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COMPARISON OF COSTS^{*} FOR TESTING A WIDE VARIETY OF DRUGS OF ABUSE PER URINE SPECIMEN IN A DRUG ABUSE URINE SCREENING PROGRAM AND FREQUENT URINE COLLECTIONS

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SUMMARY

Existing urine testing techniques in a drug abuse urine screening program with their capacity to analyze urine specimens per day are discussed. The start-up cost using each technique and cost per specimen are presented. A single step extraction technique using ion-exchange paper to absorb drugs prior to thin-layer chromatography (TLC) as reported by these laboratories will cost \$0.58 per specimen, detecting opiates and performing at least four tests per specimen, and \$0.82 per specimen, for testing the entire array of drugs of abuse (at least 9–14 tests per specimen). Sensitivity reported using TLC technique for the morphine base is $0.15 \,\mu g/ml$ (minimum volume of urine needed 20 ml), $0.10 \,\mu g/ml$ if the volume of urine available is 30–35 ml, and $0.07 \,\mu g/ml$ if the volume of urine available is 43–50 ml.

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Urine screening for abused drugs has become a necessary adjunct in prevention and treatment programs, since it provides a clinician an objective measure of drug abuse among his clients. Urine analysis is also desired for pre-employment screening of job applicants, evaluation of impaired workers, detection of drug users among criminals and for the detection of stimulant drugs in athletes. A forensic toxicologist dealing with medicolegal cases requires qualitative and quantitative data, while the primary concern of drug abuse prevention and treatment programs is to determine the progress of a particular treatment modality, hence only qualitative information is required. Furthermore, large-scale drug abuse prevention and chemotherapeutic maintenance programs require simple, rapid, sensitive, reliable, versatile and lowcost urine screening procedures.

The purpose of this communication is to report the cost of analysis per urine specimen for detecting the entire array of drugs of abuse and also to discuss in some detail the comparison of speed and analysis using currently existing detection tech-

^{*} All prices quoted are in United States dollars.

niques. During the past three years potentially useful immunoassay techniques such as radioimmunoassay ($RIA^{1,2}$), free radical assay technique ($FRAT^{3,4}$), hemagglutination, inhibition test ($H1^{5,6}$), latex flocculation test (LFT⁷), and enzyme multiplied immunoassay technique (EMIT^{3,8}), applicable to drug abuse screening programs, have been developed. These techniques are prohibitive in cost and usually selective in what drugs they are able to test. Although RIA, FRAT, and HI techniques have a sensitivity of nanograms level for the detection of morphine and structurally related narcotics, the chances of cross-reactivity with other drugs enhance at this level. Dextromethorphan and Demerol (Mepridine)^{1,2,9} are known to cross-react in most morphine tests, thus giving a false positive morphine. Codeine, which is one of the common components of cough medicine and whose presence can be misinterpreted as heroin abuse, cannot be differentiated from morphine by all the existing immuncassay techniques. In addition, people who have ingested certain foods with high content of poppy seeds^{1,2,9} often excrete urine that may give a false positive result. Therefore, all positive results obtained by immunoassay techniques are ambiguous and must be confirmed by a non-immunological procedure of comparable detection limits, while all negative results may be considered reliable.

Recently, we reported a single-step extraction and thin-layer chromatographic (TLC) identification technique for a wide variety of drugs of abuse^{10,11}, using ionexchange paper. Recent shift in emphasis from heroin abuse to poly-drug use has further necessitated the testing of entire drugs of abuse in one step. In many treatment programs serious attempt is made to rehabilitate a wide variety of drug abusers, opiates as well as non-opiate users. A significant percentage of clients take prescribed tranquilizers, antibiotics, and other types of needed drugs, it is therefore necessary that a mass screening technique should be capable of detecting a wide variety of substances and of differentiating illicit drugs and their adulterants from legitimate and prescribed drugs and their metabolities.

At present, TLC is the technique which meets the above criteria and can immediately alert the operator of the number of drugs and/or their metabolites present in a urine specimen. Gas-liquid chromatography (GLC), the only other technique that can permit simultaneous screening of a mixture of drugs, is time consuming and more expensive than TLC, since it has the inherent disadvantage of running one specimen at a time.

Due to the increased usage of drugs, more and more out-patient and in-patient treatment programs for drug-dependent individuals are being established throughout the country. To ensure that none of the heroin users are kept on a waiting list due to lack of funds (for urine testing), significant funds are being provided either to get urine analysis from outside testing facilities or to establish in-house testing facilities. However, we have noticed that in some in-house testing facilities, costly detection techniques, such as RIA, and other immunoassay techniques are being used to detect the drugs of abuse. Many programs resort to only one collection of urine per week to save the expenses which would be incurred when two or three collections of urines were made. Under the existing U.S. Federal Regulations, the urine of every client attending drug abuse prevention and chemotherapeutic maintenance programs needs to be tested randomly once a week for morphine and once a month for opiates, amphetamines, barbiturates, and other drugs as needed. However, the authors feel that frequent collection of urine has a strong deterrent effect on the use of drugs¹².

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Therefore, one collection of urine per week on random basis as proposed under the Federal Regulations for every client regardless of the length of stay with a program and without following the progress of the treatment is inadequate and can encourage the clients for use of drugs, thus vitiating the very purpose of urine surveillance in chemotherapeutic maintenance and drug abuse prevention clinics. The authors feel that frequent urine collection and data generated from urine analysis are highly imperative to assess the effectiveness and efficacy of management techniques. Hence, we suggest that a client must drop at least three urines a week for the first six months of entering a treatment program, subsequently this condition may be made less rigid to only two drops a week, depending upon the progress of each individual client in a particular treatment modality. If a client's urine report is clean for a period of six months, only then one collection of urine per week on random basis will be sufficient as a check for covert drug use. To decrease the expenses which would be incurred on frequent urine analysis, the authors recommend that only one test may be performed per week by pooling various urine specimens of different visits of the same client. The pooling of different urines can be accomplished by absorbing drugs on a cationexchange resin loaded paper at the urine collection station at the time of each visit of the client and then pooling the ion papers representing different urine specimens. Pooling of ion papers representing different urine specimens enhances the possibility of increasing the sensitivity since the human body continues the excretion of drugs and/or their metabolites in minute concentrations for more than 48 h. Furthermore, it will enable the clients' different urine specimens to be tested without entailing any extra cost (see Fig. 1).



Fig. 1. Effect of pooling ion-exchange papers representing different urines of a client using TLC and its cost in comparison to EMIT and RIA. A, Pooling of ion-papers representing different urine specimens and performing at least 4-5 tests per specimen for opiates (TLC); B, same as A but testing the entire array of drugs of abuse, *i.e.*, at least 9-14 tests per specimen (TLC); C, EMIT, each specimen has to be tested individually and the cost represents 4 tests per specimen; D, RIA, cost represents 4 tests per specimen.

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|---------|----|----|---|---|

| TLC | GLC | Spectrophotofluorome | tric tests (SPF) |
|--|---|--|---|
| | | ATS** (Farrand automated turret spectrofluorometer) | Technicon automated SPF system*** |
| 120 specimens if only opiates are tested, performing at least four to five tests per specimen. <i>i.e.</i> , morphine, codeine, methadone, quinine, etc. ¹¹ 80 specimens if the entire array of drugs of abuse ¹¹ , <i>i.e.</i> morphine, codeine, methadone, quinine, amphetamine, methamphetamine, phenmetrazine (Preludin), methylphenidate (Ritalin), secobarbital or pentobarbital, or amo- barbital or hexobarbital, phenobarbital, glutethimide (Doriden), diphenyl- hydantoin (Dilantin), propoxyphene (Darvon), meperidine (Demerol) and unchanged cocaine are tested concur- rently, thereby performing at least nine to fourteen tests per specimen. In fact, many more drugs of abuse can be tested ¹¹ per specimen without increasing the cost. | 25 Specimens per day [*] for screening of opiates and a few amphetamines. One sample takes about 20–30 min for complete elution. | 400 specimens performing one test per specimen. | 300 specimens performing one test per specimen. |

* Some laboratories may be able to process 45 samples or more per day by using two detectors and by vary-ing the various parameters, such as diameter, length, temperature of column, and carrier gas flow, etc. ** This instrument needs extraction of morphine and quinine prior to its conversion to a fluorophore. The use of ATS is limited to test morphine, quinine and meperidine only. *** This instrument has been withdrawn from the market but it can be purchased. The procedure is limited

to test morphine and methadone only.

| Immunoassay techniq | ues § | | · · · · | |
|--|--|--|---|--|
| EMIT (automated) | FRAT | RIA | НІ | LFT |
| 450–500 specimens ** performing one test per specimen. | 400 specimens ¹¹¹ performing one test per specimen. | 625 specimens [†] per- forming one test per specimen. Bivalent re- agents capable of test- ing morphine and barbiturates simulta- neously are available but all positives will | 300–400 specimens performing one test per specimen. Reagents for testing other drugs are not commercially avail- able | 300-400 specimens performing one test per specimen. This test is not com- mercially available as yet. |
| | | have to be redone for morphine and barbi- turate individually by using monovalent morphine and barbi- turate reagents. | · | |

¹ The delivery of specimens tested per day using immunoassay techniques varies as a function of the number

of tests performed per specimen. Thus an assay capable of performing 450 tests per day will do 90 specimens every day if five tests are performed per specimen. Practical considerations such as repeating certain samples and the need to include a standard of the various drug abuse calibrators will further reduce the above output.

¹⁵ EMIT automated Gilford can perform 500 tests, EMIT automated Abbot (ABA 100) can perform 1050 tests and Manual Emit Gilford can perform 300 tests per day (8h). These figures are claimed by Syva Corporation, while our experience with Manual Emit Gilford proved that a maximum number of 120 tests per day could be performed. Furthermore, practical considerations such as repeating certain samples and the need to run various calibrators reduces the output further. Reagents to test opiates, methadone, amphetamine, barbiturate, and cocaine metabolite are commercially available.

⁵¹⁵ Practical considerations such as repeating certain samples and the need to include standards will reduce the output. Reagents to test opiates, methadone, amphetamine, barbiturate, and cocaine metabolite are commercially available.

⁺ Although Roche Diagnostics claims the above figure of 625 tests per day, we feel that the feasible number of tests that can be performed per day is 350-400. Practical considerations such as repeating certain samples and the need to include standards will reduce the output.

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| | TLC | | GLC | | SPF techniques | | | r . |
|--|--|--|--|--|----------------------------------|-------------------|--|---------------------|
| | | | | | ATS | - A Barrow | Technicon automatea SPF system | 1 |
| Labor cost per day (7.5 h) approx. | | | | | | | · · | |
| S 4.56 per hour. Reagents and per- tinent supplies | (i) Chemicals and TLC supplies annrox, \$ 0.20 | 34.20 | Chemicals and oth materials appro \$ 0.12 per | \$ 34.20 ter K. | Reagents and su plies approx. | \$ 34.20 p- | Reagents and sup- plies approx. | \$ 34.20 |
| | per specimen (ii) SA-2 cation- | \$ 24.00 | specimen | \$ 2.64 | men | \$ 400.00 | \$ 0.10-\$ 0.18 | \$ 30.00 |
| | exchange resin loaded paper | | Total | \$ 36.84 | Total | \$ 434.20 | Total | \$ 64.20 |
| | approx. \$ 0.0675 per* | | per 25 specimens c | r \$ 1.48 | per 400 specimen | s or \$ 1.09 | man 200 annaimean - | |
| | 6 × 6 cm sheet (iii) Minigrip bags (plastic bags) to transport ion-exchange paper approx. \$ 0.02 per bag** | \$ 8.10 \$ 2.40 | specimen if 45 s are analyzed per performing at le to seven tests pe specimen. | o.as per pecimens day for ast five r | per specimen. | one test | 5 0.02 to \$ 0.29 ft performing one te specimen. | or Or Ost per |
| | Total | \$ 68.70 | | | | | | |
| | per 120 specimens o for performing at four to five tests p for opiates only, a \$ 0.82 per specime testing the entire a commonly abused as listed in Table performing at leas fourteen tests per men (eighty speci- per day); chemica layer supplies cale rate of \$ 0.30 per | r \$ 0.58 least ber specified array of 1 drugs I for st nine to speci- mens ils and the culated a specime | men D lin- t the n. | | | | | |
| • | The price per box of | 100 shee | ets each of 6 × 6 cm | n goes con | siderably down de | pending up | on the quantity purch | ased. |
| | Price per box \$ 6.75 \$ 5.85 \$ 5.30 \$ 5.00 \$ 4.75 \$ 4.45 | Quantity 1-99 100-49 500-99 1000-14 1500-19 2000-ov | • <i>of boxes to be purc</i> 9 9 99 99 99 | hased | | | | |
| ** purch | The price per carton ased. | of 1000 | Minigrip bags each | of 3 × 4 | in. goes consideral | oly down de | pending upon the qua | intity |

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| P | rice per carton | Quantity of cartons to be purchased |
|----|-----------------|-------------------------------------|
| э | 25.80 | |
| \$ | 19.55 | 5 |
| \$ | 13.50 | 10 |
| \$ | 8.60 | 25 |
| \$ | 7.85 | 50 |
| \$ | 7.60 | 100 |

TABLE II COST COMPARISON USING VARIOUS TECHNIQUES

| Immunoassay techniques*** | | | | |
|---|--|---|--|---|
| EMIT | FRAT | RIA | HI | LFT |
| • | | | | |
| \$ 34.20 Reagents cost approx. \$ 0.50 per test \$ 225.00 Ancillary supplies including buffer. batteria, drug abuse calibra- tors, disposable beukers approx. \$ 0.02 per test \$ 9.00 Total \$ 268.20 per 450 specimens or \$ 0.60 for performing one test per specimen \$ A urine specimen will cost \$ 1.20 to perform two tests per specimen. Reagents cost per too assay is \$ 0.74 per test but if single reagent worth 1000 assay is purchased at a time, it will cost \$ 0.50 per test. | \$ 34.20 Reagent cost ^{§§} approx. \$ 1.36 per test \$ 544.00 Ancillary supplies approx. \$ 0.12 per test \$ 48.00 Total \$ 626.20 per 400 specimens or \$ 1.57 for performing one test per specimen. If a single reagent worth 1000 assays is purchased at a time, the price per assay is \$ 0.50 and then the cost per specimen for per- forming one test per specimen comes to be about \$ 0.71, and \$ 2.84 for performing four tests per specimen. | \$ 34.20 Reagent cost approx. \$ 1.10 per assay \$ \$ 625.00 Ancillary supplies approx. \$ 0.20 per assay \$ \$ 125.00 Total \$ 784.20 Total \$ 784.20 per 625 specimens^{††} or \$ 1.26 for performing one test per specimen. A urine specimen will cost \$ 4.64 if four tests are performed per specimen. A bivalent reagent capable of testing morphine and barbiturates simultaneous- ly will cost \$ 1.50 per test but all positives will have to be redone for morphine and barbiturates by using monovalent morphine and barbiturate reagents. | \$ 34.20 Reagent cost approx. \$ 0.34 per test ^{†††} \$ 136.00 Ancillary supplies and shipping cost approx. \$ 0.08 per test \$ 32.00 Total \$ 202.20 per 400 specimens or \$ 0.51 for performing one test per specimen. | \$ 34.20 Latex flocculation test similar to pregnancy test is placed on the market by Roche Diagnostics and its price per test is still to be fixed when it becomes commer- cially available, Authors are validating the results obtained by LFT with TLC and EMIT. |

*** Positive results obtained by immunoassay techniques have to be validated by a non-immunological back-up procedure, thereby resulting in substantial increase in the cost per test.
 Since this method is based on lyso-enzyme, which is chemically bound to the drug in question, urine specimens having naive or endogeneous lyso-enzyme activity will give false positives for all drugs detected using this system. Therefore, all low-positive EMIT readings must be rechecked by running a blank of the same urine specimen without using antibody and enzyme reagents. This recheck will further increase the cost of analysis per test. Also refer to footnote *** given above on the validation of all positive results.
 §8 The regular price is \$1.50 per assay but the purchaser is entitled to a special rate of \$1.36 per assay if federal money is used to perform the test". This price needs no commitment on the part of the purchaser.
 §8 \$1.0 per assay if reagents worth 2300 tests are committed to purchase*. The cost of reagent per assay goes considerably down depending upon the quantity purchased.

| Cost per assay | Quantity to be purchase | 1 |
|----------------|--------------------------|-------|
| \$ 1.0 | 100 assays (1 | kit) |
| \$ 0.75 | 2,400 assays (24 | kits) |
| \$ 0.60 | 9.600 assays (96 | kits) |
| \$ 0.52 | 48,000 assays (480 | kits) |
| \$ 0.46 | 240.000 assays (2400 | kits) |
| \$ 0.43 | 500,000 assays (5000 | kits) |
| \$ 0.41 | 1 million assays (10,000 | kits) |

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50.41 If minion assays (10,000 kits)
 To perform 48,000 assays a year (930 test per week) will cost about \$ 25,000.
 The cost varies from \$ 0.17 to \$ 0.32 per test
 This figure of 625 tests per day is according to Roche Diagnostics but we feel that the feasible number of tests that can be performed per day is 350-400.
 †† The cost varies according to the number of tests purchased per month and the particular way the test is used. If concentrated serum is used, the price of reagent per test lowers down to \$ 0.27. There is a 5% reduction if the reagents purchased per month exceed 3000°. Methadone reagent is likely to be available in the near future.

TABLE III

START-UP COSTS OF VARIOUS TECHNIQUES

| TLC | GLC | SPF techniques | |
|---|---|--|---|
| | | ATS | Technicon automated SPF system |
| The start-up cost of a toxicology laboratory using the TLC technique was reported recently ^{13,14} ; equipment about \$2200; expendables and glassware sufficient for handling 500 specimens per week about \$1800; chemicals and re- agents approx. \$400. | A gas chromatograph with dual FID costs \$4000-\$8000. Columns, column packings and miscellaneous supplies cost \$500. | Farrand ATS costs about \$6000, but can be leased or rented (Farrand Optical Co., Valhalla, N.Y., U.S.A.). | Technicon Auto Analyzer costs about \$25 000. The instrument has been with- drawn from the market but the investigators interested in automation can still purchase this instrument; it can also be leased or rented (Technicon Instruments Corp., Tarrytown, N.Y., U.S.A.). |

Immunoassay techniques

week on yearly basis.

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| EMIT | FRAT | RIA | HI | LFT |
|--|---|---|--|--|
| Emit manual Gilford costs about \$7100; an- cillary reagents, cali- brators, and hardware needed with the spectro- photometer cost about \$200. EMIT automated Gilford costs about \$10 900 and EMIT automated Abbot (ABA 100) costs about \$26 000. Syva Corporation, Palo Alto, Calif., U.S.A. will supply EMIT manual Gilford free if the user commits to buy reagents worth 1000 tests every week on a yearly basis; it will sup- ply the automated Gilford free if the user commits to buy reagents worth 2000 tests every week on yearly basis; and it will supply the automated Abbot (ABA 100) free if the purchaser commits to buy reagents worth 7000 tests every | ESR spectrometer by Syva Corpora- tion costs about \$26 000. | A gamma counter is needed to use the ¹²⁵ I RIA system and a liquid scintillation counter is needed to use the ³ H RIA sys- tem. A gamma counter with teletype writer costs about \$9500; a liquid scintillation counter costs about the same price. A centrifuge machine will be needed, which costs about \$500 or less. Roche Diagnostics can ammortize the gamma counter, micro-medic automatic pipetting station and centrifuge machine with reagents cost. | This technique does not need ex- pensive and compli- cated equipment; it needs a simple centrifuge, titer trays and a few Pasteur pipets. | This technique needs heating blocks (specially designed to perform this test); 400 µl and 100 µl automatic pipets, and disposable specially designed test tubes. The start-up cost is less than \$500. |

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TABLE IV SENSITIVITY OF VARIOUS TECHNIQUES TLC

morphine (base) can be detected at a level of 0.10 µg/ml of urine and using 43-50 ml of urine, morphine (base) can be detected

/g/ml of urine for morphine base using a

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at a level of 0.07 μ g/ml of urine. Laboratories other than proficient laboratories can also achieve the above sensitivities if the steps reported are followed. Kullberg and Gorodetzky¹⁵ have recently reported a sensitivity of 0.07

XAD-2 resin column.

| TLC | GLC | SPF techniques | |
|--|---|---|--|
| | | Farrand ATS | Technicon automated system |
| The sensitivity of TLC identification techniques using ion-exchange paper to absorb the drugs from urine as reported recently by these laboratories ¹¹ for a wide variety of drugs of abuse was: morphine base, 0.15μ g/ml (0.20μ g/ml morphine HCl, H ₂ O); codeine phos- phate, 0.5μ g/ml; methadone HCl, 1.0μ g/ml; amphetamine sulfate, 1.0μ g/ml; methamphetamine HCl, 0.5μ g/ml; methylphenidate (Ritalin), 1.0μ g/ml; phenmetrazine HCl (Preludin), 0.5μ g/ml; phenobarbital, 0.5μ g/ml; and secobarbital, 0.36μ g/ml of urine. All these sensitivities were achieved using 20 ml of urine. Using $30-35 \text{ml}$ of urine, | Morphine 0. 1–0.5 µg/ml; barbiturates and amphetamines, 1.0–2.0 µg/ml of urine. | Mulé and Hushin ¹⁶ have reported a sen- sitivity of 0.22 µg/ml of urine for morphine base. | Technicon claims a sensitivity of 0.20 µg/ml of urine for morphine base; how- ever, these data need validation. |

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| Immunoassay technique | ······································ | | · · · · · · · · · · · · · · · · · · · | •••••••••••••••••••••• |
|---|---|--|---|---|
| EMIT | FRAT | RIA | HI | LFT |
| Morphine, 0.5 μ g/ml; methadone, 0.5 μ g/ml; amphetamine, 1–2 μ g/ml; barbiturate, 1–2 μ g/ml; and benzo- yl ecgonine, 1.0 μ g/ml (Syva Corporation re- commends a cut-off limit of 0.3 μ g/ml for morphine and metha- done; 1.0 μ g/ml for amphetamine and bar- biturate for urine specimens submitted for Proficiency Testing by Center for Disease Control (CDC) Atlanta, Ga., U.S.A.). | Morphine, 0,1–0.5 µg/ml (incidence of false positives for morphine at a higher sensitivity level of 0,1 µg/ml is possible), amphetamine, barbi- turate, and benzoyl ecgonine, 1.0 µg/ml; methadone, 0.5 µg/ml, as claimed by Syva Corporation. | 25–100 ng/ml of urine for morphine (the incidence of cross-reactivity with other drugs at 25–40 ng level could be high). | 25-50 ng/ml of urine for morphine (the incidence of cross-reactivity with other drugs at 25-50 ng level could be high but by selecting a decreased sensitivity of 100-200 ng/ml this incidence of false positives can be minimized). | 100–200 ng/ml of urine (by purchasing concentrated anti- body, user can select any sensitivity be- tween 100–300 ng/ml of urine). |
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| TABLE V SUMMARY | | | | | |
|---|--|--|---|--|---|
| | Delivery of urine specimens per day (7.5 h) | Cost per specimen | No. of tests performed per specimen | Start-up cost | Sensitivity |
| LIC | 120 80 | \$0.58 \$0.82 | 4-5 9-14 or more | Equipment, expendables and chemicals, 54,400 (refs. 13, 14) | Morphine base, 150 ng; methadone HCl, 1.0 /ug; ampitetamine sulfate, 1.0 /ug; methamphetamine HCl, 0.5 /ug; phenobarbital, 0.5 /ug/ml of urine (unine needed 20 ml); morphine base, 70 ng/ml of urine (urine needed 43–50 ml); morphine base 100 ng/ml of urine (urine needed 30–35 ml). Refer to Table IV. |
| GLC | 25-45 (see foot- note *, Table I) | S1.48-S0.88 | S-7 | S4,500-S8,500 | Morphine base, 100–500 ng/ml; barbiturates and amphetamines, 1.0–2.0 µg/ml of urine. |
| ATS (Farrand automated turret spectrofluorometer) | 400 | S1.09 | - | S6,000 | Morphine base, 220 ng/ml of urine ¹⁶ |
| Technicon auto- mated SPF system | 300 | S0.22-S0.29 | l | \$25,000 | Morphine base, 200 ng/ml of urine |
| EMIT | 450-500 (see foot- note ^{§ §} , Table I) | S0.60 (see foot- notes ••• and §, Table 11) | - | Manual S7, 100: Gilford automated, S10,900; Abbott automated (ABA- 100), S26,000 plus S200 ancillary sup- plies and hardware | Morphine, 500 ng: methadone, 0.5 /ng; amphet- amine, 1–2 /ng; barbiturates, 1–2 /ng; and benzoyl ecgonine, 1.0 /ng/ml of urine (Syva recommends a cut-off of 300 ng/ml of urine for morphine and methadone for Proficiency Testing of Urine Specimens). |
| FRAT | 400 (see foot- note ¹¹³ , Table I) | S0.71–S1.57 (see Table II under FRAT and also footnotes *** and *\$, Table II) | | S26,000 | Morphine, 100–500 ng: amphetamine, barbiturate, and benzoyl ecgonine, 1.0 /ng: and methadone, 0.5 /ng/ml of urine |
| RIA | 625 (see footnote ⁺ , Table I) | S1.26 S1.50 (see Table II under RIA and also footnote ***, Table II | 1 2 (see Table II under R1A) 1) | S10,000 | Morphine, 25-100 ng/ml of urine (incidence of cross-reactivity with other drugs at 25-40 ng level could be high). |
| · · | 300-400 | S0.51 (see footnote ***, Table II) | _ | \$500.0 approx. | Morphine, 25–50 ng/ml of urine (incidence of cross-reactivity with other drugs at this level could be high, but this can be minimized by selecting a decreased sensitivity of 100–200 ng/ml of urine) |
| LFT | 300-400 | Not known as yet | - | S500.0 approx. | 100-200 ng/ml of urine |

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Pooling of different urines is not feasible using the EMIT since it involves the risk of diluting the sensitivity of the test by mixing a positive urine with one or more negative urines. Similarly, urine monitoring using Amberlite XAD-2 (nonionic) polymeric resin columns at the clinics is not possible as this would need the services of a trained operator. Furthermore, it will be virtually impossible to pool the various urine specimens for different visits of one client using the same resin column since it has to be stored in a refrigerator after the urine has been passed through to avoid the formation of channels due to drying of the resin. In addition, the shipping of the above wet columns to the laboratories will create technical problems.

Data regarding existing techniques, delivery of urine specimens per day, cost of monitoring various drugs per specimen, start-up cost of each technique and their sensitivities are presented in Tables I–V. Table I shows the delivery of urine specimens using each technique. Thus far, TLC eminently appears to be the only technique which is simple, inexpensive, reliable and versatile. A technician using the singlestep extraction technique as reported by these laboratories^{10,11} can detect a minimum of fourteen drugs at a time in a single urine specimen costing approximately \$0.82, while testing for opiates performing four to five tests per specimen will cost \$0.58. These figures include labor, reagents, chemicals and TLC supplies calculated on the basis of 600 urine specimens per technician per week for opiates and 400 urine specimens for detecting the entire array of drugs of abuse. On the other hand, immunoassay techniques are exorbitant in cost: A single test per urine specimen using EMIT will cost \$0.60 and will cost more than a \$1.0 using FRAT or RIA. The total



Fig. 2. Relationship between number of tests per urine specimen and cost per test. A, TLC; B, EMIT; C, RIA; D, RIA, showing that two tests (morphine and barbiturates) may be performed simultaneously using bivalent reagents (positives have to be re-done using monovalent reagents).

cost of testing a urine specimen for more than one drug increases according to the number of tests performed, thus a urine specimen will cost \$3.0 for testing morphine, methadone, cocaine metabolite, amphetamine and barbiturate using EMIT and will cost more than \$4.0 using RIA (see Fig. 2). Furthermore, the need to include standards, or to run various drug abuse calibrators, the necessity to confirm all positives by a nonimmunological procedure or practical considerations such as repeating certain samples (to the extent of 20-30%) will substantially increase the total cost of analysis per specimen. These data also prove that no savings of tax payers' dollars can be achieved by replacing the personnel employed for performing TLC with automated immunoassay systems. In fact, using TLC techniques, we can have daily and speedy delivery of urine results by employing adequate staff and by adjusting the daily collection of urines according to the needs of a particular program. The readers are further advised that immunoassay techniques are unable to differentiate amphetamine from methamphetamine, phenobarbital from secobarbital and diphenylhydantoin (Dilantin), and morphine from codeine, and cannot detect amphetamine-type drugs such as phenmetrazine (Preludin), and methylphenidate (Ritalin), and sedativehypnotics like glutethimide (Doriden).

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REFERENCES

- 1 S. Spector and C. W. Parker, Science, 168 (1970) 1347.
- 2 D. S. Skelly, L. P. Brown and P. K. Besch, *Clin. Chem.*, 19 (1973) 146; D. Catlin, R. Cleeland and E. Grunberg, *Clin. Chem.*, 19 (1973) 216.
- 3 R. K. Leute, E. F. Ullman, A. Goldstein and L. Herzenberg, *Nature (London)*, *New Biol.*, 236 (1972) 93.
- 4 R. K. Leute, E. F. Ullman and A. Goldstein, J. Amer. Med. Ass., 211 (1972) 1231.
- 5 F. L. Adler and C. T. Liu, J. Immunol., 106 (1971) 1684.
- 6 F. L. Adler, C. T. Liu and D. H. Catlin, Clin. Immunol. Immunopathol., 1 (1972) 53.
- 7 H. Hager and M. Usategui, Roche Diagnostics, Division of Hoffmann-La Roche Inc., Nutley, N.J. 07110, personal communication.
- 8 R. E. Rubenstein, R. J. Schneider and E. F. Ullman, *Biochem. Biophys. Res. Commun.*, 47 (1972) 846.
- 9 A Guide to Urine Testing for Drugs of Abuse, Special Action Office Monograph, Series B, No. 2, November 1973, Washington, D.C.
- 10 K. K. Kaistha, R. Tadrus and R. Janda, Natl. Drug Abuse Conf., Chicago, Ill., March 30-31, 1974. 11 K. K. Kaistha, R. Tadrus and R. Janda, J. Chromatogr., 107 (1975) 359.
- 12 A. A. Kurland, L. Wurmser, F. Kerman and R. Kokoski, Meet. Comm. Problems Drug Dependence, 29th, National Academy of Sciences, National Research Council, Lexington, Ky., Feb. 14–16, 1967.
- 13 K. K. Kaistha and J. H. Jaffe, Int. J. Addict., 7 (1972) 585.
- 14 K. K. Kaistha, J. Pharm. Sci., 61 (1972) 655.
- 15 M. P. Kullberg and C. W. Gorodetzky, Clin. Chem., 20 (1974) 117.
- 16 S. J. Mulé and P. L. Hushin, Anal. Chem., 43 (1971) 708.