the opium poppy.

Most "street" exhibits of heroin and cocaine contain adulterants and diluents. Samples taken from large scale, brick size, kilogram seizures will be relatively pure. Except for some by-products from the opium poppy and the coca leave, there will be little in the way of foreign materials. Adulterants are encountered, in increasing proportions, as the heroin and cocaine progress down the distribution chain from the main supplier to the dealers to the users.

Adulterants commonly encountered in heroin include quinine, procaine, acetaminophen, caffeine, diphenhydramine, aspirin, phenobarbital, and lidocaine. Adulterants commonly encountered in cocaine include procaine, benzocaine, and lidocaine. Diluents found in heroin include different kinds of starches. It is not uncommon to find in heroin substances such as calcium carbonate which had been added during the morphine extraction processes. Diluents found in both cocaine and heroin include lactose, mannitol, sucrose, and dextrose.

The identification of adulterants and diluents may or may not be a requirement as a part of the identification scheme in the forensic science laboratory. In most instances, the requirements of the judicial system will be limited to the identification of the controlled substance. This will usually be accomplished by separating the sample into its component parts, and then identifying all or some of these components. In the case of a heroin exhibit, cut with quinine and mannitol, a capillary GC/MS examination might result in a chromatogram and corresponding spectra with an acetylcodeine peak, an acetylmorphine peak, a morphine peak, a quinine peak, and a heroin peak. The first two peaks are most probably processing by-products; the morphine is from the opium poppy; the heroin is the main peak of interest, and the quinine has probably been added as an adulterant. There is no need to separate the components by extractions to make the identifications. However, if the analyst is desirous of conducting an IR examination or a NMR examination to identify the heroin, an extraction of the heroin from a 3 N hydrochloric acid medium using chloroform is an option. Depending upon whether the heroin exists as a salt (heroin hydrochloride) or as heroin base, a set of serial extractions can be conducted to isolate the heroin from the quinine and the other substances. The identification of cocaine in a mixture follows the same procedures. Depending upon the type of analysis, the cocaine may or may not need to be chemically separated from the adulterants for an identification.

The simplest way to identify diluents in controlled substance mixtures is by microscopic identification. Common diluents along with the sugars/carbohydrates/starches described above include sodium chloride, calcium carbonate, and various types of amorphous materials. Because of their optical properties, these materials lend themselves well to a microscopic identification. Chemical separations are fairly easy because these materials are usually insoluble in solvents such as diethyl ether or hexane, and slightly soluble in solvents such as methanol. Most organic materials are soluble in methanol or some other polar solvent. The sugars/carbohydrates/starches can be further identified using IR following the separation if only one sugar is present. If not, HPLC can be used to identify the sugars.

Even if the identification of all adulterants, diluents, and by-products are not required in the final report generated by the analyst, such information can prove useful in evaluating trends and possible distribution patterns.

1.7.3.3 Quantitating Controlled Substances

A number of different methods can be used to quantitate controlled substances. Capillary column GC or HPLC are probably the two most utilized instrumental methods to accomplish this task. The choice of which instrumental method to use depends upon the chemical properties of the substance in question. GC works well with those compounds that are not highly polar, are relatively stable at high temperatures, and are soluble in organic solvents such as methanol or chloroform. Even if these conditions exist, GC can still be used if a derivatizing agent is used.

If GC is used, the most common analytical method for quantitation involves the use of an internal standard, providing a consistent concentration of a known chemical in solution. In order to avoid the obvious problem of choosing an internal standard which might be present in the sample as an adulterant or diluent, the internal standard can be a straight chain hydrocarbon (tetracosane, eicosane, or dodecane) which is added in equal amounts to both the sample being analyzed and the calibration samples. The internal standard method is especially advantageous because the expected flame ionization detector response for the internal standard to the drug can be checked for each and every injection. The critical factor for each injection is the ratio of the detector response of the internal standard to the calibration solution of known concentration. This is especially critical if the sample size of the injection is off target

by a minuscule amount. The absolute integration values for the known peak and the internal standard peaks may vary. However, the ratio will not be affected. If the detector is responding properly to the internal standard in solution, it is also responding properly for the substance being quantitated.

Controlled substances can also be quantitated using what is referred to as the external standard method. In this method, calibration standards of known concentrations are prepared. Injections are then made into the GC injection port, and a calibration table is established. The accuracy of this method is quite good, provided that the injection amounts used in establishing the calibration table are exactly the same from injection to injection. Even small variations of less than 10% volume, when dealing with a 1 μl injection, can lead to less than optimized results. This problem can be overcome by making multiple injections and checking the consistency of the detector response and the injection volume. The ability to be consistent can be developed by an analyst with a good eye. The ability to read the sample size on the microsyringe is, for some, as much an art as a scientific technique. Automatic injectors are now available on many gas chromatographs which approach consistency from one injection to the next. However, this method will work only when there is a verifiable linear response of the detector within a specified concentration range.

In both the internal and external standard methods, there must be a linear response of the detector to the solutions of different concentrations. This is determined by injecting solutions of known concentrations and establishing a calibration table. With most instrument data stations, this is relatively simple. The instrument will then calculate the response ratio of internal standard to drug for the solution of unknown concentration and compare this to the response ratios of internal standard to drug for the solutions of known concentrations in the calibration table. This ratio can then be used to calculate the concentration of the drug that is being analyzed.

HPLC can be useful for quantitating controlled substances in solution. This instrumental method also measures the response of different compounds at different ultraviolet/visible absorption bands. These responses are then compared to calibration table values. Internal standards can be used in the same way they are used in GC quantitations. The limitations and comparisons of HPLC and GC are discussed elsewhere.

Ultraviolet/visible spectrophotometry (UV/VIS) is a technique that has been in use for many years. UV/VIS uses one of the basic tenets of physics — Beer's Law. Absorption of monochromatic light is proportional to the concentration of a sample in solution. The concentration of an exhibit in solution can be determined by comparison with calibration tables. This type of analysis is dependent upon the solubility properties of the substance being quantitated in acid, basic, and organic solutions. The UV/VIS method is accurate and reliable only when the compound of interest is pure with no interfering substances. GC and HPLC are used more often because of the added reliability check provided by the internal standard methodology.

NMR spectrometry can also be used for the quantitation of controlled substances. The quantitative analytical techniques in NMR are more complicated than those discussed above and require a specialized instrumental expertise.

All of the methods discussed above are reliable and accurate when properly and conscientiously conducted. There is one very important difference which applies to any quantitative method when compared to an identification method. With proper methods, an analyst can make an identification of a controlled substance with scientific certainty. The quantitation of a controlled substance will usually result in values falling within a narrowly defined "window" of from one-tenth to one or two absolute percent. The reported value will usually be an average value.

1.7.3.4 Reference Standards

The first step in ensuring the accuracy of the identification of any controlled substance should be a collection of authenticated reference standards. Reference standards for the forensic science examinations should be 98+% pure. They can be purchased from a reputable manufacturer or distributor, synthesized by an organic chemist within the laboratory, or purified from a bulk secondary standard by using an appropriate methodology. "Reference Standards" that have been authenticated are available from the United States Pharmacopeia (USP) and National Formulary (NF). Samples obtained from any other source should be authenticated using the appropriate methodology. This authentication process will involve a two step process of first positively identifying the proposed reference standard and then determining the purity of this standard.

At a minimum, the identification of a reference standard should be conducted using IR and MS. The resulting spectra are then compared with reference spectra in the literature. The chemist should be able to evaluate data from both of these instruments and be able to explain the major peaks using, respectively, a functional group analysis or a molecular fragmentation analysis. If no literature spectra are available, a more sophisticated structural analysis such as NMR spectroscopy will be necessary to verify the chemical structure. Additional methods that can be used to supplement, but not replace, IR, MS, and NMR, include optical crystallography, X-ray crystallography, and a melting point analysis.

The next step in the process is to quantitate the reference standard against a "primary standard". A primary standard is a sample that has been subjected to the authentication process and meets the criteria of a positive identification and 98%+ purity. The quantitation methods of choice are GC or HPLC. With either method, the concentrations of the injections of both the primary standard and the authentication sample must be within the linear range of the detector. The method should utilize an internal standard. The results of all injections should have a relative standard deviation of less than 3%.¹

If a primary standard is not available, a purity determination can be accomplished by a peak area percent determination using capillary GC with a flame ionization detector and HPLC using a photo-array ultraviolet detector. A third instrumental method using a differential scanning calorimeter (DSC) should also be considered. In a peak area percent analysis, the area percent of the standard compound is determined vs. any impurities that are present in the batch. A blank injection of the solvent is done prior to the standard injection to detect peaks common to both the solvent and the authentication standard. The GC solution is checked for insolubles. If these insolubles are present, they can be isolated and identified by IR. Of course, if there are insolubles, the sample is no longer considered an authentication standard until it is purified and the foreign material is removed.

HPLC can also be used in a peak area percent analysis. For basic drugs, the analyst would use a gradient mobile phase using methanol and an acidic aqueous phosphate buffer. For neutral and acidic drugs, he would use a gradient with methanol and an acidic aqueous phosphate buffer containing sodium dodecyl sulfate. For anabolic steroids, he would use a methanol/water gradient mobile phase. As is the case with GC, with HPLC a blank injection of the solvent always precedes the injection of the authentication standard. Three wavelengths, 210 nm, 228 nm, and 240 nm, are monitored for most drugs. For anabolic steroids, the analyst should monitor 210 nm, 240 nm, and 280 nm. If the resulting UV spectra of all pertinent peaks are similar, the integration of the peaks with the most sensitive wavelengths are used for the calculation of purity.

DSC is a method of adding heat to a preweighed sample and monitoring temperature and heat flow as the sample goes through its melting point.² If decomposition does not occur during the melt, the peak shown on the thermogram can be used to determine melting point

and the molar concentration of any melt soluble impurities present. With this data, the analyst can determine the purity of the authentication standard. One drawback of DSC is that structurally dissimilar impurities such as sugars in a supposed heroin “standard” are not always detected by this method. This is because the impurity does not go into solution in the melting main component. With almost all authentication standards, most impurities will be structurally similar to the drug of interest. The dissimilar compounds should have been removed prior to the DSC analysis or detected by GC or HPLC.

REFERENCES

1. *CRC Handbook of Tables for Probability and Statistics*, CRC Press, 2nd ed., 1968, p.5.
2. McNaughton, J.L. and Mortimer, C.T., Differential scanning calorimetry, *IRS; Physical Chemistry Series*, 2, 1975, vol. 10.

1.8 COMPARATIVE ANALYSIS

1.8.1 DETERMINING COMMONALITY OF SOURCE

Two different kinds of controlled substance analyses are routinely conducted in the forensic science laboratory. The first is the “identification”. The goal is self-evident — to identify a controlled substance by name. The second, less common, type of analysis is the “comparative analysis”. Its purpose is to determine a commonality of source. A comparative analysis will include a comprehensive examination of the sample's chemical and physical characteristics, with the goal of demonstrating, with a high degree of certainty, a common origin for two or more samples.¹

Sometime it is possible to determine when two items of evidence have a common origin just by physically fitting them together. This applies to exhibits such as a screwdriver and a broken blade, two large paint chips that have broken apart, or a piece of paper torn in two or more pieces. In the forensic examination of illicit drugs, it is possible to state with a high degree of certainty that two exhibits of a white powder share a common source. The wording in stating such a conclusion is critical. Words must be carefully selected so as to convey the conclusion clearly and concisely, without overstepping the scientific certainty that exists. The following quote, about two samples of cocaine, is from the transcript of drug trial held in 1991. It illustrates the appropriate language to be used on such occasions.

After a review of all analytical data, it can be stated with a high level of scientific certainty and beyond a reasonable doubt that a close chemical relationship exists between [the two samples] strongly suggesting that they were derived from the same manufacturing process...and that they were probably derived from the same batch.²

Before undertaking a detailed examination of two samples, a broad overview is desirable. The color and granularity of the exhibits should be examined, and then the components of the sample identified and quantitated. If all of the data from one exhibit compare favorably with all of the data from the second exhibit, the analyst can proceed to a second set of procedures to evaluate the processing by-products and trace materials in the exhibits. It is important to realize that in order to successfully evaluate two exhibits to determine commonality of source, each exhibit must be analyzed in the same way using the same methodology, instruments, and chemicals and solvents from the same containers.

Controlled substances such as cocaine and heroin are the simplest to compare because they are derived from botanical substances (the coca leaf and the opium poppy, respectively).^{3,4} Many naturally occurring by-products from the plants are carried through the processing stages of the drugs, and these can be used to confirm the existence of a common source.

1.8.2 COMPARING HEROIN EXHIBITS

Capillary column gas chromatography (ccGC) and HPLC are the two methods most often utilized in comparing two or more heroin exhibits to determine whether they came from the same source. HPLC can be utilized in the first part of the analytical scheme because the components being evaluated usually are present in substantial amounts. The major components including heroin, acetylmorphine, acetylcodeine, morphine, codeine, noscapine, papaverine, thebaine, and most diluents can be identified and quantitated. A high degree of resolving power is not required at this point in the analytical scheme. If the HPLC analysis demonstrates that the samples being compared are similar, the analyst proceeds to the second part of the analytical scheme.

In the second part of this scheme to evaluate the trace components of the exhibits, ccGC is usually the method of choice, both because of its resolving power and because of its ability to detect minute quantities of the component of interest. The second step of the isolation process involves multiple extractions and derivatizations to isolate the acidic and neutral compounds for analysis and evaluation. This process isolates the precursors, solvents, and respective contaminants, by-products, intermediates, and degradation products. It is desirable to remove the heroin from the sample during the extraction processes in order to keep most of the trace components at the same level of chromatographic attenuation. Once the heroin has been identified and quantitated, only then are the other elements analyzed. If after these two processes the analyst sees no chromatographic differences in the samples being evaluated, a conclusion can be formulated. The number of components from this second part of the process can number from 100 to 300. If all of these components are present in both exhibits at similar relative levels, a conclusion regarding commonality of source is warranted.

1.8.3 COMPARING COCAINE EXHIBITS

The process is different for cocaine comparisons. For one thing, the cocaine need not be removed from the sample. Four different ccGC examinations can be conducted which evaluate and compare the by-products and impurities down to trace levels by:

1. Flame ionization gas chromatography (GC-FID) to evaluate cocaine hydrolysis products, manufacturing impurities, and naturally occurring alkaloids;⁵
2. GC-FID to determine trimethoxy-substituted alkaloids as well as other minor naturally occurring tropanes;⁶
3. Electron capture gas chromatography (GC-ECD) to determine the hydroxycocaines and N-nor related compounds;⁴ and
4. GC-ECD to determine the 10 intact truxillines.⁷

These four gas chromatographic methods provide an in-depth evaluation of trace level components and allow the precise comparison of two different cocaine exhibits. The number of components evaluated range in the hundreds. This data provides the analyst with an abundance of analytical points to form a conclusion regarding commonality of source.

Extraction of the impurities and by-products can be accomplished using a derivatizing reagent.^{8,9} Heptafluorobutyric anhydride (HFBA) is often used for this purpose. The GC-FID

and GC-ECD analyses that follow will result in organic profiles of the many compounds from the cocaine and heroin samples being analyzed. A further MS analysis may serve to identify the chemical composition of many of the components of each exhibit. Many of the resulting peaks represent compounds formed during the manufacturing process; others will be oxidation or hydrolysis products of known compounds; and other peaks will have a degree of uncertainty regarding their exact chemical structure. However, what will be known is that these peaks are present in both exhibits being compared using the ccGC methods and represent cocaine and heroin manufacturing impurities or by-products.

REFERENCES

1. Perillo, B.A., Klein, R.F.X., and Franzosa, E.S., Recent advances by the U.S. drug enforcement administration in drug signature and comparative analysis, *Forensic Sci. Int.*, 69: 1-6, 1994.
2. Moore, J.M., Meyers, R.P., and Jiminez, M.D., The anatomy of a cocaine comparison case: a prosecutorial and chemistry perspective, *J. Forensic Sci.*, 38: 1305-1325, 1993.
3. Moore, J.M. and Cooper, D.A., The application of capillary gas chromatography-electron capture detection in the comparative analyses of illicit cocaine samples, *J. Forensic Sci.*, 38: 1286-1304, 1993.
4. Moore, J.M. and Casale, J.F., In-depth chromatographic analyses of illicit cocaine and its precursor, coca leaves, *J. Chromatography*, 674: 165-205, 1994.
5. Casale, J.F. and Waggoner, R.W., A chromatographic impurity signature profile analysis for cocaine using capillary gas chromatography, *J. Forensic Sci.*, 36: 1321-1330, 1991.
6. Casale, J.F. and Moore, J.M., 3', 4', 5'-Trimethoxy-substituted analogues of cocaine, cis-/trans-cinnamoylcocaine and tropacocaine: Characterization and quantitation of new alkaloids in coca leaf, coca paste and refined illicit cocaine, *J. Forensic Sci.*, 39: 462-472, 1994.
7. Moore, J.M., Cooper, D.A., Lurie, I.S., Kram, T.C., Carr, S., Harper, C., and Yeh, J., Capillary gas chromatographic-electron capture detection of coca leaf related impurities of illicit cocaine: 2,4-diphenylcyclobutane-1,3-dicarboxylic acids, 1,4-diphenylcyclobutane-2,3-dicarboxylic acids and their alkaloidal precursors, the truxillines, *J. Chromatography*, 410: 297-318, 1987.
8. Moore, J.M., Allen, A.C., and Cooper, D.A., Determination of manufacturing impurities in heroin by capillary gas chromatography with electron capture detection after derivatization with heptafluorobutyric acid, *Analt. Chem.*, 56: 642-646, 1984.
9. Moore, J.M., The application of chemical derivatization in forensic drug chemistry for gas and high performance liquid chromatographic methods of analysis, *Forensic Sci. Rev.*, 2: 79-124, 1990.

1.9 CLANDESTINE LABORATORIES

There are two kinds of clandestine laboratories. The first is the **operational** clandestine laboratory. This laboratory, usually operating in secrecy, is engaged in the production of controlled substances, precursors to controlled substances, or controlled substance homologues or analogues. The second is the **non-operational** clandestine laboratory. This usually is a storage facility that is under investigation because of information obtained from precursor and essential chemical monitoring.¹

For the forensic scientist involved in the seizure of a clandestine laboratory, the task of evaluating the possibilities and probabilities begins prior to arrival at the laboratory site. The individual tasked with securing the laboratory for the purpose of collecting evidence must, for his own protection, be trained and certified competent in dealing with the safety and technical considerations of clandestine laboratory seizures. Forensic chemists may be asked to provide assistance in preparing search warrants based on available information, as when investigators know that certain chemicals and pieces of analytical equipment such as gas cylinders, and

glassware such as large triple neck round bottom flasks have been purchased. This sort of information is critical in determining what kind of synthesis is taking place. The forensic scientist will also provide technical advice regarding the importance of specific safety considerations and offer suggestions on handling situations such as on-going reactions.

After the clandestine laboratory site has been secured by the appropriate law enforcement authorities, the forensic scientist may enter the site to evaluate the environment and decide on the most appropriate actions. The investigator's most important function is to minimize any health risk to enforcement personnel. This may involve ventilating the environment by opening doors, windows, and using a fan; securing open containers, turning off gases and water; and removing obstacles on the floor which may prove hazardous to anyone entering the site. The investigator may also decide on whether chemical reactions in progress should be stopped or allowed to proceed. After all of these and other decisions are made and the site is secure, the forensic analyst will begin to sample, package, and mark evidence containers. This process will usually proceed slowly and methodically to ensure accuracy and completeness.

Once the clandestine laboratory has been seized and the evidence collected, the forensic analyst will proceed to the laboratory to complete the administrative processes of ensuring accountability and security. When the time approaches for the analytical procedures to commence, the person tasked with this process will attempt to identify as many of the samples as deemed necessary for the required judicial action. This may mean identifying any and all exhibits that were seized, or it may mean that only those exhibits required to form a conclusion as to an identification of the final product are necessary. The extent of the analysis can be more of a legal question than a scientific question. The forensic scientist should be able to provide the basics of the reaction mechanisms. This information will be based on the chemicals at the site and those identified in the reaction mixtures. He should also be able to provide a theoretical yield of the final product based on the amounts of the chemical precursors.

After the work in the laboratory has been completed, the forensic scientist has the responsibility of assisting the legal authorities in understanding what was happening in the clandestine laboratory — what was being synthesized, how was it being synthesized, and what environmental ramifications existed due to the disposing of waste solvents and other chemicals found in the soil or plumbing. The forensic analyst must recognize his responsibilities as an expert witness and provide factual information in as much detail as necessary. However, this task carries with it the responsibility of avoiding unsubstantiated speculation.

Evaluating a clandestine laboratory, from the time of notification until the time of testimony in the courtroom, requires an open-minded and analytical approach. As information is gathered and data collection proceeds, the analyst may be involved in an ever evolving decision-making process. This will probably require him to change his strategies as more information becomes available. Conclusions should be reserved until all the necessary exhibits have been collected and analyzed, the clandestine laboratory operator has been debriefed, the analytical data has been evaluated, and, if necessary, consultations with colleagues have been completed. In the courtroom, the forensic analyst will preserve his status as a credible expert witness by basing his testimony on factual data and possibilities that are within the realm of scientific probability.

1.9.1 SAFETY CONCERNS

A hazard evaluation is an absolute requirement prior to entering a clandestine laboratory. This should involve an evaluation of the physical and environmental hazards that may be present. This evaluation is usually the result of questioning other law enforcement personnel familiar with the laboratory, or the laboratory operator. Great care should be exercised in evaluating and acting on information from the laboratory operator. The forensic analyst should determine the minimum level of safety equipment required for entry into the laboratory. If there is

knowledge regarding the type of drug being synthesized in the clandestine laboratory and the processing methodology, the forensic scientist will have some idea as to the types of chemicals that may be encountered. If records are available regarding the purchasing activity of the clandestine laboratory operator, the quantities of the chemicals facing the investigators will be available.

All this information should be documented and used to decide the safest and most prudent manner in which to enter the clandestine laboratory. Other concerns that must be considered are the weather conditions, and entry and egress options. Extremes in either heat or cold can affect the way the safety and sampling equipment will function. These conditions will also effect how long the forensic chemist can be expected to work in the appropriate clothing. Egress options from a clandestine laboratory must be determined before entry. In the event of a fire or explosion, those individuals processing the clandestine laboratory must know how to exit the dangerous environment. As a part of the planning scenario for processing the clandestine laboratory, the appropriate authority should make the nearest medical facility aware of the fact that if an investigator is injured, medical attention will be sought. The medical facility may have some requirement for treating a chemical injury. This should be determined beforehand and a protocol to meet these requirements should be established.

The most important responsibility of the forensic analyst involved in a clandestine laboratory investigation and seizure is safety. Safety must be considered from a number of perspectives. The forensic scientist must be concerned with the safety and well-being of anyone entering the suspected clandestine laboratory. His training and experience will have prepared him to recognize many of the obvious dangers of the chemical hazards and physical hazards at the site. This awareness is not stagnant. There will usually be a condition that requires an immediate adjustment and reevaluation. He must be constantly aware of the possible hazards when the combination of two minimally unsafe conditions result in fatalities. This results from a failure to recognize that while each condition is dangerous in its own right, combining the dangers is a recipe for disaster if certain precautions are not followed.

For instance, if the odor of ether is detected in an enclosed dark room, a possible first step might be to turn on the lights. However, any short circuit in the light switch resulting in a spark could cause the ether vapors in combination with the oxygen in the air to explode. The correct action would be to obtain an outside lighting equipment to determine the source of the ether vapors, rectify the conditions resulting in the ether vapors, ventilate the room, check the light switch and wiring, and then turn on the lights. This situation is one in which a chemical hazard in combination with a physical hazard could combine and result in serious injury or death.

Before entering the clandestine laboratory, the forensic analyst must take precautions to ensure eye, lung, and skin protection. This will usually mean proper clothing including head gear, boots, outerwear and gloves; safety glasses and/or a face shield; and the appropriate air purification and breathing apparatus. Consideration should also be given to use of air monitoring devices which can detect concentrations of combustible gases or vapors in the atmosphere, oxygen deficiencies, and gas concentrations to lower explosive limits. There are also devices available in the form of glass tubes filled with specific detection granules which allow for the reasonable determination of airborne chemical hazards in the atmosphere. When these devices are used properly, the forensic scientist entering the clandestine laboratory maximizes his chances for protecting the safety of the seizure team, including himself.

Even after the atmosphere has been sampled and ventilation has progressed, once inside the clandestine laboratory, the forensic chemist should be aware of the many possibilities posing a threat. The potential chemical dangers include an explosion potential, flammable and combustible chemicals, corrosive chemicals, oxidizers, poisons, compressed gases, irritants, and booby traps. Physical hazards include but are certainly not limited to broken glass, bare electrical wiring, slippery floors, and loud noises. These chemical and physical hazards can be

accentuated by a reduction in dexterity because of safety equipment and clothing, a narrow field of vision due to a breathing apparatus, diminished communications, physical and mental stress, heat or cold stress, a confined work space environment, and a prolonged period of time spent processing the clandestine laboratory.

After the laboratory processing has been completed, the forensic scientist should be a part of the team which reduces the level of environmental contamination to a controllable level. This will usually involve prior planning for the proper disposal of hazardous chemicals and protective clothing by a waste disposal authority. There should be a standard operating procedure for the decontamination of anyone who entered the clandestine laboratory. This should include provisions for an emergency shower and an eyewash station, first aid kits, and decontamination procedures for injured workers.

One of the most important factors anyone processing a clandestine laboratory must remember is the following — no matter how much protective clothing is available, no matter how much pre-planning is done, no matter how careful a person might be in collecting chemicals and assessing danger, if that person fails to recognize his limitations in knowledge or physical ability, a disaster is waiting to happen. The greatest danger facing anyone who processes a clandestine laboratory is a false sense of security.

1.9.2 COMMONLY ENCOUNTERED CHEMICALS IN THE CLANDESTINE LABORATORY

The following tabulation of data is intended as an overview of those chemicals most frequently encountered as precursors in clandestine laboratory settings. A **precursor** is a chemical that becomes a part of the controlled substance either as the basis of the molecular skeleton or as a substituent of the molecular skeleton. This list is not all inclusive. Modifications to typical synthetic routes on the parts of ingenious organic chemists are typical and cannot always be predicted.

1.9.3 TABLES OF CONTROLLED SUBSTANCES

1.9.3.1 Generalized List by Category of Physiological Effects and Medical Uses of Controlled Substances

Precursor	Controlled substance
Acetic anhydride	Heroin Methaqualone Phenyl-2-Propanone (P2P)
Acetonitrile	Amphetamine
N-Acetylanthranilic acid	Methaqualone Mecloqualone
Acetylacetone	Methaqualone
4-Allyl-1,2-methylenedioxybenzene	3,4-Methylenedioxyamphetamine (MDA)
Ammonium formate	Amphetamine MDA
Amphetamine	alpha-Methyl fentanyl
Aniline	alpha-Methyl fentanyl
Anthranilic acid	Methaqualone
Benzaldehyde	Amphetamine P-2-P

Benzene	Amphetamine
	P-2-P
Benzyl cyanide	Methamphetamine
Bromobenzene	N-Ethyl-1-phenylcyclohexylamine (PCE)
	Phencyclidine (PCP)
	1-Phenylcyclohexylpyrrolidine (PCPy)
	P-2-P
1-Bromo-2,5-dimethoxybenzene	4-Bromo-2,5-dimethoxyamphetamine (DOB)
Bromohydroquinone	DOB
5-Bromoisatin	Lysergic Acid
ortho-Bromophenol	4-Bromo-2,5-dimethoxyphenethylamine (Nexus)
Bromosafrole	3,4-Methylenedioxyethylamphetamine (MDEA)
	3,4-Methylenedioxymethamphetamine (MDMA)
2-Bromothiophene	1-[1-(2-Thienyl)cyclohexyl]piperidine (TCP)
Chloroacetic acid	P-2-P
Chloroacetone	P-2-P
1-Chloro-2,5-dimethoxybenzene	Nexus
2-Chloro-N,N-dimethylpropylamine	Methadone
2-Chloroethylbenzene	Fentanyl
alpha-Chloroethylmethyl ether	P-2-P
Chlorohydroquinone	DOB
Chlorosafrole	MDEA
	MDMA
ortho-Cresol	4-Methyl-2,5-dimethoxyamphetamine (STP)
Diethylamine	Diethyltryptamine
	Lysergic Acid Diethylamide (LSD)
Ephedrine	Methamphetamine
	Methcathinone
Ergonovine	LSD
Ergotamine	LSD
Ethylamine	Ethylamphetamine
	3,4-Methylenedioxyethylamphetamine (MDEA)
N-Ethylephedrine	N-Ethyl-N-methylamphetamine
N-Ethylpseudoephedrine	N-Ethyl-N-methylamphetamine
ortho-Ethylphenol	4-Ethyl-2,5-dimethoxyamphetamine
Formamide	Amphetamine
	MDA
Isosafrole	4-Methylenedioxyamphetamine (MDA)
	3,4-Methylenedioxymethamphetamine (MDMA)
	MDEA
Lysergic acid	LSD
Methylamine	Methamphetamine
	MDMA

3,4-Methylenedioxyphenyl- 2-propanon	MDA MDMA MDEA
N-Methyephedrine	N,N-Dimethylamphetamine
N-Methylpseudoephedrine	N,N-Dimethylamphetamine
Nitroethane	P-2-P Amphetamine MDA
1,2-Methylenedioxy-4- propenylbenzene	MDEA
N-Methylephedrine	P-2-P
N-Methylformamide	Methamphetamine
N-Methylformanilide	STP
2-Methyl-4-[3H]-quinazolinone	Methaqualone
Methyl-3,4,5-trimethoxybenzoate	Mescaline
Norpseudoephedrine	4-Methylaminorex
Phenethylamine	Fentanyl para-Fluoro fentanyl 2-Methyl fentanyl
N-(1-Phenethyl)-Piperidin-4-one	Fentanyl para-Fluoro fentanyl
N-(1-Phenethyl-4-piperidinyl)-aniline	Fentanyl
Phenylacetic Acid	P-2-P
Phenylacetone	P-2-P
Phenylacetyl Chloride	P-2-P
D-Phenylalanine	Amphetamine Methamphetamine
2-Phenyl-1-bromoethane	Fentanyl
1-Phenyl-2-bromopropane	alpha-Methyl fentanyl
Phenylmagnesium Bromid	PCP PCPy P-2-P
Phenylpropanolamine	Amphetamine 4-Methylaminorex
Phenyl-2-propanone (P-2-P)	Amphetamine Methamphetamine
Piperidin	Phencyclidine (PCP)
N-(4-Piperidinyl)aniline	Fentanyl alpha-Methyl fentanyl
Piperonal	MDA MDMA MDEA
Piperonylacetone	N-Hydroxy MDA
Propionic Anhydride	Fentanyl analogues

Propiophenone	Methamphetamine
Pyrrolidine	PCPy
Pseudoephedrine	Methamphetamine
Safrole	MDA
	MDMA
	3,4-Methylenedioxy P-2-P
3,4,5-Trimethoxybenzaldehyde	Mescaline
	3,4,5-Trimethoxyamphetamine

Table 1.9.3.1 Controlled Substances

Below is a categorized listing of the most commonly encountered controlled substances.

Drug	CSA Schedules	Trade or other names	Medical uses
<i>Narcotics</i>			
Heroin	I	Diacetylmorphine, Horse, Smack	None in U.S., analgesic, antitussive
Morphine	II	Duramorph, MS-Contin, Roxanol, Oramorph SR	Analgesic
Codeine	II, III, IV	Tylenol w/Codeine, Empirin w/Codeine, Robitussin A-C, Fiorinal w/Codeine, APAP w/Codeine	Analgesic, antitussive
Hydrocodone	II, III	Tussionex, Vicodin, Dycodan, Lorcet	Analgesic, antitussive
Hydromorphone	II	Dilaudid	Analgesic
Oxycodone	II	Percodan, Percocet, Tylox, Roxicet, Roxidone	Analgesic
Methadone and LAAM	I, II	Dolophine, Levo-alpha-acetylmethadol, Levomethadyl acetate	Analgesic, treatment of dependence
Fentanyl and analogues	I, II	Innovar, Sublimaze, Alfenta, Sufenta, Duragesic	Analgesic, adjunct to anesthesia, anesthetic
Other narcotics	II, III, IV, V	Percocan, Percocet, Tylox, Opium, Darvon, Talwin ² , Buprenorphine, Meperidine (Pethidine)	Analgesic, antidiarrheal
<i>Depressants</i>			
Chloral hydrate	IV	Noctec, Somnos, Felsules	Hypnotic
Barbiturates	II, III, IV	Amytal, Fiorinal, Mebutal, Seconal, Tuinal, Penobarbital, Pentobarbital	Sedative hypnotic, veterinary euthanasia agent

Drug	CSA Schedules	Trade or other names	Medical uses
Benzodiazepines	IV	Ativan, Dalmane, Diazepam, Librium, Xanax, Serax, Valium, Tranxene, Verstran, Versed, Halcion, Paxipam, Restoril	Antianxiety, sedative, anticonvulsant, hypnotic
Glutethimide	II	Doriden	Sedative, hypnotic
Other depressants	I, II, III, IV	Equanil, Miltown, Noludar, Placidyl, Valmid, Methaqualone	Antianxiety, sedative, hypnotic
<i>Stimulants</i>			
Cocaine ¹	II	Coke, Flake, Snow, Crack	Local anesthetic
Amphetamine/ methamphetamine	II	Biphetamine, Desoxyn, Dexedrine, Obetrol, Ice	Attention deficit disorder, narcolepsy, weight control
Methylphenidate	II	Ritalin	Attention deficit disorder
Other stimulants	I, II, III, IV	Adipex, Didrex, Ionamin, Melfiat, Plegine, Captagon, Sanorex, Tenuate, Tepanil, Prelu-2, Preludin	Weight control
<i>Cannabis</i>			
Marijuana	I	Pot, Acapulco Gold, Grass, Reefer, Sinsemilla, Thai Sticks	None
Tetrahydrocannabinol	I, II	THC, Marinol	Antinauseant
Hashish and hashish oil	I	Hash, Hash Oil	None
<i>Hallucinogens</i>			
LSD	I	Acid, Blotter Acid, Microdots	None
Mescaline and peyote	I	Mescal, Buttons, Cactus	None
Phenethylamines	I	2,5-DMA, STP, MDA, MDMA, Ecstasy, DOM, DOB	None
Phencyclidine and analogues	I, II	PCP, PCE, PCPy, TCP, Hog, Loveboat, Angel Dust	None
Other hallucinogens	I	Bufotenine, Ibogaine, DMT, DET, Psilybin, Psylocin	None
<i>Anabolic steroids</i>			
Testosterone	III	Depo-testosterone,	Hypogonadism

Drug	CSA Schedules	Trade or other names	Medical uses
		Delatestryl (Cypionate, Enanthate)	
Nandrolone	III	Nandrolone, Durabolin, Deca-Durabolin, Deca	Anemia, breast cancer
Oxymetholone	III	Anadrol-50	Anemia

¹Designated a narcotic under the CSA.

²Not designated a narcotic under the CSA.

REFERENCE

1. Frank, R.S., The clandestine laboratory situation in the United States, *J. Forensic Sci.*, 28: 18-31, 1993.

1.9.3.2 Listing of Controlled Substances by Schedule Number

Listed below are those substances specifically controlled under the Controlled Substances Act as of January 26, 1996. This list does not include all controlled steroids or controlled substance analogues. These are classes of compounds that are controlled based on chemical and pharmacological criteria which have been discussed earlier in this chapter.

Table 1.9.3.2 Controlled Substances by Schedule Number

Drug name	CSA sch.	Synonyms
1-(1-Phenylcyclohexyl)pyrrolidine	I	PCPy, PHP, rolicyclidine
1-(2-Phenylethyl)-4-phenyl-4-acetoxypiperidine	I	PEPAP, synthetic heroin
1-Methyl-4-phenyl-4-propionoxypiperidine	I	MPPP, synthetic heroin
1-[1-(2-Thienyl)cyclohexyl]piperidine	I	TCP, tenocyclidine
1-[1-(2-Thienyl)cyclohexyl]pyrrolidine	I	TCPy
2,5-Dimethoxy-4-ethylamphetamine	I	DOET
2,5-Dimethoxyamphetamine	I	DMA, 2,5-DMA
3,4,5-Trimethoxyamphetamine	I	TMA
3,4-Methylenedioxy-N-ethylamphetamine	I	N-ethyl MDA, MDE, MDEA
3,4-Methylenedioxyamphetamine	I	MDA, Love Drug
3,4-Methylenedioxymethamphetamine	I	MDMA, Ecstasy, XTC
3-Methylfentanyl	I	China White, fentanyl
3-Methylthiofentanyl	I	China White, fentanyl
4-Bromo-2,5-dimethoxyamphetamine	I	DOB, 4-bromo-DMA
4-Bromo-2,5-dimethoxyphenethylamine	I	Nexus, 2-CB, has been sold as Ecstasy, i.e., MDMA
4-Methoxyamphetamine	I	PMA
4-Methyl-2,5-dimethoxyamphetamine	I	DOM, STP
4-Methylaminorex (cis isomer)	I	U4Euh, McN-422
5-Methoxy-3,4-methylenedioxyamphetamine	I	MMDA

Drug name	CSA sch.	Synonyms
Acetorphine	I	
Acetyl-alpha-methylfentanyl	I	
Acetyldihydrocodeine	I	Acetylcodone
Acetylmethadol	I	Methadyl acetate
Allylprodine	I	
Alpha-Ethyltryptamine	I	ET, Trip
Alpha-Methylfentanyl	I	China White, fentanyl
Alpha-Methylthiofentanyl	I	China White, fentanyl
Alphacetylmethadol except levo-alphacetylmethadol	I	
Alphameprodine	I	
Alphameprodine	I	
Alphamethadol	I	
Aminoex	I	Has been sold as methamphetamine
Benzethidine	I	
Benzylmorphine	I	
Beta-Hydroxy-3-methylfentanyl	I	China White, fentanyl
Beta-Hydroxyfentanyl	I	China White, fentanyl
Betacetylmethadol	I	
Betameprodine	I	
Betamethadol	I	
Betaprodine	I	
Bufotenine	I	MAPPINE, N,N-dimethylserotonin
Cathinone	I	Constituent of “khat” plant
Clonitazene	I	
Codeine methylbromide	I	
Codeine-N-oxide	I	
Cyprenorphine	I	
Desomorphine	I	
Dextromoramide	I	Palfium, Jetrium, Narcolo
Diampromide	I	
Diethylthiambutene	I	
Diethyltryptamine	I	DET
Difenoxin	I	LYSPAFEN
Dihydromorphine	I	
Dimenoxadol	I	
Dimepheptanol	I	
Dimethylthiambutene	I	
Dimethyltryptamine	I	DMT
Dioxaphetyl butyrate	I	
Dipipanone	I	Dipipan, phenylpiperone HCL,
Diconal, Wellconal	I	
Drotebanol	I	Metebanyl, oxymethebanol
Ethylmethylthiambutene	I	

Drug name	CSA sch.	Synonyms
Etonitazene	I	
Etorphine (except HCL)	I	
Etoxadine	I	
Fenethylamine ethyltheophylline amphetamine	I	Captagon, amfetyline
Furethidine	I	
Heroin	I	Diacetylmorphine, diamorphine
Hydromorphanol	I	
Hydroxypethidine	I	
Ibogaine	I	Constituent of "Tabernanthe iboga" plant
Ketobemidone	I	Cliradon
Levomoramide	I	
Levophenacymorphan	I	
Lysergic acid diethylamide	I	LSD, Lysergide
Marijuana	I	Cannabis, Marijuana
Mecloqualone	I	Nubarene
Mescaline	I	Constituent of "Peyote" cacti
Methaqualone	I	Quaalude, Parest, Somnafac, Opitamil, Mandrax
Methcathinone	I	N-Methylcathinone, "cat"
Methyldesorphine	I	
Methyldihydromorphine	I	
Morpheridine	I	
Morphine methylbromide	I	
Morphine methylsulfonate	I	
Morphine methylsulfonate	I	
Morphine-N-oxide	I	
Myrophine	I	
N,N-Dimethylamphetamine	I	
N-Ethyl-1-phenylcyclohexylamine	I	PCE
N-Ethyl-3-piperidyl benzilate	I	JB 323
N-Ethylamphetamine	I	NEA
N-Hydroxy-3,4-methylenedioxyamphetamine	I	N-hydroxy MDA
N-Methyl-3-piperidyl benzilate	I	JB336
Nicocodeine	I	
Nicomorphine	I	Vilan
Noracymethadol	I	
Norlevorphanol	I	
Normethadone	I	Phenyldimazone
Normorphine	I	
Norpipanone	I	
Para-fluorofentanyl	I	China White, fentanyl

Drug name	CSA sch.	Synonyms
Parahexyl	I	Synhexyl
Peyote	I	Cactus which contains mescaline
Phenadoxone	I	
Phenampramide	I	
Phenomorphane	I	
Phenoperidine	I	Oparidine, Lealgin
Pholcodine	I	Copholco, Adaphol, Codisol, Lantuss, Pholcolin
Piritramide	I	Piridolan
Proheptazine	I	
Properidine	I	
Propiram	I	Algaril
Psilocybin	I	Constituent of "Magic Mushrooms"
Psilocyn	I	Psilocin, constituent of "Magic Mushrooms"
Racemoramide	I	
Tetrahydrocannabinols	I	THC, Delta-8 THC, Delta-9 THC, and others
Thebacon	I	Acetylhydrocodone, Acedicon, Thebacetyl
Thiofentanyl	I	China White, fentanyl
Tilidine	I	Tilidate, Valoron, Kitadol, Lak, Tilsa
Trimeperidine	I	Promedolum
1-Phenylethylamine	II	Precursor of PCP
1-Piperidinoethylamine	II	PCC, precursor of PCP
Alfentanil	II	Alfenta
Alphaprodine	II	Nisentil
Amobarbital	II	Amytal, Tuinal
Amphetamine	II	Dexedrine, Biphatamine
Anileridine	II	Leritine
Benzoylcegonine	II	Cocaine metabolite
Bezitramide	II	Burgodin
Carfentanil	II	Wildnil
Coca Leaves	II	
Cocaine	II	Methyl benzoylcegoni, Crack
Codeine	II	Morphine methyl ester, methyl morphine
Dextropropoxyphene, bulk (non-dosage forms)	II	Propoxyphene
Dihydrocodeine	II	Didrate, Parzone
Diphenoxylate	II	
Diprenorphine	II	M50-50

Drug name	CSA sch.	Synonyms
Dronabinol in sesame oil in soft gelatine capsule	II	Marinol, synthetic THC in sesame oil/soft gelatine
Ecgonine	II	Cocaine precursor, in coca leaves
Ethylmorphine	II	Dionin
Etorphine HCL	II	M 99
Fentanyl	II	Innovar, Sublimazw, Duragesic
Glutethimide	II	Doriden, Dorimide
Hydrocodone	II	Hycodan, dihydrocodeinone
Hydromorphone	II	Dilaudid, dihydromorphinone
Isomethadone	II	Isoamidone
Levo-alphaacetylmethadol	II	LAAM, long acting methadone, levomathadyl acetate
Levomethorphan	II	
Levorphanol	II	Levo-Dromoran
Meperidine	II	Demerol, Mepergan, pethidine
Meperidine intermediate-A	II	Meperidine precursor
Meperidine intermediate-B	II	Meperidine precursor
Meperidine intermediate-C	II	Meperidine precursor
Metazocine	II	
Methadone	II	Dolophine, Methadose, Amidone
Methadone intermediate	II	Methadone precursor
Methamphetamine	II	Desoxyn, D-desoxyephedrine, ICE, Crank, Speed
Methylphenidate	II	Ritalin
Metopon	II	
Moramide-intermediate	II	
Morphine	II	MS Contin, Roxanol, Duramorph, RMS, MSIR
Nabilone	II	Cesamet
Opium extracts	II	
Opium fluid extract	II	
Opium poppy	II	Papaver somniferum
Opium tincture	II	Laudanum
Opium, granulated	II	Granualted opium
Opium, Powdered	II	Powdered opium
Opium, raw	II	Raw opium, gum opium
Oxycodone	II	Percodan, Percocet, Tylox, Roxicodone, Roxicet
Oxymorphone	II	Numorphan
Pentobarbital	II	Nembutal
Phenazocine	II	Narphen, Prinadol
Phencyclidine	II	PCP, Sernylan

Drug name	CSA sch.	Synonyms
Phenmetrazine	II	Preludin
Phenylacetone	II	P2P, phenyl-2-propanone benzyl methyl ketone
Piminodine	II	
Poppy straw	II	Opium poppy capsules, poppy heads
Poppy straw concentrate	II	Concentrate of poppy straw, CPS
Racemethorphan	II	
Racemorphan	II	Dromoran
Secobarbital	II	Seconel, Tuinal
Sufentanil	II	Sufenta
Thebaine	II	Precursor of many narcotics
Amobarbital and noncontrolled active ingredients	III	Amobarbital/ephedrine capsules
Amobarbital suppository dosage form	III	
Anabolic steroids	III	“Body Building” drugs
Aprobarbital	III	Alurate
Barbituric acid derivative	III	Barbiturates not specifically listed
Benzphetamine	III	Didrex, Inapetyl
Boldenone	III	Equipoise, Parenebol, Vebonol, dehydrotestosterone
Butabarbital	III	Butisol, Butibel
Butalbital	III	Fiorinal, Butalbital with aspirin
Chlorhexadol	III	Mechloral, Mecoral, Medodorm, Chloralodol
Chlorotestosterone (same as clostebol)	III	If 4-chlorotestosterone then clostebol
Chlorphentermine	III	Pre-Sate, Lucofen, Apsedon, Desopimon
Clortermine	III	Voranil
Clostebol	III	Alfa-Trofodermin, Clostene, 4-chlorotestosterone
Codeine and isoquinoline alkaloid 90 mg/du	III	Codeine with papaverine or noscapine
Codeine combination product 90 mg/du	III	Empriin, Fiorinal, Tylenol, ASA or APAP w/codeine
Dehydrochlormethyltestosterone	III	Oral-Turinabol
Dihydrocodeine combination product 90 mg/du	III	Synalgos-DC, Compal
Dihydrotestosterone (same as stanolone)	III	See stanolone
Drostanolone	III	Drolban, Masterid, Permastril
Ethylestrenol	III	Maxibolin, Orabolin, Durabolin O, Duraboral
Ethylmorphine combination product 15 mg/du	III	
Fluoxymesterone	III	Anadroid-F, Halotestin, Ora-Testryl
Formebolone (incorrect spelling in law)	III	Eaiclene, Hubernol

Drug name	CSA sch.	Synonyms
Hydrocodone and isoquinoline alkaloid 15 mg/du	III	Dihydrocodeinone+papaverine or noscapine
Hydrocodone combination product 15 mg/du	III	Tussionex, Tussend, Lortab, Vicodin, Anexsia and many more
Lysergic acid	III	LSD prcursor
Lysergic acid amide	III	LSD prcursor
Mesterolone	III	Proviron
Methandienone (see Methandrostenolone)	III	
Methandranone	III	?Incorrect spelling of methandienone?
Methandriol	III	Sinalsex, Stenediol, Troformone
Methandrostenolone	III	Dianabol, Methabolina, Nerobol, Parbolin
Methenolone	III	Primobolan, Primobolan Depot, Primobolan S
Methyltestosterone	III	Android, Oreton, Testred, Virilon
Methyprylon	III	Noludar
Mibolerone	III	Cheque
Morphine comgination product/ 50 mg/100 ml or gm	III	
Nalorphine	III	Nalline
Nandrolonoe	III	Deca-Durabolin, Durabolin, Durabolin-50
Norethandrolone	III	Nilavar, Solevar
Opium combination product 25 mg/du	III	Paegoric, other combination products
Oxandrolone	III	Anavar, Lonavar, Provitar, Vasorome
Oxymesterone	III	Anamidol, Balnimax, Oranabol, Oranabol 10
Oxymetholone	III	Anadrol-50, Adroyd, Anapolon, Anasteron, Pardroyd
Pentobarbital and noncontrolled active ingredients	III	FP-3
Pentobarbital suppositry dosage form	III	WANS
Phendimetrazine	III	Plegine, Prelu-2, Bontril, Melfiat, Statobex
Secobarbital and noncontrolled active ingredients	III	Various
Secobarbital suppository dosage form	III	Various
Stanolone	III	Anabolex, Andractim, Pesomax, Dihydrotestosterone
Stanozolol	III	Winstrol, Winstrol-V
Stimulant compunds previously excepted	III	Mediatric
Sulfondiethylmethane	III	
Sulfonethylmethane	III	

Drug name	CSA sch.	Synonyms
Sulfonmethnae	III	
Talbutal	III	Lotusate
Testalactone	III	Teslac
Testosterone Dalatestryl	III	Android-T, Adrolan, Depotest,
Thiamylal	III	Surital
Thiopental	III	Pentothal
Tiletamine and zolazepam combination product	III	Telazol
Trnbolone	III	Finaplix-S, Finajet, Parabolan
Vinbarbital	III	Delvinal, Vinbarbitone
Alprazolam	IV	Xanax
Barbital	IV	Veronal, Plexaonla, Barbitone
Bromazepam	IV	Lexotan, Lexatin, Lexotanil
Camazepam	IV	Albego, Limpidon, Paxor
Cathine	IV	Constituent of “Khat” plat
Chloral betaine	IV	Beta Chlor
Chloral hydrate	IV	Noctac
Chlordiazepoxide	IV	Librium, Libritabs, Lombitrol, SK-Lygen
Clobazam	IV	Urbadan, Urbanyl
Clonazepam	IV	Klonopin, Clonopin
Clorazepate	IV	Tranxane
Clotiazepam	IV	Trecalmo, Rizo
Cloxazolam	IV	Enadal, Sepazon, Tolestan
Delorazepam	IV	
Dextropropoxyphene Dosage Forms	IV	Darvon, Propoxyphene, Darvocet, Dolene, Propacet
Diazepam	IV	Valium, Valrelease
Diethylpropion	IV	Tenuate, Tepanil
Difenoxin 1 mg/25 ug ATS04/du	IV	Motofen
Estazolam	IV	ProSom, Domnamid, Eurdin, Nuctalon
Ethchlorvynol	IV	Placidyl
Ethinamate	IV	Valmid, Valamin
Ethyl loflazepate	IV	
Fencamfamin	IV	Reactivan
Fenfluramine	IV	Pondimin, Ponderal
Fenproporex	IV	Gacilin, Solvolip
Fludiazepam	IV	
Flunitrazepam	IV	Rohypnol, Narcozep, Darkene, Roipnol
Flurazepam	IV	Dalmane

Drug name	CSA sch.	Synonyms
Halazepam	IV	Pexipam
Haloxazolam	IV	
Ketazolam	IV	Anxon, Loftran, Solatran, Contamex
Lorpazolam	IV	
Lorazepam	IV	Ativan
Lormetazepam	IV	Noctamid
Mazindol	IV	Sanorex, Mazanor
Mebutamate	IV	Capla
Medazepam	IV	Nobrium
Mefenorex	IV	Aneorexic, Amaxate, Doracil, Pondinil
Meprobamate	IV	Miltown, Equanil, Deprol, Equagesic, Meprospan
Methohexital	IV	Brevital
Methylphenobarbital (mephobarbital)	IV	Mebaral, Mephobarbital
Midazolam	IV	Versed
Nimetazepam	IV	Erimin
Nitrazepam	IV	Mogadon
Nordiazepam	IV	Nordazepam, Demadar, Madar
Oxazepam	IV	Serax, Serenid-D
Oxazolam	IV	Erenal, Convertal
Paraldehyde	IV	Paral
Pemoline	IV	Cylert
Pentazocine	IV	Talwin, Talwin NX, Talacen, Talwin Compound
Petrichloral	IV	Pentaerythritol, Chloral, Periclor
Phenobarbital	IV	Luminal, Donnatal, Bellergal-S
Phentermine	IV	Ionamin, Fastin, Adipex-P, Obe-NIX, Zantryl
Pinazepam	IV	Domar
Pipradrol	IV	Detaril, Stimolag Fortis
Prazepam	IV	Centrax
Quazepam	IV	Doral, Dormalin
SPA	IV	1-Dimethylamino-1,2diphenylethane, lefetamine
Temazepam	IV	Restoril
Tetrazepam	IV	
Triazolam	IV	Halcion
Zolpidem	IV	Ambien
Buprenorphine	V	Buprenex, Temgesic
Codeine preparations — 200 mg/100 ml or 100 gm	V	Cosanyl, Robitussin A-C, Cheracol, Ceroce, Pediacof

Drug name	CSA sch.	Synonyms
Difenoxin preparations — 0.5 mg/25 ug ATS04/du	V	Motofen
Dihydrocodeine preparations — 10 mg/200 ml or 100 gm	V	Cophene-S, various others
Diphenoxylate preparations — 2.5 mg/25 ug ATS04	V	Lomotil, Logen
Ethylmorphine preparations — 100 mg/100 ml or 100 gm	V	
Opium preparations — 100 mg/100 ml or 100 gm	V	Parepectolin, Kapectolin PG, Kaolin Pectin P.G.
Pyrovalerone	V	Centroton, Thymergix

The author gratefully acknowledges the assistance of Dr. Judy Lawrence, Pharmacologist, DEA office of Diversion Control, for providing the information utilized in compiling this listing of controlled substances.