MICROGRAM

Laboratory Operations Division
Office Of Science And Drug Abuse Prevention

BUREAU OF NARCOTICS & DANGEROUS DRUGS / U.S. DEPARTMENT OF JUSTICE / WASHINGTON, D.C. 20537

Vol. III, No. 5 Aug., 1970

BNDD will expand its laboratory service to state, local and federal law enforcement agencies starting October 1, 1970. The Bureau will provide travel and expenses of BNDD forensic chemists incidental to court testimony. In the past, only free analyses have been furnished.

"Laboratory Services to Law Enforcement Agencies," a leaflet available at no cost from BNDD Regional Laboratories and Regional Offices, has been revised to reflect the added service. It also explains how laboratory examinations can be requested.

Forensic laboratories can furnish us with valuable drug intelligence. Instead of destroying all tablet and capsule evidence, send a portion of it to us after adjudication of a case. Forensic chemists in our Special Testing and Research Laboratory will attempt to identify the product and its manufacturer. This examination is of value in identifying counterfeit and other clandestinely made drugs; to detect newly abused products; and to determine if a specific sample is part of a domestic or international problem.

Send only tablets and capsules. Send up to fifty tablets, or up to twenty-five capsules to:

Chief Chemist
Special Testing and Research Laboratory (SCILR)
Bureau of Narcotics and Dangerous Drugs
Washington, D.C. 20537

When submitting samples of controlled drugs, such as, LSD, PCP, STP and methamphetamine, we would appreciate any intelligence information you may have about the samples. The intelligence information in which we are specifically interested includes;

1. Subject's name
2. City and State where purchased

3. Date purchased
4. Amount purchased
5. Amount paid for the sample if purchased. If not purchased indicate how acquired, such as, seized, money flashed, or if the sample was a gift.

This type of information will help BNDD to determine if the source of the samples is local, or part of a larger domestic or international problem.

The following is some of the intelligence information that has been developed from ballistics examinations.

1. There have been identified 77 clandestine punch operations producing LSD, PCP,and STP tablets. All are believed to be located in the United States.

2. Samples submitted by foreign enforcement groups have matched tablets purchased in the United States. So far, samples have been received from Hawaii; London, England; Rome, Italy; San Juan, Puerto Rico; and the Virgin Islands.

3. Samples from foreign sources have been identified as originating from nine of the 77 clandestine punch operations that are known to exist.

Coned-Shaped LSD Tablets were seized by BNDD agents in Detroit, Michigan in June. These were the first LSD tablets encountered in this shape. The seizure consisted of 10,000 brick-red tablets. Analysis revealed approximately 40 micrograms of LSD per tablet. The method of packaging was also a first. The tablets were in plastic bags (1000 per bag), folded in such a way as to form a cone. A description of the tablets is: cone measures 6 milliliters from base to apex, and the base is slightly larger than the cone giving a collared effect. Collar is 6.8 millimeters diameter, and 1.8 millimeters thick. On the collar face opposite the cone is a truncated cone approximately the same thickness as the collar.

PCP-LSD Combination Capsules were recently encountered by the BNDD New York Regional Laboratory. The mixture consisted of a #4 hard gelatin transparent capsule filled with a fine light brownish-pink colored powder. Agents reported that the preparation is referred to as "Product IV." Analysis showed the product to contain 200 micrograms of LSD and 2.7 milligrams of PCP per capsule.

Heroin-Caffeine was identified in two recent submissions of heroin to the BNDD New York Regional Laboratory. One submission, white granular powder weighing 7.9 grams, contained 41.2% Caffeine and 51.2% Heroin hydrochloride. No other diluents were present. The other submission, consisting of 8.8 grams of white powder in glassine bags, contained 6.4% Caffeine, 7.2% Heroin Hydrochloride and milk sugar. Both samples came from the same person and it is believed they represent a Hong Kong source.

MEETINGS:

Second World Meeting on Medical Law, Washington, D.C., August 18-21, 1970. Contact: R. Dierkens, Dr. Jr., Agrege Law Faculty, Secretary General, 5 Apotheekstraat B-9000, Ghent, Belgium.

Canadian Society of Forensic Science 18th Annual Meeting, Banff, Alberta, Canada, September, 23-25, 1970. Contact: Mr. Anthony, Chief Crown Prosecutor, Municipal Courts Building, Edmonton, Alberta, Canada.

Association of Official Analytical Chemists 84th Annual Meeting October 12-15, 1970, Marriott Motor Hotel, Twin Bridges, Washington, D.C. Special features of the meeting will be two symposia. The first one, Tuesday afternoon, October 13, will have presentations and discussion on international standardization of analytical methods. On October 15, a symposium, "Analytical Methods in Forensic Science," will be held to give technical advancements in the area of scientific crime detection.

American Academy of Clinical Toxicology annual meeting, San Francisco, California, October 24-26, 1970. Will include two one-day symposiums. One on the "Clinical Toxicology of Substances of Abuse" (other than narcotics), the other on "Legal Aspects of Clinical Toxicology." Address: P.O. Box 2565, Houston, Texas 77001.

National Association of Police Laboratories-BNDD joint symposium on drug identification, November 18-20, 1970, New Yorker Hotel, New York City. Registration fee $20, includes a luncheon and cost of printing and mailing copies of techniques presented.

The program is designed to present the practical aspects of drug analytical procedures in the forensic laboratory. Techniques presented will pertain to the analysis of narcotics, depressants, stimulants and hallucinogens.

Questions relating to the subject matter can be sent in advance or submitted during the first two days of the symposium. The inquiries will be given to the appropriate lecturer, who, if present, will answer them in the concluding segment of the presentation. Questions will also be answered at the conclusion of each talk.

Contact: National Association of Police Laboratories, c/o Suffolk County Police Laboratory, Veterans Highway, Hauppage, New York 11787

1971 American Academy of Forensic Sciences annual meeting in Phoenix, Arizona. Contact: Robert J. Joling, A.B., J.D., 612 Kenosha National Bank Building, 625 57th Street, Kenosha, Wisconsin 53140

It's a Girl! Interpol Officials in Switzerland recently seized a twelve centimeter cigar containing cannabis, mailed from America. The band on the cigar read "It's a Girl."

Glassine Envelope production in sized 1-1/2 x 1-1/2 and 1-3/4 x 1-3/4 inches, has been discontinued by one of the largest manufacturers, as the result of Congressional hearings.

NOTE: The BNDD Forensic Chemist seminar scheduled for December 7-11, 1970, has been cancelled.

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PROCEDURE FOR THE SCREENING OF DRUGS OF ABUSE IN URINE

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New York Regional Laboratory

Bureau of Narcotics & Dangerous Drugs

A combination extractive, chromatographic and spectrophotometric method was developed and used for detecting drug abuse.(a) This method was useful in the detection of hypnotics and sedatives, stimulants, tranquilizers and narcotics in the urine of patients in various stages of rehabilitation.

DIRECT SOLVENT EXTRACTION

In the past, direct solvent extraction was infrequently used except for the extraction of a known drug. However, with the introduction of reliable spectrophotometric instruments and the development of chromatographic techniques, as thin-layer and gas chromatography, there has been an increase interest in direct solvent extraction. The direct extraction methods are for the most part, rapid and convenient. The most popular solvents used are ether and/or chloroform. One of the serious complications of direct solvent extraction is the formation of emulsions. In this respect, chloroform is the worst. However, from a practical point of view the emulsion tend to be rather infrequent. If they do occur, the addition of a few ml. of methanol is sufficient to break the emulsion. A direct solvent extraction of urine affords a break down into five general groups, that is,

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(a) For Nassau County Drug Abuse and Addiction Commission, at Meadow Brook Hospital, Office of the Medical Examiner, East Neadow, New York.

1. strongly acidic drugs, e.g. salicylic acid, mefenamic acid.
2. weakly acidic drugs, e.g. barbiturates, glutethimide.
3. neutral drugs, e.g. ethinamate, phenacetin.
4. basic drugs, e.g. amphetamines, phenothiazines.
5. amphoteric drugs, e.g. morphine.

Other Procedures

Several methods for the detection of drugs of abuse can be found in the literature.[1,2,3,4] Recently, papers have appeared using ion-exchange paper to absorb drugs from urine followed by elution with a series of buffer-solvent systems.[5,6] However, it was acknowledged that recoveries of labeled drugs were only in the 20% range or less.[6] Therefore, considering the range of sensitivity of the ion-exchange method, it would seem unacceptable for the detection of barbiturates, amphetamines, and psychoactive drugs, e.g. psilocybin, marihuana. On the other hand, a workable direct estraction procedure can easily afford a 60-80% recovery and give a sensitivity of 1 microgram per ml. of urine 50 ml. initially). It is important to note, that in the case of LSD the chance of detection is nihl. This is primarily due to the small quantity of LSD ingested (100-150 u.g.) and the subsequent extensive metabolism.[7,8] Moreover, since the ion-exchange paper is eventually extracted with solvent, it would seem practical to use a direct solvent extraction method and take advantage of the greater per cent recovery and sensitivity.

Preliminary screening test on urine.

A. Ferric chloride test for salicylates - to 2 ml. of urine add 1 ml. of ferric chloride solution. A violet color developes if salicylate is present.(9)

B. FPN test for phenothiazines - to 2 ml. of urine add 1 ml. of FPN reagent. A variety of colors ranging through pink, red, orange, violet and blue indicates presence of a phenothiazine.(10)

The direct solvent extraction method used for the complete narcotic screening of urines is as follows:

1. Measure out 50 mls. of urine (adding a few drops of 20% H_2SO_4) into shaking flasks with 100 mls ether.
2. Shake for approximately 10 minutes.
3. Transfer contents into 500 ml. separatory funnel.
4. Let stand long enough to separate (15 minutes) (In case of emulsion, add additional 100 mls. ether).
5. Run off aqueous layer in 500 ml. shaking flask. Save for step #9.
6. To ether layer - add 25 ml. of saturated solution of sodium bicarbonate to remove strong acid - in same 500 ml. separatory funnel.
7. Shake, let stand for 10 minutes.
8. Filter ether layer into beaker; labeled WAN this is treated routinely (GLC + Koppanyi) Disregard water layer.

9. Aqueous layer from #5 - Make basic (pH 10+) with 50% NaOH (approximately 1.0 ml. will do it).
10. Add 100 mls. ether.
11. Shake for 10 minutes.
12. Return to original 500 ml. separatory funnel.
13. Let stand for 10 minutes - to separate.
14. Run off aqueous layer again into same 500 ml. flask. Save for step#20.
15. Wash ether layer (basics) with water (twice) in separatory funnel (25-50 ml. H_2O).
16. Run off and discard water; all water must be removed.
17. Add 5 ml. of 0.5 N H_2SO_4 - Shake and let stand 15 minutes.
18. Run off H_2SO_4 + water layer, into test tube (labeled) and place under hood to drive off excess ether. Discard ether layer.
19. Read in U.V. - If U.V. is positive - Make H_2SO_4 layer basic with 50% NaOH, add 25 mls. of $CHCl_3$ in large test tube. Shake, let stand, aspirate off aqueous layer. Filter $CHCl_3$ layer into 50 ml. beaker and evaporate. (Evaporate for future T.L.C.).

    If U.V. gives typical amphetamine curve add 3 drops of acid (50% 6 NHCl + 50% EtOH) to $CHCl_3$ before evaporation.

Hydroysis

20. Aqueous layer from Step #14 is neutralized with 20% H_2SO_4.

21. 2 mls. of concentrated H_2SO_4 are added and flask is placed on warm steam bath to drive off residual ether.* NOTE: Autoclave is preheated.

22. After all ether has been driven off (samples become noticeably darker). Plave flasks in autoclave and hydrolyse for thirty minutes.

23. Allow autoclave and samples to cool (preferably overnight).

24. Filter hydrolysed urine into 250 ml. shaking flask - Make basic (approximate pH 9.0) with 50% NaOH (4-6 mls. will usually do this).

25. Add solid Sodium Bicarbonate (scoop full) until pH 8.5 is achieved.

26. Add 100 mls. of $CHCl_3$ to the 250 mls. shaking flask - shake for 10 minutes.

27. Pour off into 500 ml. separatory funnel. Let stand 15 minutes.

28. Filter bottom layer ($CHCl_3$) using double filter paper into 100 ml. beaker (labeled "Hyd").

29. $CHCl_3$ is evaporated without acid and residue is ready for T.L.C.

Optional

30. A subdivision of the weak acid-neutral (WAN) fraction (step 8) is not usually necessary. Occassionally the separation of the WAN fraction may help identification. Then an addition step

should be included. The WAN ether extract is extracted with 10 ml of 0.1 N NaOH and separated. The remaining ether phase contains the neutral drugs. The separated NaOH phase is acidified with HCl and re-extracted with either. This ether phase constitutes the weak acids.

NOTE: The acid hydrolysis (step 20) has the advantage in that it liberates conjugated drugs, usually present as glucuronides, that would otherwise not be available for solvent extraction. The method enhances the sensitivity considerably.[3],[6]

Gas Chromatography

There are some 37 barbiturates of the malonylurea type, of which some 5-10 are commonly used.[11] Gas chromatography is an efficient method for the detection, separation and identification of microgram quantities quickly.[12] In the scheme used, gas chromatography was used routinely for the detection of any weak acid-neutral drugs (step 8). Throughout the literature numerous examples have demonstrated the versatility of gas chromatography. The development of silicone polymer substrates and high sensitivity detectors have extended analysis to include the separation and detection of micro quantities of barbiturates, tranquilizers, alkaloids and other drugs.[13]

Discussion

Any gas chromatograph equipped with a flame ionization detector will suffice as a basic instrument for analysis. More important is the choice of column substrate and operating temperature. A sufficient variety of column substrates and operating conditions have been reported.[12,14,15] For routine analysis, it was found that the barbiturates could be separated and identified using a 4 foot column at 200°C on SE 30, 5% by weight on 100 to 120 mesh firebrick. The retention times ranged from 1 to 6 minutes.

The apparent retention times were measured from the sharp, vertical rise of the solvent peak to the mid-point of the response peak. The column was initially conditioned at 300° overnight. Standards were prepared using 10 mg. of barbiturate per 10 ml. of chloroform resulting in 1 ug./1 ul. The instrument was so programed that a 2 ul. injection of standard produced a response of 30% or more of full scale deflection on the recorder. The injection port and detector were maintained at 225°C. The following standards were routinely injected each day to "prime" the gas chromatograph: Methyprylon (Noludar), Acetophenetidin (Phenacetin), Amobarbital, Pentobarbital, Secobarbital, Phenobarbital, Glutethimide (Doriden), Meprobamate (Miltown) and cyclopal. To the dry residue (step 8) 50 ul. of chloroform was added. A 2 ul. portion was injected.

Sensitivity

Several authors have reported the detection and separation of barbiturates at 1 ug./ul. or higher.[12,13,14,15,16,17] Using a flame ionization detector performance levels have been reported in the 0.01-0.005 ug./ul. range for various barbiturates.[18,19]

Recently, the identification of barbiturates by direct derivative formation within the gas chromatograph has been reported.[20] It appears that another parameter, the retention time of the barbiturate derivative, can be employed to make the identification of the drug more certain.

Ultraviolet Spectrophotometry

The ultraviolet spectrophotometer was routinely used for the identification of drugs in the basic fraction (step 19). It was reported that as little as 15 to 200 ug./ml. of free drug is needed for spectrophotometric analysis.(3) None of the positive samples were quantitated. A list was made of all the drugs of abuse that might be found in the basic fraction. A ultraviolet spectra of all these drugs was made and kept on file as a reference.

The region scanned in the ultraviolet was from 360 mu. to 220 mu. Initially, a quick manual scan was performed to see if the sample required dilution because of a high concentration of basic drug. In numerous cases a maximum was found at 259 mu. due to nicotine. In several cases an extremely high absorbance at 259 mu. appeared as an attempt to obscure the absorbance of other drugs at this wavelength. Re-extraction (step 19) in most cases proved this to be so. Occasionally, it was observed that in the region 240-300 mu. rather broad plateaus were obtained whose height usually never exceeded 0.2 absorbance units (0.0 to 1.0 scale). Re-extraction followed by thin-layer chromatography failed in all cases to indicate the presence of any basic drugs. However, a "positive" ultraviolet spectra has a clearly defined maximum in the region scanned.

Thin-layer Chromatography

Thin-layer chromatography can be used routinely for detection of morphine. However, other basic drugs can readily be detected, such as, codeine, quinine, nicotine, demerol, pheniramine, and the phenothiazines. The FPN test[10] used in the analysis is an indication of whether one can expect to find the characteristic phenothiazine spots in the T.L.C. Since heroin is metabolized and excreted as morphine,[21,22] the detection of morphine is usually indicative of a heroin user. Previously, the thin-layer chromatographic methods reported[23,24] require more than one developing system to resolve morphine completely from other narcotics. Recently, a thin-layer chromatographic procedure suitable for screening a large number of specimens was reported.[25] A single new developing solvent system is used. This chromatographic procedure has been extended to screen for neutral and acid drugs[26] as well as the previously mentioned basic drugs.[25] The thin-layer chromatographic screening procedure used in this work[a] was that of Davidow.[25]

Materials and Equipment

Developing solvent: ethyl acetate, 170 ml; methyl alcohol, 20 ml; and concentrated ammonium hydroxide, 10 ml.

Spray Reagents: Sulfuric acid, 5% by volume in water

Iodoplatinate solution: 1 gram of platinic chloride in 10 ml of water is added to 10 gram of potassium iodide in 200 ml. of water. This mixture is diluted to 250 ml. with water. It should be refrigerated and fresh solutions prepared every three weeks.

Equipment

500 micron pre-prepared plates (20 x 20 cm.) silica Gel G.

Developing tank with ground glass cover.

Chromatographic spray bottles

Hamilton syringes, 10 and 50 microliter

Hot air, dryer

Hot plate

Ultraviolet, short and long wave, Chromato-Vue

General Methods

1. 500 micron pre-prepared plates (20 by 20 cm.) were used.
2. Using a template, mark 13 equally spaced starting points and a 15 cm finishing line.
3. The center spot is maintained for standard controls: standards were prepared by accurately weighing out 10 mg of basic drug and dissolving in 10 ml of chloroform. Five (5) microliters of each of the standards were routinely spotted.

Morphine Codeine Quinine Nicotine Demerol Methadon Pheniramine	All added to center standard control spot.

4. Residues from step number 29 and also the positives from U.V. are concentrated in 95% ethanol and air dried.

5a. Residues from hydrolysis are now dissolved in 0.5 ml. of ETOH and 50 microliters (1/10 of total residue) are spotted at starting line.

b. Entire residue from a positive U.V. is spotted at starting line.

6. The plate is developed in the Davidow solvent system: 170 ml. ethyl acetate, 20 ml. methanol, 10 ml. concentrated ammonium hydroxide, which has equilibrated in a filter paper lined developing tank for thirty minutes.
7. After complete development of plate (45 minutes), it is removed from tank and allowed to air-dry.
8. Observe under U.V. light (3660 Å)
9. Spray plate with 5% H_2SO_4
10. Observe again under U.V. light. Drugs like quinine will fluoresce strongly; phenothiazines appear highly colored (pinks and purples).
11. Over-spray with platinic-iodide reagent. (Fresh solution should be prepared every three weeks.
12. Standards and positives appear as colored spots.

Sensitivity

In the case of morphine 0.5 µg. per one ml. of urine can easily be detected. However, the limits of other basic drugs are approximately 1-2 micrograms per ml. of urine. Quinine which fluoresces under U.V. light may be detected in amounts of one microgram per 10 ml. of urine. The detection of amphetamine is feasible at concentrations of at least 100 micrograms per ml. of urine.

As codeine is generally metabolized to morphine,[27] the urine from codeine addicts generally gives weak morphine spots and also a codeine spot.

A negative for morphine does not mean that the individual has not used heroin or morphine earlier. Morphine can usually be detected for at least two days after a 15 mg. intramuscular injection.[21] However, quinine which often is used to adulterate heroin, is easily detected at considerably lower levels than morphine. Often it is therefore, not surprising to find a quinine positive and a morphine negative.

In general, the absence of a detectable spot would imply that the individual is currently not using any of the basic drugs. that is, codeine, heroin or demerol. A positive spot would be evidence of illicit drug use.

The Davidow thin-layer chromatographic procedure offers the advantages of one developing solvent system and is generally a rapid, sensitive method.

Spectrophotofluorometry

Spectrofluorometric analysis has certain advantages over absorptiometric analysis. It is from 100 to 1,000 times more sensitive.(28) It offers two spectra (activation and emission) for identification instead of one. However, not all molecules that absorb light fluoresce. For a molecule to fluoresce it must absorb energy (light) and be activated or raised to an excited state and then return to the ground state by emitting the excess energy as light of a longer wave length.

Spectrophotofluorometry has been used as a means of identification for phenothiazines.(29) The phenothiazines have their fluorescence peaks in the 450 to 475 mu range and show a two-wave fluorescence excitation pattern in the ultraviolet. When these compounds are oxidized with potassium permanganate, they form a very distinct four-wave crescendo-like excitation pattern and their fluorescence shifts toward lower wavelengths. Compounds which resemble the phenothiazines structurally, as chlorprothixene and imipramine do not yield the typical four-wave excitation pattern so typical for phenothiazine compounds. Hence, phenothiazine-like drugs can readily be distinguished from the phenothiazines.

The fluorescence spectrophotometer was not incorporated as an analytical tool in the scheme presented. However, it is apparent that some highly potent drugs, such as L.S.D., are initially ingested in microgram quantities. One may assume the range of detection would be at the nanogram (10^{-9}g.) level. It would appear that the spectrophotofluorometer affords the sensitivity for this range of detection with an excellent degree of accuracy.

Additional Methods

The previously detailed procedure for the isolation and identification of drugs of abuse has one important advantage over other existing procedures. Refinements of existing instrumental techniques or completely new instrumental methods can readily be incorporated in or used as an addition to those presently in the procedure. Likewise, microcrystal tests, additional thin-layer chromatography methods, and the use of chromatography methods, and the use of ultraviolet spectrophotometry for specific drugs may be taken advantage of when situations require it.

Recently, a rapid ultraviolet spectrometric method for the detection of chlorprothixene was reported.(30) This method permits the analysis of chlorprothixene from biological specimens even in the presence of its metabolites and other alkaline drugs without preliminary separation. The procedure is based upon the oxidation of the drug and its metabolites by alkaline permanganate. It was found that in hexane the products have a characteristic ultraviolet absorption and maximum at 233 mu. The method is sensitive enough to allow the detection of the drug in urine three (3) days after ingestion of a single 50 mg. dose. A similar method has been reported for the detection of amitriptyline and nortriptyline.(31)

A complete survey of the recent literature reveals that several interesting applications of thin-layer chromatography for the detection of narcotic drugs in the urine have been published. Also, a procedure which employs microcrystal tests as well as thin-layer chromatography for the identification of narcotic drugs has been reported.[32] However, it must be understood that these procedures must be evaluated before they can be used to supplement or replace those in current use.

It would be most advisable to periodically survey the literature so that the present scheme could be updated when necessary. This would hopefully result in the most efficient and effective program of analysis possible.

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Equipment and Cost

Today many forensic science laboratories are very well equipped. Therefore, much of the equipment listed below will already be available for use. Therefore, the initial cost of the narcotic screening program on urines should be far less than the totals listed.

The recommended features of the ultraviolet spectrophotometer be that it is equipped with a manual scan. In addition, a stationary or fixed chart paper would also be of value such that at least five spectra can be run per single chart paper. This would decrease the volume of stored ultraviolet spectra data considerably.

The recommended gas chromatograph should be equipped with dual hydrogen flame ionization, dual recorder, and hydrogen generator.

Special Equipment

Lamp, Ultraviolet, short and Long-Wave	180.00
Rotating shaker	435.00
Flask carriers	95.00
Laboratory cart	70.00
Hot plate	28.00
Variable transformer	28.00
Numbering machine	16.00
Analytical balance	830.00

Triple beam balance	25.00
Dryer, hot air	44.00
Water bath	142.00
Refrigerator 5 cu. ft.	150.00
Autoclave	600.00
U.V. Spectrophotometer	7,000.00
	-9,000.00
Gas chromatograph	3,600.00
Recorder	1,600.00
Hydrogen generator	660.00
	15,503.00

Glassware

500 ml. separatory funnels (32)	272.00
Screw cap flasks, Erlenmeyer (36)	75.00
Funnels, powder (12)	7.00
Chromatographic plates, 20 x 20 cm.(initial)	13.00
Chromatographic Developing Batter Jar (2)	33.00
Syringes, 25 ul. (2)	36.00
Beakers 250 ml. (144)	86.00
Test tubes and racks	20.00
	542.00

Chemicals (Initial investment)

$NaHCO_3$	5 lbs.	2.40
NaOH	5 lbs.	6.70
H_2SO_4	9 lbs.	4.40
Chloroform	32 pt.	34.00
Ether	20 lbs.	25.00
		72.50

The most expendable materials are ether and chloroform. The average cost of these are $60 per week for 90 samples. Hence, the solvent cost is far less than one dollar per sample. The cost of the inorganic chemical would average approximately $5 a week.

Personnel

The urine screening program can be effectively managed by two technical people and a chemist with an excellent background in instrumentation. In time the technicians can learn to operate the ultraviolet spectrophotometer and gas chromatographs and to spot the thin-layer plates. However, it is advisable to have the interpretation of all the analytical methods done by a competent chemist. This typical three man laboratory team can complete ninety (90) samples per week.

General Laboratory Procedure

With this rather large number of samples the paper work can present somewhat of a problem. To facilitate matters it is suggested that a rubber stamp be made containing the following:

$FeCl_3$ _____

F.P.N. _____

U.V. _____

G.L.C. _____

T.L.C. _____

basic T.L.C. _____

Other _____

An additional stamp reading, No Drugs Detected, is also necessary.

The work sheet should contain the following information on an 8 x 11 inch sheet:

Name of patient _____ Date _____

Residence _____

Specimen collected by _____

Time _____ Date _____

Specimen received by _____

Time _____ Date _____

All specimens received are given a laboratory number which corresponds to the work sheet number. The ultraviolet spectra curves from all specimens are kept on file in the laboratory. The gas chromatograph of the specimen is attached to the work sheet. A folder is required for each individual. The completed work sheet is placed in the folder and kept on file. A short typewritten report on each case indicating the results is forwarded to the appropiate agency.

Where possible, specimens should be refrigerated within 24 hours after collection. Since 50 ml. of urine is necessary for a complete analysis, the specimen collected should contain no less than this volume.

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Chapter II—Bureau of Narcotics and Dangerous Drugs, Department of Justice

PART 320—DEPRESSANT AND STIMULANT DRUGS; DEFINITIONS, PROCEDURAL AND INTERPRETATIVE REGULATIONS

Meprobamate; Exemption of Certain Combination Drugs

By an order published in the FEDERAL REGISTER on June 6, 1970, the Director of the Bureau of Narcotics and Dangerous Drugs ended the stay of the effective date of the final order published in the FEDERAL REGISTER on December 6, 1967 (32 F.R. 17473), listing meprobamate as a drug subject to control under the Drug Abuse Control Amendments of 1965. This order is to take effect July 6, 1970.

Notice is hereby given that the order published June 6, 1970, is hereby supplemented in that the following combination drugs will not be controlled and thereby do not have to meet the requirements of section 511(c) (a) and (e), and the recordkeeping requirements of section 511(d)(1) of the Federal Food, Drug, and Cosmetic Act:

Milprem—200	Tablet: Meprobamate 200 mg. Conjugated Estrogens—equine 0.4 mg.	Wallace Pharmaceuticals.
Milprem—400	Tablet: Meprobamate 400 mg. Conjugated Estrogens—equine 0.4.	Do.
Milpath—200	Tablet: Meprobamate 200 mg. Tridihexethyl Chloride 25 mg.	Do.
Milpath—400	Tablet: Meprobamate 400 mg. Tridihexethyl Chloride 25 mg.	Do.
Miltrate—10	Tablet: Meprobamate 200 mg. Pentaerythritol tetranitrate 10 mg.	Do.
Miltrate—20	Tablet: Meprobamate 200 mg. Pentaerythritol tetranitrate 20 mg.	Do.

Title 21, Chapter II, § 320.8(b) of the Code of Federal Regulations is hereby amended by adding the above listed combinations to the end of that paragraph. Since this supplement to the order published in the FEDERAL REGISTER on June 6, 1970 is nonrestrictive, it will become effective on July 6, 1970.

Dated: June 29, 1970.

JOHN E. INGERSOLL,
Director, Bureau of Narcotics and Dangerous Drugs.

[F.R. Doc. 70-8509; Filed, July 2, 1970; 8:48 a.m.]