



TOX TALK

Society of Forensic Toxicologists, Inc.

1013 THREE MILE DRIVE • GROSSE POINTE PARK • MICHIGAN 48230-1412

VOLUME 12, No. 2

JUNE 1988

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FROM THE EDITOR'S DESK ; . .

JOSEPH R. MONFORTE, PH.D.

I want to take this opportunity to thank the contributors to this issue of ToxTalk. A special "thank you" goes to Chip Walls for submitting the section on Literature/Publications. Hopefully, this will become a regular feature of ToxTalk, depending upon the interest and number of submissions.

The NIDA Guidelines for Federal Workplace Drug Testing were published in their final form in the Federal Register on April 11, 1988. These guidelines detail comments from reviewers and incorporate some changes from the original guidelines, particularly in the area of qualifications of personnel. SOFT has issued a position statement relative to the NIDA Guidelines, and forensic toxicologists should obtain and familiarize themselves with the contents of the final guidelines. These may be obtained by telephoning (301) 443-6780.

The existence of the guidelines has become apparent in Michigan. At a recent arbitration hearing concerning a positive urine cannabinoid metabolite result, questions were asked to determine how closely the laboratory adhered to the NIDA Guidelines. The questions were supplied to the attorney by a local university "expert." Eventually, we will all be responding to similar questions.

SOFT has formed a committee under the capable direction of Mike Peat to develop guidelines for the operation of a post mortem forensic toxicology laboratory. The committee has had one telephone conference call and will meet as a group in August. This is a very timely committee, and you will be kept informed of their activities.

IN THIS ISSUE

REGULAR FEATURES: PROFESSIONAL CALENDAR

NEW FEATURE: PUBLICATIONS/LITERATURE CITATIONS

OF SPECIAL INTEREST: SOFT MEETING PRELIMINARY PROGRAM
MEETING REVIEW - ASCPT

TECHNICAL HIGHLIGHTS: ELIMINATING MASS SPECTROMETRY
BASE PEAKS

INSERT: CALL FOR PAPERS - SOFT MEETING

MEETING REVIEW: A REPORT ON THE NATIONAL MEETING OF THE AMERICAN SOCIETY
FOR CLINICAL PHARMACOLOGY & THERAPEUTICS - MARCH 7-11, 1988

ABSTRACTED FROM MATERIAL SUBMITTED BY VINA SPIEHLER, DIAGNOSTIC PRODUCTS
CORP., 5700 WEST 96TH STREET, LOS ANGELES, CA 90045

A two-day Consensus Conference on the Scientific Principles Underlying Non-medical Urine Drug Testing was held under the auspices of the Committee on Substance Abuse which found it easier to come to a consensus on the analytical shortcomings, legal questions and ethical problems of urine drug testing rather than on the scientific principles. In brief, the consensus was that a positive urine test provides limited information with respect to drug dose, route of administration, or patterns of use. The probability of pharmacological effect and time of effect cannot often be determined; therefore, interpretation of urine drug results should be done by a physician with clinical pharmacology training.*

The specific research recommendations were for 1) quantitative urine drug metabolite profiles after known dose and time, 2) quantitative methods for drugs in saliva as well as blood and urine, 3) brain receptor research, 4) the relationship between pharmacokinetics and pharmacodynamics for these drugs, 5) direct tests for drug induced behavior changes, and 6) epidemiological studies of drug use, safety and impact of urine drug testing.

In the ASCPT plenary sessions, the scientific papers reflected the definition of substance abuse as alcohol and nicotine addiction or misuse of sedative/hypnotics such as the benzodiazepines. Smoking was banned from the meeting, but alcohol was served at the receptions. Alcohol is currently postulated to act via the GABA-Cl⁻ channel complex like the benzodiazepines and barbiturates rather than by disruption of cell membrane fluidity. Some benzodiazepine antagonists apparently act as alcohol antagonists. Benzodiazepine reverse agonists, such as the beta carbolines, block this antagonism.

Presentations on nicotine effects demonstrated hysteresis effects including hysteresis in relating pharmacokinetics and pharmacodynamic models. This may be due to a lag time in the drug reaching or leaving the receptor sites, acute tolerance at the receptor level, rate limiting steps in the post-receptor biochemical cascade or other causes, and it means that urine, serum, blood or saliva drug concentrations might not correlate directly with the drug effect on behavior at the time of the sampling. This is the scientific basis of the Consensus Conference's call for direct tests of drug effect on behavior instead of chemical tests on body fluids to establish intoxication or impairment.

In the sessions on pharmacometrics Sheiner presented an algorithm for modeling hysteresis. Papers were presented on fentanyl, alfentanil, nicotine and hydromorphone. In addition to research presentations on Bayesian forecasting of individual pharmacokinetic parameters, results with the ABBOTBASE programs for compatible PC's for individualization of dosing for aminoglycosides were presented.

* EDITOR'S NOTE: Any comments on this? JRM

ELIMINATION OF MASS SPECTROMETRY BASE PEAKS

SUBMITTED BY JOSEPH R. MONFORTE, PH.D., ROBERT GAULT, PH.D., AND KAREN KATALINICH, B.S., WAYNE COUNTY MEDICAL EXAMINER'S OFFICE, 400 EAS LAFAYETTE, DETROIT, MI 48226

An article appeared in ToxTalk (Vol.11, #1, pg 3, 3/87), later published in JAT (V11#5, 235, 1987) describing the usefulness of eliminating the base peak of $m/e = 58$ as an aid in distinguishing amitriptyline from cyclobenzaprine. This technique seemed applicable to other drugs where virtually only a base peak of 58 appears in the mass spectrum, and retention times are too similar to make the distinction. Examples are shown in Table 1.

The mass spectra of these drugs are shown in Figure 1 and are virtually indistinguishable.

TABLE 1

DRUG	RETENTION TIME
Propoxyphene	7.50 minutes
Amitriptyline	7.55 minutes
Doxepin	7.69 minutes

Column: Hewlett Packard 15 meter cross-linked methyl silicone
Column Temperature: 90°C to 270°C at 20°/minute; hold at 270°C for 6 minutes

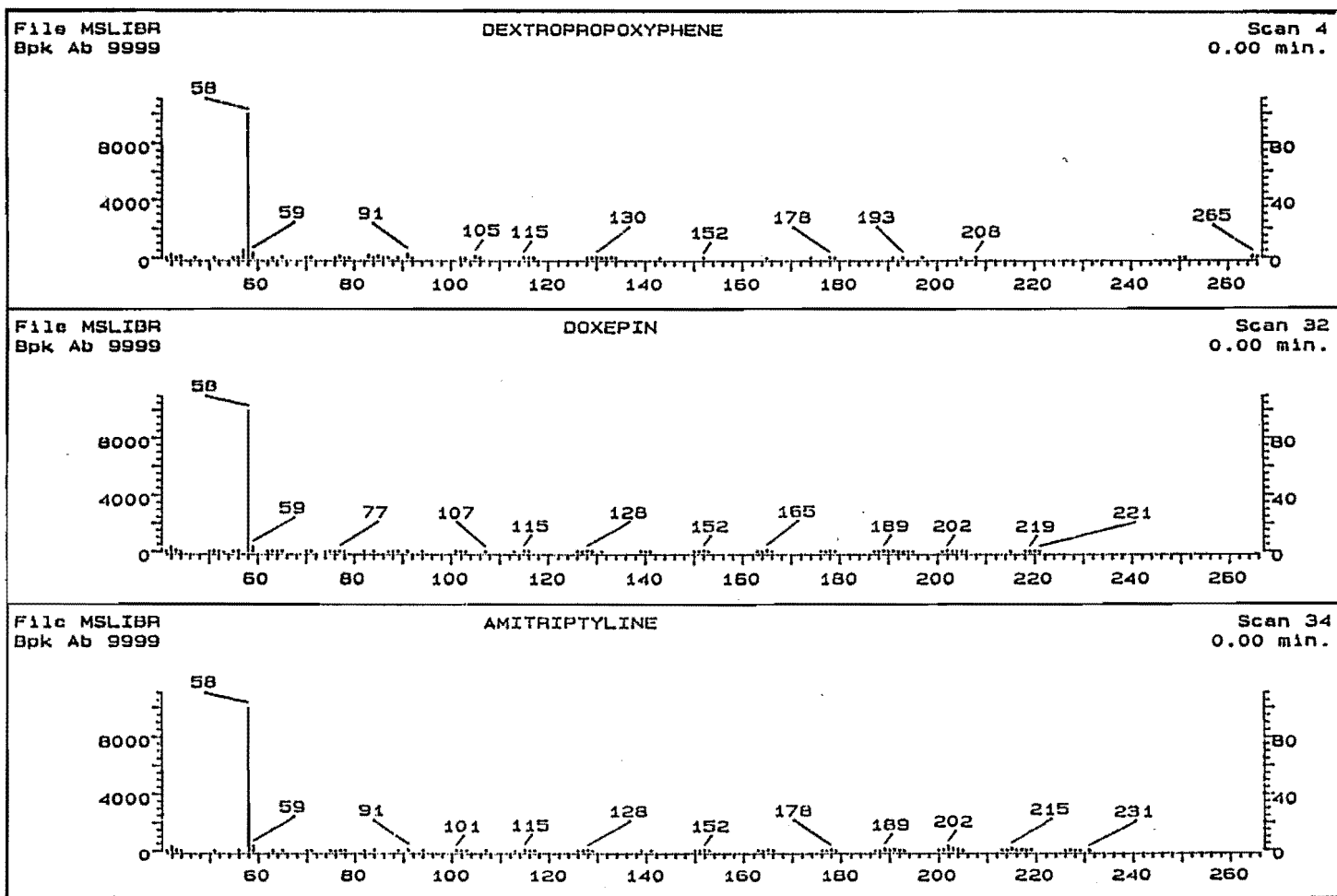


FIGURE 1

Elimination of the $m/e = 58$ base peak creates new "base" peaks for each drug, as shown in Figure 2. The identifications are now much clearer, particularly when the entire mass spectrum is evaluated.

The above data were obtained on a Hewlett Packard 5996A GC/MS combined with the RTE-6 Rev.E Data system. Since the system is autoscaling, removal of the initial base peak automatically results in a new base peak as shown below.

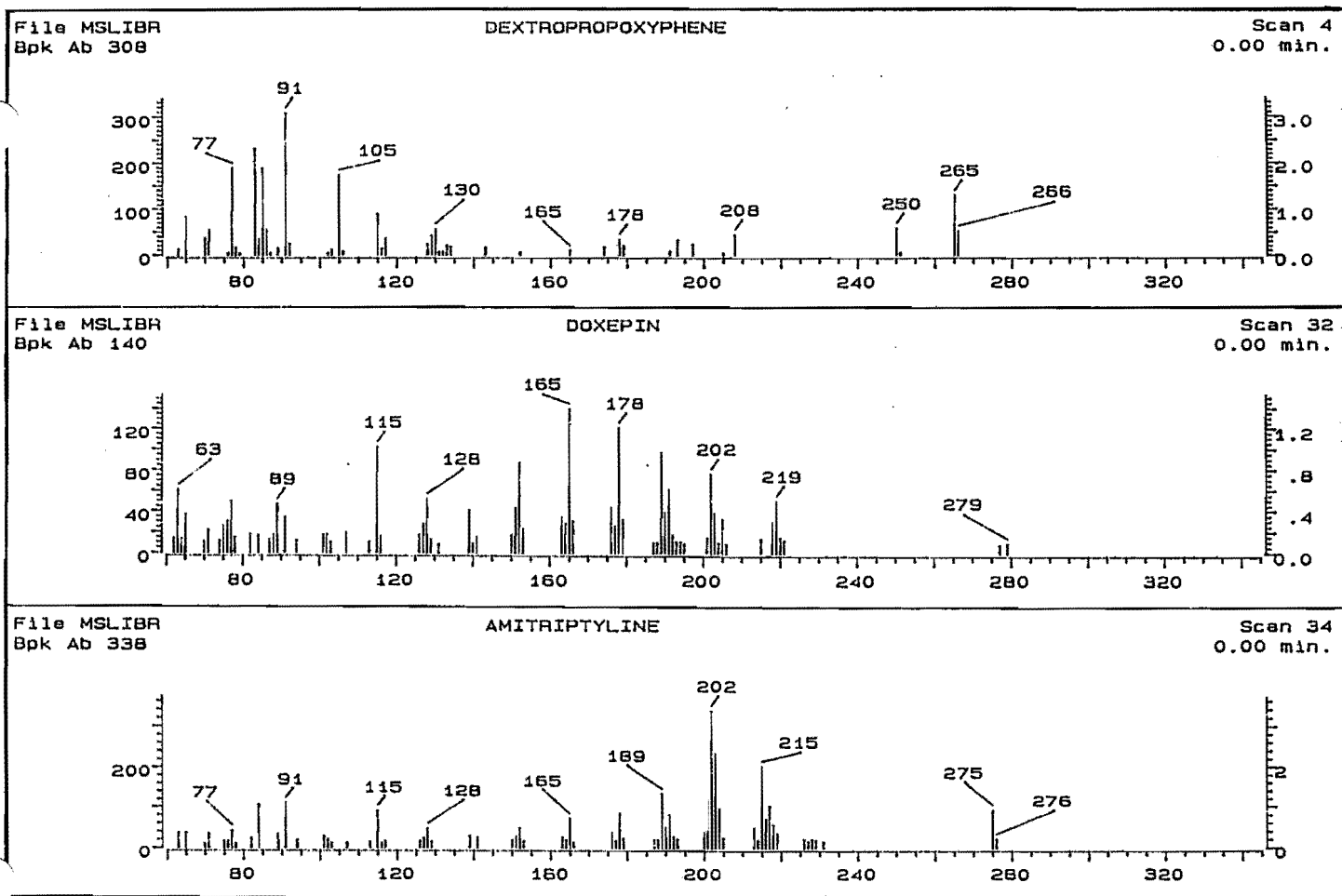
To the right is a short transfer file for the HP RTE-6 System which will remove the base peak from a spectrum, independent of m/e . The spectrum must be in the X register; Y, Z and T registers are preserved. Here's how to do it!

```

:SV,4,,IH
:RU,RPN
:RU,QQ,X,0
:IF,1P,NE,1,8
:RU,SAV,REGT,T
:RU,ENT
:RU,BIG,1
:RU,SUB,T
:RU,RCL,REGT
:RU,RD
:SV,0,,IH
::
:DP
:DP, The X Register must contain
      a mass spectrum with this
      command!
:DP
:SV,0,,IH
::

```

FIGURE 2



It is the intent of this column to call attention to unusual or highly interesting articles, not a systematic review of selected journals such as available through other recognized sources (Chem Abstracts - Forensic Sciences, CAT, TIAFT, etc.).

MORE ON PROFICIENCY TESTING. Gambino, S.R., O'Brien, J.E., and Malon, P.; *Clinical Chemistry*, 34:2, 1988. This is a brief presentation by MetPath Teterboro examining proficiency test failures and discussing why failures on proficiency tests may not equate with actual clinical performance. Failures may be tracable to (1) the sample, (2) materials or statistical parameters set by the testing agency, and (3) errors by the lab being tested. The authors submit some suggestions to correct problems related to numbers (1) and (2) and conclude that while this type of testing is valuable, some steps must be taken to assure its validity.

PRELIMINARY TESTS FOR DRUGS OF ABUSE. Sunshine, I.; *Clin Chem* 34:2, 1988. An employee drug-testing program is best designed by consultation between representatives of the laboratory and associates from all client departments (personnel, security, legal, medical, safety, public relations and labor unions). The test procedures selected for the specific drugs in question will depend on sensitivity/specificity/"cut-off" values, equipment available, specimens required, and turnaround time. Preliminary screening is required to separate the large number of negatives from presumptive positives, which require subsequent confirmation. Immunoassays (usually semi-automated) are procedures of choice for initial screening. In some clinical situations, thin-layer chromatography may be preferable. This article discusses some assets and liabilities of various analytic procedures and presents guides to the selection of suitable procedures for particular clients.

EMPLOYEE TESTING AND THE LAW. A new journal aimed at the controversy of employee drug testing. "Reporting legal, technical, and policy developments in employee testing," a recent article by David Plack on "TESTING FOR ABUSED DRUGS: A PRIMER FOR EXECUTIVES" is worthy of attention since its numerous charts bring together a lot of information.

DRUG ABUSE IN THE WORKPLACE: PREVENTION AND CONTROL - PROCEEDINGS OF THE 1987 ARNOLD O. BECKMAN CONFERENCE (Special Issue of *Clin Chem* 33(11-B), October 1987.

COCAINE: PHARMACOLOGY, EFFECTS AND TREATMENT OF ABUSE (NIDA Monograph M-50). It's a freebie packed with information. The chapters written by Reese Jones ("The Pharmacology of Cocaine") and Marian Fischman ("The Behavioral Pharmacology of Cocaine in Humans") are concise summaries of the subject. Call the National Clearinghouse on Alcohol & Drug Abuse Information at (301) 468-2600 for your copy.

ABUSE LIABILITY OF BENZODIAZEPINES (PHARMACOLOGICAL REVIEWS 39(4):251. The important sections of this extensive review cover evidence of the behavioral changes induced by benzodiazepines. Of particular interest are the sections related to psychomotor performance (p 293) and effects of benzodiazepines on the risk of accidents (p 308, 312). This issue can be ordered for \$16 from Williams & Wilkins, 428 E. Preston St., Baltimore, MD 21202.

TWO SOFT MEETING WORKSHOPS
QC for Postmortem Samples
Artificial Intelligence

THE EFFECT OF BIOLOGICAL SPECIMEN TYPE ON THE GC HEADSPACE ANALYSIS OF ETHANOL AND OTHER VOLATILE COMPOUNDS. Watts and McDonald, Am J Clin Path 87:79-85, 1987. This article reviews the effect of specimen "solids content" salting out and choice of internal standard. They found without at least a 5:1 dilution of "blood" there were differences between the headspace result and the "dilute & shoot" method. This article should be considered with the work presented at the 1988 AAFS meeting by Vicki Watts (abs.#K63) and Gene Rugotzke (abs.#K47).

CONSIDERATIONS IN ENHANCING RESOLUTION, SPEED, AND SENSITIVITY IN CAPILLARY CHROMATOGRAPHY AND GC/MS. Hyver and Phillips, J Chrom 399:33-46, 1987. Cap columns with 100 um ID for the fast times of your life. (Or big is not always better.)

ARTIFACTS IN THE DEFINITION OF TOXICITY BY CYANIDES AND CYANOGENS. Ballantyne, B, Fundam Appl Toxicol 3(5):400-408, Sept-Oct 1983. Information from one of the leading experts on the subject. Discusses storage conditions, artifacts, analytical considerations, and whole blood -vs- plasma.

More publications will be featured in future issues of ToxTalk as the information is made available and space permits. You are encouraged to send contributions for this column to ToxTalk. Be sure to include proper citation or source address/telephone number.

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DEADLINE FOR THE NEXT

ISSUE OF ToxTALK:

AUGUST 1, 1988

SUBMIT YOUR MATERIAL EARLY

PLASMA CONCENTRATIONS OF BENZODIAZEPINES - A REVIEW OF CLINICAL FINDINGS AND IMPLICATIONS. Norman & Burrows, Prog Neuropsychopharmacol Biol Psychiatry 8(1):115-126, 1984. Brief discussion of methods of analysis, pharmacokinetics, and plasma concentrations -vs- anxiolytic response.

DETERMINATION OF BENZOYLECGONINE AND COCAINE IN BIOLOGIC FLUIDS BY AUTOMATED GC. Peyton, Jones et al, J Chrom Biomed Appl 417:277-286, 1987. For those of you living in a high cocaine use area and have lots of confirmations/quants take heed to the tips in this article. Particular attention should be paid to problems of long autosampler runs. One would wonder what else the gremlins take during the night.

CAREER OPPORTUNITIES

Do you have a position available that may be of interest to SOFT members? Please submit the information to ToxTalk. There is no fee for this service.

MEMBERSHIP DIRECTORY UPDATE

Scuttle-butt abounds, but ToxTalk has received no official address changes. If you have moved, notify Secretary Pinder so you won't miss a future exciting issue of ToxTalk!

PROFESSIONAL CALENDAR

CALIFORNIA ASSOCIATION OF TOXICOLOGISTS 1988 quarterly meetings: August 6 - Northern California; November 5 - Los Angeles. Contact: Paul Sedgwick, Orange County Sheriff-Coroner, Forensic Science Services, P.O. Box 449, Santa Ana, CA 92702 telephone: (714) 647-7481.

June 27-30, 1988: THE INTERNATIONAL ASSOCIATION OF FORENSIC TOXICOLOGISTS, Groningen, The Netherlands. Scientific program includes a special one-day session on "Interpretation of Analytical Results." One day a parallel session is planned on mass spectrometry and mass selective detection together with the Department of Clinical Chemistry, Section Mass Spectrometry of the University Hospital Groningen. All other aspects of forensic toxicology will be covered in proffered papers and posters. On request round table conferences can be held. Contact: Dr. Donald R. A. Uges, Chairman, University Hospital Groningen, P.O. Box 30.001, NL-9700 RM Groningen The Netherlands; telephone: (0)50 61.4080; Telex: 53942 AZGN NL

September 10-14, 1988: INTERNATIONAL SYMPOSIUM/WORKSHOP ON DOPING IN SPORTS, Seoul, Korea. Contact Dr. Jongsei Park, Technical Director, Doping Control Center/KAIST, 144-29, Samsung-dong, Kangnam-Ku, Seoul, Korea.

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* September 28 - October 1, 1988: S.O.F.T. 1988 ANNUAL MEETING, Hershey *
* Hotel, Philadelphia, contact Jane Speaker, Ph.D., 2112 Cherry Street, *
* Philadelphia, PA 19103. (215) 563-9779 *
* * * * *

October 21-22, 1988: 14th Annual Meeting of the NORTHEASTERN ASSOCIATION OF FORENSIC SCIENTISTS, Mystic Hilton, Mystic, CT. Contact: Steve Sottolano, D.E.A. - Northeast Laboratory, 555 West 57th Street, Suite 1886, New York, NY 10019; telephone (212) 399-5137.

Fall 1989: S.O.F.T. ANNUAL MEETING, Chicago.

November 1989: PAN AMERICAN ASSOC. OF FORENSIC SCIENCES, Bogota, Colombia. Theme: "The Sciences and Justice." Contact: President Dr. Egon Lichtenberger, Carrera 11 A 96-26, Bogota, Colombia.

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ToxTalk is mailed quarterly to members of the Society of Forensic Toxicologists, Inc. For membership information contact: Richard D. Pinder, Ph.D., SOFT Secretary, Office of the Chief Medical Examiner, 11 Shuttle Road, Farmington, CT 06032 Telephone: (203) 679-3980

All members and others are invited to contribute to ToxTalk. Submit all materials (original plus 3 copies, if possible) for publication consideration to: ToxTalk, 1013 Three Mile Drive, Grosse Pointe Park, MI 48230-1412. Deadlines: February 1, May 1, August 1, and November 1.

M E M O R A N D U M

Handwritten initials



DATE: JUNE 24, 1988
 TO: EDITORS CAPLAN AND MONFORTE
 FROM: PATRICIA MOHN-MONFORTE, ToxTALK PUBLICATIONS EDITOR
 RE: JUNE 1988 TOXTALK - PRODUCTION REPORT

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ACCORDING TO MY RECORDS, THE 4 PREVIOUS ISSUES (JUNE '87, SEPT. '87, DEC. '87, AND MARCH '88) AVERAGED \$725.01 PER ISSUE SO WE ARE CONTAINING COSTS. THIS ISSUE WAS ALSO LESS EXPENSIVE BECAUSE IT WAS ONLY 4 PAGES INSTEAD OF 8; HOWEVER, IF MAJOR MATERIAL (MEETING MINUTES, ETC.) IS SUBMITTED IN PRINT-READY FORM, WE SHOULD BE ABLE TO CONTINUE TO KEEP COSTS DOWN.

c: M. McGEE

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