Society of Forensic Toxicologists, Inc.

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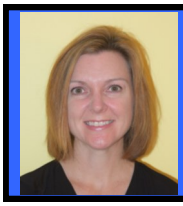

PRESIDENT'S MESSAGE

Submitted by **Jennifer Limoges, M.S., DABC**

The forensic community is quickly advancing with official standards in the field, and there are many different ways to participate in the process. The NIST OSAC has begun placing standards and guidelines on the Registry, and numerous documents are in the works. The original members of the OSAC were appointed for staggered terms, and the first terms will be ending later this year, so there will be opportunities to apply. The American Academy of Forensic Sciences (AAFS) has become an ANSI accredited Standards Development Organization (SDO) – the AAFS Standards Board (ASB). The ASB is starting to create Consensus Bodies for the various types of standards submitted. Within the next few months I would expect the ASB to be convening a Toxicology Consensus Body, so there will be opportunities for participation in that group. The most essential part of standards development is the public comment period, and I strongly encourage everyone to participate in that part of the process. SOFT will take an active role in letting our membership know when all these various opportunities for participation are available.

The planning for the 2016 SOFT annual meeting in Dallas is well underway. Our hosts Erin Spargo and Chris Heartsill have assembled an excellent planning committee and are starting to put the details in motion. Check the website regularly for all the latest information.

We have had some changes to our Annual Meeting Treasurer roles. Each annual meeting has a Treasurer assigned by the Board of Directors. Brad Hepler had stepped down from this role after several years, and SOFT is extremely grateful for his years of service as a Meeting Treasurer. Laurel Farrell (2016) and Marc LeBeau (2017) will continue in

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PRESIDENT'S MESSAGE (CONTINUED)

the role, and we have added Denice Teem and Melissa Kennedy to the team.

The Board also approved the 2020 annual meeting to be held in September of that year at the Marriott Marquis San Diego Marina. It will be the 50th anniversary of the SOFT annual meeting, and this is an extraordinary location. The Marriott is on the waterfront within walking distance or just a quick trip on the light rail to tons of great attractions including the Gaslamp Quarter, the Embarcadero, USS Midway, San Diego Zoo, SeaWorld, Balboa Park, and Petco Stadium to name just a few. And the Meeting Resource Committee is already working on the 2021 location to be selected later this year.

Many of our members just returned from another excellent AAFS meeting. Thank you to SOFT members Sarah Kerrigan (Section Chair) and Dan Anderson (Section Secretary) for representing the Tox section of the AAFS, and to Fiona Couper and Nikolas Lemos for coordinating an excellent Tox program. Thanks also to the many SOFT members who contributed to the high quality scientific presentations, posters, and workshops.

2015 SOFT BUSINESS MEETING MINUTES

The 2015 SOFT Business Meeting Minutes will be published in the June 2016 issue of ToxTalk®.

The California Association of Toxicologists (C.A.T.) 50th Anniversary Meeting

The California Association of Toxicologists (C.A.T.) proudly announces its 50th Anniversary Meeting, to be held in 2017.

C.A.T.'s first meeting was May 27, 1967. To celebrate, we will be returning to San Diego to honor the past, enjoy the present, and to shape the future of toxicology.

The meeting will be held May 5th and 6th, 2017, at Paradise Point Resort in San Diego. Drs. Lionel Raymon and Jan Ramaekers are tentatively scheduled to speak.

Please consult the website, www.cal-tox.org, for more information or to become a member. You may also contact host Dan Coleman at dan.coleman@doj.ca.gov

TREASURER'S REPORT 2016

Submitted by **Michelle Peace, Ph.D.,** SOFT Treasurer

I completed my first year as SOFT's Treasurer and have an even deeper appreciation for the hard work of those who have led this organization and who continue to grow its capacity and lead into the future. Specifically, as SOFT's Treasurer, I am thankful to the commitment of individuals like Bonnie Fulmer and the Committee of Annual Meeting Treasurers, Laurel Farrell, Marc Lebeau, and Brad Hepler, who constantly have the fiscal health of this organization on their minds. We owe deep thanks to Dr. Hepler who has committed at least 17 years to leadership in SOFT and just wrapped up his final duties as the Meeting Treasurer for the very successful meeting in Atlanta. As we say goodbye to Brad in treasury duties, we welcome Denice Teem and Melissa Kennedy into the rotation on this committee to help manage the annual meetings. They will train with Laurel and Marc and take their rotations in a couple of years.

Organizational Initiatives of Note:

- This year, we performed an internal review of SOFT's business practice by the Audit Committee, chaired by Tom Kupiec. This came with the decision that undertaking an external audit for a newly elected Treasurer while that person was on the steep learning curve for business practices and fiscal management for the organization was unduly burdensome. Therefore, I asked the Board to approve a change to the Policies and Procedures to move the external audit to the second year of the Treasurer's term. The Audit Committee found that there have been "no material misstatements of the books and records".

- The Wells Fargo Merchant Account, which was used to manage dues, was closed after the dues were moved into our operational budget. The Board decided that managing the two merchant accounts was unnecessary given that there is a single portal on the website to conduct business. Therefore, a single merchant account will be used to manage all credit card transactions. PayPal is also being considered to ease some transactions.

- I recommended to the Board that the organization's Treasurer should not chair the Strategic Planning Committee (SPC), but serve as a member. Ted Shults agreed to chair the committee and has led the committee through significant conversations regarding the hiring of an Executive Director. They have made several recommendations to the Board for consideration in hiring an Executive Director. Fiscally, the impact of those recommendations is reflected in the approved 2016 Budget Proposal and will be discussed below in the category analyses.

- Considerations that have been brought to the Board for discussion in 2016 include a potential re-organization of funds in our bank accounts and dispersing an RFP to banks in order to garner best rates for our practices.

The Board of Directors approved the 2016 Annual Budget at the interim meeting on February 24, 2016. The SOFT account balances, approved 2016 budget, and 2015 budget vs actuals are presented in this report. The organization is fiscally healthy and administratively compliant. As such, the Board continues to discuss leveraging our balances to provide meaningful benefits and services to the membership. Items of note in the budget analysis and proposal are below.

Operations

- Proposed operational income was adjusted to reflect the number of SOFT members and member dues of $80.

- Professional fees are proposed to be higher than the previous year as a result of moving the external audit from 2015 to 2016.

- SOFT Officer and Committee

TREASURER'S REPORT 2016 (CONTINUED)

Expenses has a significantly increased line item in the proposal due to anticipating one on-site meeting in Phoenix for the President, Secretary, and Audit Committee Chair, at least one on-site visit for planning an annual meeting, and to cover potential expenses incurred during the anticipated hiring process for an Executive Director. Expenses were less in 2015 as a result of a Convention Bureau fully supporting the travel for the on-site team.

- Website and software expenses were more than anticipated in 2015 in order to make critical improvements for security, member access, and to improve delivery of certificates.

- Two categories were added in operations for the hiring of an Executive Director. The SPC recommended that salary plus fringe plus office set-up be $105,000. If an Executive Director is hired in 2016, the actual will be less than the proposed, but the line item was supported for impact analysis and future planning. The SPC also strongly recommended that SOFT employ a search firm with a seasoned and successful record of placements to facilitate our process. Projections for the cost of the search for an executive director are $30,000.

Awards

- Two Leo Dal Cortivo Award recipients were selected. One winner has not yet cashed the award check.

Professional Investment

- The category of "Other Professional Investment Income" is the result of a credit from the hotel in 2014 and a pre-pay for 2016.

- SOFT Continuing Education Committee held a successful workshop in 2015 and are projecting 4 regional workshops in 2016.

- Young Forensic Toxicologists Committee performed an analysis of their activities at SOFT. With data to support their request, the Board approved additional funds to support their activities.

If you have any comments, questions, or suggestions on SOFT's finances, please contact me at mrpeace@vcu.edu.

Account Balances	CURRENT (Feb 15, 2016)	Dec 31, 2015 (per bank statements)	Dec 31, 2014
Operations	680,488	533,617	575,512
Reserve	150,193	150,167	151,032
ERA	168,077	164,664	160,224
Leo DalCortivo	44,291	44,288	45,244
Meeting Checking	78,530	164,156	6950
Merchant Account	52,810	500	500
Web Dues	0	0	51,952
	1,174,389	**1,057,392**	**991,415**

TREASURER'S REPORT 2016 (CONTINUED)

OPERATIONS			
INCOME	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
Application Fees	5500	7360	5000
Late Fees (Dues)	500	90	500
Membership Dues	100000	69756	64000
Other Operations Income	0	4	0
TOTALS	**106000**	**77210**	**69500**
EXPENSES	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
AAFS Midyear BOD Meeting Expenses	1200	856	1200
Appreciation Gifts	1500	554	1500
Bank and Credit Card Service Fees	3500	2918	3500
Charitable Contributions	1000	1820	800
Insurance	3000	2563	4500
Lease SOFT Office	4000	3788	3000
Office Equipment	500	274	500
Office Telephone/Internet	3000	2669	2500
Office/General Administrative Expenses	2500	1742	2500
Admin Assistant Payroll Expenses	45000	38262	45,000
Postage/Shipping Expenses	800	553	800
Professional Fees: Accounting and Legal	12000	1560	12000
QuickBooks Online + Fees	700	880	650
SOFT Officer/Committee Expenses	20000	5286	13000
Software/Website Programing	5000	10066	7500
State of Delaware: Incorporation Expenses	250	227	100
Website Hosting Expenses	1600	1542	1400
Exec Director Salary + Set-up	105000		
Exec Director Search	30000		
TOTALS	**240550**	**75560**	**100450**
NET OPERATIONS	***(134550)***	***1650***	***(30950)***
AWARDS			
INCOME	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
ERA Donations	2000	3400	1500
Interest Earned - ERA Account	250	197	250
Leo Dal Cortivo Donations	0	0	0
Interest Earned - LDC Account	50	44	50
TOTALS	**2300**	**3641**	**1800**
EXPENSES	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
ERA/YSMA Awards	6000	6000	6000
Leo Dal Cortivo Awards	2000	1000	2000
TOTALS	**8000**	**7000**	**8000**
NET AWARDS	***(5700)***	***(3359)***	***(6200)***

TREASURER'S REPORT 2016 (CONTINUED)

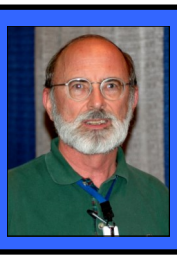
PROFESSIONAL INVESTMENT			
INCOME	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
Annual Meeting Income	1010000	1122106	975000
ToxTalk Advertisements	1500	2900	1000
SOFT Logo Sales	1500	2771	1000
Silent Auction Proceeds	2500	6923	2500
Interest Earned - Reserve Account	200	180	200
SOFT Con Ed Income	3000	1670	0
Other Prof Investment Income	0	15825	0
TOTALS	**1018700**	**1152375**	**979700**
EXPENSES	**2016 PROPOSAL**	**2015 ACTUAL**	**2015 BUDGET**
Meeting Expenses	975000	997456	970000
CFSO Membership	10000	10000	10000
Oxford University Press	40000	38580	40000
SWGTOX	200	180	0
SOFT Logo'd Item Expenses	1500	3202	3000
SOFT Con Ed committee Expenses	20000	3006	5000
Young Toxicologists Committee/SSEP	14000	7697	6000
Survey Monkey	300	250	200
TOTALS	**1061000**	**1060371**	**1034200**
NET PROFESSIONAL INVESTMENT	***(42300)***	***92004***	***(54500)***
OVERALL			
NET INCOME	***(182550)***	***90295***	***(91650)***

DUID Drug Testing Guidelines Survey Coming Soon

Submitted by **Mandi Mohr**

The National Safety Council, through NHTSA, is supporting an update to the recommendations for toxicology testing in impaired driving and motor vehicle fatality investigations, last published in 2013 (Logan et al. Recommendations for toxicological investigation of drug-impaired driving and motor vehicle fatalities. J Anal Toxicol. 2013 Oct;37(8):552-8). The recommendations have achieved widespread recognition among laboratorians, toxicologists and management, as well as Federal Agencies such as SAMHSA, NTSB, and ONDCP, and NHTSA as well as groups such as the NSC and GHSA.

In order to update the guidelines, laboratories performing toxicology testing in these types of cases will be sent a survey regarding current practices and drug prevalence in impaired driving and motor vehicle fatalities. The survey is expected to be sent out in May 2016. Laboratory participation in completion of the survey is a critical component to ensure published guidelines are reflective and representative. Your participation in the completion of the survey is greatly appreciated.



CASE NOTES

Send interesting *"Case Notes"* to Section Editor

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In Vitro Formation of Ethyl Glucuronide in Meconium Samples

Submitted by **Irene Shu, Aileen Baldwin, Valencia Sagnia, Mary Jones, Joseph Jones, Douglas Lewis, Adam Negrusz***

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Alcohol is one of the most commonly used drugs in the world, and currently ranks among the top leading risk factors for global burden of disease, disability and death. Approximately 30% of pregnant women reported drinking alcohol during the pregnancy, 8.3% of which reported binge drinking. After the first month of pregnancy, 22.5% of women reported alcohol consumption, 2.7% of women were drinking during all trimesters of pregnancy, and 7.9% during the third trimester (1). The prevalence of a very serious conglomerate of developmental and cognitive disabilities known as Fetal Alcohol Spectrum Disorders (FASD) is estimated to be as high as 2 to 5% of school children, making prenatal alcohol exposure the most preventable source of birth defects in the U.S.

Early diagnosis of prenatal alcohol exposure by testing specimens collected from the neonate allows for intervention services to be immediately provided to the affected newborn. Meconium is the first stool passed by the neonate within the first 48 hours after birth. It begins to accumulate in the fetus's intestine between 12 and 16 weeks of pregnancy. The excretion of meconium can be delayed in premature or low birth weight neonates (2). Some direct biomarkers, ethyl alcohol metabolites, accumulating in meconium have been studied as objective measures of prenatal alcohol exposure. Fatty acid ethyl esters (FAEEs) were the first suggested for that purpose in the early 1990s with the proposed summed cutoffs ranging from 0.5 to 2 nmol/g (2,3). The most frequently mentioned FAEEs are ethyl laurate, myristate, palmitoleate, linolenate, arachidonate, linoleate, palmitate, oleate, and stearate (4). It has been shown that late meconium samples collected from non-exposed neonates contained FAEEs above 2 nmol/g comparing to first-collected specimens tested negative. In the same study, incubation of meconium collected from neonates born to non-drinking mothers with glucose or ethyl alcohol resulted in significantly elevated concentrations of FAEEs (2). Similar experiments performed in our laboratory (unpublished data) also revealed *in vitro* formation of FAEEs in meconium samples. The results, therefore, have to be interpreted with caution when FAEEs are used to diagnose prenatal alcohol exposure. In the recent years, ethyl glucuronide (EtG) and ethyl sulfate (EtS), both ethyl alcohol Phase II metabolites, have been studied as viable biomarkers of *in utero* exposure to alcohol (4,5,6,7). Unlike FAEEs, EtG showed an association with alcohol history (5). In another study, the highest clinical sensitivity and specificity with EtG ≥30 ng/g of maternal self report at ≥ 19 weeks' gestation was observed comparing to FAEEs and EtS. Only for EtG, a significant dose-meconium concentration correlation was seen (EtG≥30 ng/g) (4). None of the studies, however, addressed the issue of *in vitro* formation of EtG in meconium over proposed cutoff 30 ng/g potentially leading to false interpretation of maternal drinking behavior.

The purpose of our study was to investigate the possibility of EtG *in vitro* formation in meconium followed environmental exposure to alcohol. Twenty authentic meconium specimens were selected. The analytical method for EtG in meconium consisted of sample homogenization, strong anion exchange solid phase extraction, and liquid chromatography-tandem mass spectrometry (LC-MS/MS) using D_5-EtG as the internal standard for quantification. The limit of detection (LOD) and the lower limit of quantification (LLOQ) was 6 and 12 ng/g, respectively. The linearity range was 12-600 ng/g for a calibration model established by a single-point 30 ng/g calibrator. A 0.1 g sample from each specimen was weighed out for EtG analysis (time zero). At the same time an-

In Vitro Formation of Ethyl Glucuronide in Meconium Samples (CONTINUED)

other 0.5 g meconium aliquot from each specimen was taken and 50 microliters of anhydrous 200-proof ethyl alcohol was added and mixed (approximately 0.08 g of ethanol in 1 g of meconium). The ethanol-meconium mixture from each specimen was stored at room temperature. A 0.1 g of ethanol-fortified meconium aliquot was subsequently weighed out from each sample at 24- and 48-hour time points for EtG analysis. The results are presented in Table 1.

As shown, at time zero all meconium samples had EtG concentrations below the LLOQ. After 24 hours of ethanol exposure, all 20 meconium aliquots tested positive; 18 of them were above the recommended EtG cutoff of 30 ng/g. In addition, inter-individual variability of the amount of EtG synthesized *in vitro* was observed when meconium was fortified with ethanol. EtG concentration thus did not correlate with the degree of alcohol exposure. In summary, as this experiment shows, significant amounts of EtG can be synthesized in meconium when environmentally exposed to alcohol. For that reason it is not an ideal biomarker for maternal alcohol use during pregnancy.

Table 1. EtG formation in meconium after exposure to ethanol

Sample number	EtG Concentration [ng/g]		
	0 h	24 h	48 h
1	ND	279	318
2	<LLOQ	1295	2164
3	ND	395	894
4	ND	369	802
5	ND	107	226
6	ND	295	363
7	ND	1153	1321
8	ND	12	14
9	<LLOQ	1063	1162
10	ND	1028	916
11	ND	713	653
12	ND	872	1149
13	ND	996	1654
14	ND	829	2643
15	ND	936	2413
16	ND	867	959
17	ND	23	35
18	ND	1196	1419
19	ND	471	585
20	ND	1150	2076
ND – not detected			

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In Vitro Formation of Ethyl Glucuronide in Meconium Samples (CONTINUED)

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Authors' Disclosures of Potential Conflicts of Interest: *No authors declared any potential conflicts of interest.*

Two Fatalities Involving the Use of the Synthetic Opioid U-47700

Submitted by **Erin A. Spargo, Ph.D., F-ABFT**
Southwestern Institute of Forensic Sciences, Dallas, TX

Introduction

A recent report stated that overdose deaths involving synthetic opioids excluding methadone increased by 80% from 2013 to 2014[1]. A number of jurisdictions have reported an increase in deaths in recent years from fentanyl and analogs including acetylfentanyl[2]. Reports of fatalities from AH-7921, another synthetic opioid, have also appeared in the literature beginning in 2014[3]. More recently, drug user forums have included discussions of a new synthetic opioid, U-47700, (*trans*-3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide) (Figure 1, www.cayman chem.com).

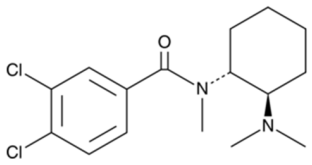

Figure 1: Structure of U-47700

It is generally reported that U-47700 was synthesized from AH-7921 in the 1970s by Upjohn Laboratories. It is currently marketed as a research chemical.

Our laboratory encountered two cases of U-47700 in 2015.

Case History and Autopsy

Case Study #1

A 27 year old white male was found dead at 2:18 pm in the kitchen area of a local high end hotel where he was staying with his mother; video last showed him alive at 3:00 am. He was found in a kneeling position with his face on the hotel floor. The face and head were congested and a bloody purge drained from his airways. Rigor was present; lividity was not set. Drug evidence, including two bags of unknown white powder, was present on the decedent. There were no signs of a struggle or foul play. The decedent had a history of depression, pill abuse, suicidal thoughts, hypertension and possible illegal drug use. According to the father of the deceased, his son ordered the white powder via the internet from China. At autopsy, cardiomegaly (heart weight of 380 grams) and pulmonary edema were observed. The left and right lungs weighed 660 and 810 grams, respectively. No tablets or capsules were identified in the gastric contents.

Case Study #2

A 20 year old white male was found unresponsive in bed at home at 10:50 am; he was last known alive at 9:30 pm the previous evening. Emergency personnel pronounced the man dead at 11:00 am. The decedent was lying on his back and purge was observed on his mouth and nose. Lividity was present on his chest, back and lower extremities. The decedent was heard to be breathing heavily throughout the night.

Two Fatalities Involving the Use of the Synthetic Opioid U-47700 (CONTINUED)

He had a known history of cocaine and marihuana use and according to friends, used an "opiate-like substance [purchased] over the internet that wouldn't show up on a drug test". The decedent's father reported that he had been in good spirits and had been sober the past six months. He was currently placed on a "medical discharge" from a local university. Gross pulmonary congestion and edema with heavy lungs (1080 grams right and 680 grams left) were observed at autopsy. The decedent had concentric left ventricular hypertrophy. Cardiomegaly (505 grams) and hepatosplenomegaly (2290 gram liver and 210 gram spleen) were evidence of terminal circulatory failure. Gastric contents contained no tablets or capsules.

Methods

Specimen collection

Both autopsies were performed at the Dallas County Medical Examiner's Office. Femoral blood, collected in gray top Vacutainer® tubes, was obtained in each case. In addition, subclavian blood was drawn in a gray top Vacutainer® in Case Study #2. Urine, vitreous humor, skeletal muscle, and blood in a red top Vacutainer® also were obtained in each case.

Toxicology testing approach

Both cases were subjected to the standard drug and alcohol postmortem testing panel performed at the in-house toxicology laboratory. Alcohols and acetone analysis were performed by headspace gas chromatography with dual column flame ionization detection (GC/FID/FID). Preserved femoral blood was screened by ELISA for three classes of drugs (cannabinoids, opiates and cocaine metabolite) and by gas chromatography mass spectrometry (GC/MS) for alkaline and acid/neutral drugs. Confirmation of positive screening results was performed either by a different technique or a second extraction.

Analysis

The procedure used by the laboratory for alkaline drug testing has been published previously[4]. Briefly, two milliliters of purified water were added to labeled 15 mL screw top culture tubes. Fifty microliters of internal standard (alphaprodine) were pipetted into each tube. A screening QC solution and three milliliters of blank blood were added to the QC tube. Three milliliters of sample were added to each case tube. Tubes were vortex mixed. Ten milliliters of n-butyl chloride were added to each tube and tubes were rotated for five minutes. Two hundred and fifty microliters of concentrated ammonium hydroxide were added and tubes were rotated for five minutes and then centrifuged. Nine milliliters of the supernatant were transferred into a clean labeled screw top culture tube to which 5 mL of 1.0 N hydrochloric acid were added; tubes were rotated for five minutes and centrifuged. The top layer was removed and 4 mL of the bottom aqueous layer were added to labeled tubes containing 60 uL of external standard (cholestane in chloroform) and 800 uL of concentrated ammonium hydroxide. Tubes were capped, vortex mixed and hand inverted at approximately 15 second intervals. After centrifugation, all but ~0.5 mL of the aqueous layer was removed and the chloroform layer was transferred to an autosampler vial containing a glass insert for analysis. Samples were analyzed by GC/MS/FID (DB-1 columns, 90 to 310°C at 12°C/min). Results were deemed acceptable when the screening QC passed and the cholestane/alphaprodine ratio was within 20% of target. Drugs reported as detected were reported from the screening analysis. When the laboratory quantitated a drug using the alkaline method, a second sample was extracted and quantitated by GC/FID/FID, equipped with DB-1 and DB-5 columns.

Drug Analysis Laboratory Testing

The Medical Examiner's Office submitted to the in house Drug Analysis Laboratory drug evidence that was found on the decedent in Case Study #1. Qualitative testing was performed by placing each piece of evidence in methanol, vortexing, transferring an aliquot to an autosampler vial and testing by GC/MS/FID. Identification was determined by mass spectral and retention time (within ± 0.05 minutes) matches to a known standard.

Two Fatalities Involving the Use of the Synthetic Opioid U-47700 (CONTINUED)

Results and Discussion

Toxicology testing results for Case Study #1 and Case Study #2 can be found in Table 1. The mass spectrum of U-47700 from Case Study #2 is shown in Figure 2. U-47700 eluted at 16.910 minutes. In Case Study #1, U-47700 co-eluted with diazepam (not shown). In both cases, multiple peaks were present slightly prior to this retention time in both the blood and urine; their mass spectra were consistent with one and two demethylations of the compound.

Table 1: Toxicology Laboratory Results

Assay	Case Study #1	Case Study #2
Alcohols and acetone	negative	negative
Alcohols and acetone (vitreous)	negative	negative
ELISA	negative	negative
Acid/neutral drug screen (femoral)	ibuprofen detected	negative
Alkaline drug screen	U-47700 detected	U-47700 detected
Alkaline drug screen (urine)	U-47700 detected oxymetazoline detected demethyldiazepam detected olanzapine detected	U-47700 detected
Alkaline drug quantitation	diazepam: 0.60 ± 0.09 mg/L demethyldiazepam: 0.52 ± 0.07 mg/L	not performed
Benzodiazepines quantitation	oxazepam: 0.076 ± 0.019 mg/L temazepam: 0.108 ± 0.016 mg/L	not performed

Case Study #1: all results are from preserved femoral blood unless otherwise noted.
Case Study #2: all results are from preserved subclavian blood unless otherwise noted.
Uncertainty is reported at a coverage probability of 95.45%.

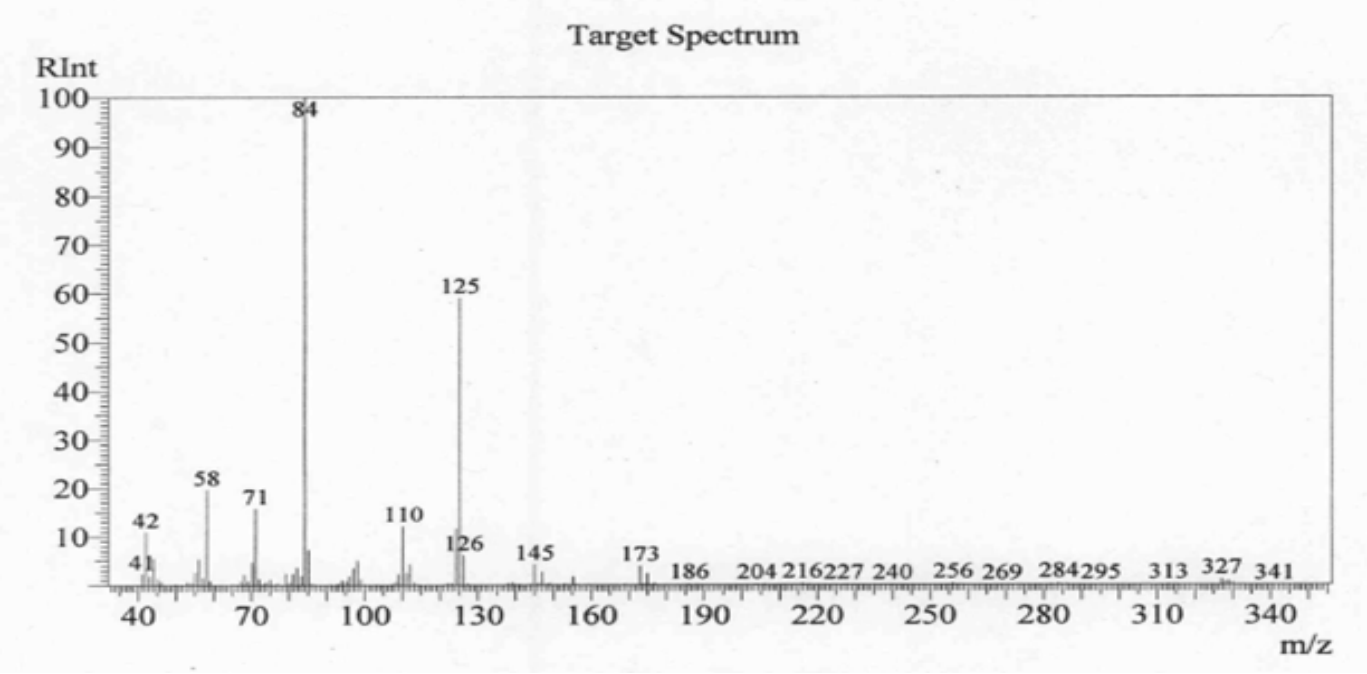

Figure 2: Mass Spectrum of U-47700 from Case Study #2

Two Fatalities Involving the Use of the Synthetic Opioid U-47700 (CONTINUED)

Table 2: Drug Analysis Laboratory Results for Case Study #1		
Exhibit	Weight	Material Contained
White powder (labeled Hh3)	3.0590 ± 0.0038 grams	etizolam
White powder (labeled LW1)	2.4331 ± 0.0038 grams	U-47700
Green round tablet with markings MYLAN477 (23 additional pills with same logo not tested)	0.1574 ± 0.0038 grams	diazepam
Clear liquid contained in a nasal spray bottle labeled Afrin PumpMist	2.3219 ± 0.0038 grams	oxymetazoline

Uncertainty is reported at a coverage probability of 99.73%.

These peaks were present only in the case sample, not a neat or extracted standard. A similar pattern of two primary demethylated metabolites also was reported for AH-7921[3,5].

Results of testing performed by the Drug Analysis Laboratory are presented in Table 2. One of the white powders contained the benzodiazepine etizolam; although this drug can be detected in the toxicology alkaline drug screen, it was not identified in the blood sample tested.

It should be noted that at the time of initial testing of these cases (July and December 2015) there was no commercially available standard for U-47700. The Drug Analysis Laboratory supervisor was able to obtain a copy of the U-47700 mass spectrum from a colleague which allowed us to tentatively report the identification of the drug in the white powder from Case Study #1 and in the blood sample from Case Study #2. This information was not available at the time of the toxicology testing of Case Study #1 and so the identity of the unknown peak in the alkaline drug screen (later identified to be U-47700) was not initially reported. Once the standard was available in late February 2016, the standard was run and the identity of U-47700 confirmed by retention time and mass spectrum. In addition, the urine was run at this later time in both cases.

Currently, Case Study #1 is signed out as a natural death due to hypertensive cardiovascular disease, but this is under review by the medical examiner due to the subsequent identification of the U-47700 peak in the blood and urine. In Case Study #2, the medical examiner ruled that the manner of death was accident and the cause of death was toxic effects of U-47700.

The Belgium Early Warning System on Drugs of the Scientific Institute of Public Health reported in February 2016 that they received information on a fatality involving U-47700 and fentanyl; according to the report, both drugs were found in a white powder (obtained over the internet) and postmortem samples[6]. Morphine-like behavioral effects were observed after administration of U-47700 to male mice; binding assays conducted using the brains of these mice showed U-47700 to be 7.5x more potent than morphine[7]. The drug acts as a strong μ-opioid receptor agonist, with a much lower affinity for the κ receptor[8]. Users report that the drug is short acting and can cause respiratory depression/breathing suppression[9]. As U-47700 is closely structurally related to AH-7921 it could by hypothesized that their effects would be similar. AH-7921 is reported to induce effects similar to traditional opioids including relaxation, mild euphoria, and pruritis[10]. In deaths from AH-7921, pulmonary edema and heavy lungs often were observed[5].

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Midwestern Association of Forensic Scientists' Annual Meeting
October 3-7, 2016

The MAFS 2016 Fall Meeting will be held October 3rd - 7th, 2016 in Branson, Missouri. Hosted by The Missouri State Highway Patrol, the meeting will consist of workshops, break-out sessions, and posters for analysts in Drugs, Toxicology, Trace Evidence, Crime Scene, Biology, Questioned Documents, Latent Prints, and Firearms/Toolmarks.

Hosted by The Missouri State Highway Patrol

Contact: Program Chair Abigail Lehman 573-526-6134 x2529 abigail.lehman@mshp.dps.mo.gov
http://www.mafs.net/news-feeds-1/mafs-2016-meeting

Hilton Branson Convention Center
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FROM THE TOXICOLOGY LITERATURE

Submitted by **Kevin G. Shanks, M.S., D-ABFT-FT**
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AIT Laboratories, Indianapolis, IN

Clinical Toxicology (Philadelphia)
Volume 54, Issue 2
Flubromazolam – A New Life-Threatening Designer Benzodiazepine

Łukasik-Głebocka *et al*. reported the case of a 27 year old male who was found unconscious at home. Upon arrival at the hospital, he was intubated and mechanically ventilated. Clinical chemistry laboratory tests showed leukocytosis, respiratory acidosis, increased serum glucose, increased creatine kinase (15,960 U/L), increased aminotransferase alanine (406 U/L), and increased aspartate aminotransferase (502 U/L). IV fluids were given for hypotension and tachycardia. Ephedrine and naloxone were administered. Norepinephrine was administered via a central port into the subclavian vein. Blood pressure increased to 120/80 mmHg. After a positive benzodiazepine urine screen, flumazenil was administered intravenously. The patient woke up, reacted to pain stimuli, but did not react to voice. He again became unconscious after about 30 minutes. The patient recovered and was extubated after four days. On the ninth day of hospitalization, he was moved for further examination. Toxicological analysis of a serum sample acquired 19 hours post-admission revealed flubromazolam (59 ng/mL). After recovery, the patient admitted to consuming 2 mg of flubromazolam in combination with PCP about 48 hours prior to the incident and an additional 3 mg of flubromazolam about 19 hours prior to the incident.

Journal of Analytical Toxicology
January 2016
Volume 40, Issue 1
Sudden Cardiac Death Following Use of the Synthetic Cannabinoid MDMB-CHMICA

Westin *et al*. reported the death of a 22 year old male after he was found unconscious after smoking a brown synthetic cannabinoid powder. He was in asystole when emergency personnel arrive and transferred by air to the intensive care unit. He was declared dead following day due to brain hypoxia. Anoxic brain damage, pneumonia, and circulatory collapse were noted. Toxicological analysis of a serum sample acquired 2 hours post-admission was positive for MDMB-CHMICA (1.4 ng/mL), mirtazapine (5.3 ng/mL), THC (1.5 ng/mL), and cetirizine (qualitative). Postmortem spleen blood was positive for MDMB-CHMICA (0.1 ng/mL).

Forensic Science International
January 2016
Volume 259
Drug Facilitated Sexual Assault with Lethal Outcome: GHB Intoxication in a Six-Year-Old Girl

Mehling *et al*. reported the case of a 6 year old girl who was sedated with GHB and sexually violated by her uncle over approximately nine months. The perpetrator obtained the GHB as a liquid via the internet and synthesized solid GHB salt from GBL via instructions off the internet. About 9 months into the assaults, the uncle mixed GHB into some spaghetti and apple juice. The child became sedated and unconscious. After four hours and several sexual assaults, she stopped breathing. Toxicological analysis revealed GHB in the cardiac blood (1.5 mg/L), bile (2.92 mg/L), vitreous fluid (5.8 mg/L), liver (100 mg/kg), kidney (125 mg/kg), and brain (110 mg/kg). Cause of death was ruled as GHB intoxication.

Clinical Toxicology
Volume 54, Issue 2
Cardiovascular Toxicity with Levetiracetam Overdose

Page *et al.* reported the case of a 43 year old female who presented to the hospital 8 hours after consuming 60-80 1000 mg tablets of levetiracetam, 20 tablets of 30 mg codeine/500 mg acetaminophen, and ethanol. She was prescribed 1000 mg levetiracetam twice per day for epilepsy. On arrival, heart rate was 45 beats per minute and blood pressure was 86/57 mmHg. She was given atropine and saline and her heart rate and blood pressure increased for a short time before decreasing to 40 beats per minute and 88/62 mmHg. Admission serum ethanol was 0.147 g/dL. At 8 hours post ingestion, acetaminophen was 41mcg/mL. Over the next 1-2 days, she recovered and was discharged (48 hours post ingestion). Heart rate was 60 beats per minute and blood pressure was 142/81 mmHg. Toxicological analysis of the serum sample 8 hours post ingestion was positive for levetiracetam (462.5 mcg/mL).

FROM THE TOXICOLOGY LITERATURE (CONTINUED)

Journal of Analytical Toxicology
March 2016
Volume 40, Issue 2
An Acute Butyr-Fentanyl Fatality: A Case Report with Postmortem Concentrations

McIntyre *et al*. report the case of a 44 year old male who was found unresponsive on the bathroom floor. A syringe with plunger was found in the bathroom and a box with used syringes, foil, residue, etc. was found in the house. The man had a history of heroin abuse and was going to join an experimental drug program for controlled released buprenorphine. Autopsy findings included a recent puncture site on the left antecubital fossa. The right antecubital fossa, forearms, wrists, and ankles showed a history of injection sites and damage. Pulmonary edema and congestion was observed. Aspiration of gastric contents was also noted. Toxicology analysis of the peripheral blood revealed butyr-fentanyl (58 ng/mL), acetyl-fentanyl (38 ng/mL), benzoylecgonine (80 ng/mL), and levamisole (qualitative). The cause and manner of death was determined to be accidental acute butyr-fentanyl, acetyl-fentanyl, and cocaine intoxication.

Forensic Science Library Service — Information Alerts

You are invited to take advantage of a no-cost opportunity to improve awareness of developments and discoveries in the forensic sciences.

Jeff Teitelbaum, of the Washington State Patrol Crime Laboratory, is one of very few professional librarians in the world specializing in forensic science information resources. Services that he offers include:

Tables of Content for all forensic science-related journals
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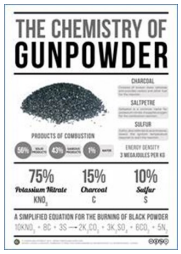
Send an email to Jeff.Teitelbaum@wsp.wa.gov and request to be added to the email list.



DRUGS IN THE NEWS

Send interesting ***"Drugs In The News"*** articles to Section Editor

Laureen Marinetti, Ph.D., F-ABFT,
Lmarinetti@redwoodtoxicology.com

"One person is brain dead and five others are seriously ill after taking part in a drug trial for the Portuguese pharmaceutical firm named Bial at a clinic in north-west France."

Here is an article that caught my attention. The story was first reported in January of this year. This article combines the subsequent stories that have been reported through March with a short discussion at the end to try to clarify some conflicting information.

This clinical trial turned to tragedy when five men, between 28 and 49 years old, were sent to the hospital in Rennes. One was declared brain dead and later died, while the four others suffered neurological disorders. A sixth person was hospitalized as a precaution. The Chief Neuroscientist at the hospital, Professor Gilles Edan, stated that there is no known antidote to the experimental drug they were testing. The drug was designed to act on the body's endocannabinoid system; it was developed by the Portuguese pharmaceutical company Bial to treat anxiety or problems linked to degenerative diseases. Biotrial, a private pharmaceutical group, was chosen to carry out the French trial of the drug. French Health Minister Marisol Touraine told reporters that all those hospitalized were healthy men when the trial began. The French prosecutor's office has opened an investigation into what the Health Ministry is calling a "serious accident during a clinical test" at the Biotrial laboratory in Rennes.

Biotrial released a statement that serious adverse side effects have occurred in one of its trials. The drug had been administered orally (later in another article it was reported that the drug was injected) to six healthy adult volunteers resulting in a serious accident and the patients are now being treated in hospital in France. The tests were conducted in full compliance with the international regulations and that those procedures were followed at every stage of the trial, especially the emergency procedures for transferring the subjects to the hospital.

According to a source close to the case, the drug was a painkiller containing cannabinoids, (this has been disputed by France's Health Ministry which stated that the drug does not contain cannabinoids) an active ingredient found in cannabis plants. The study has been halted and all volunteers taking part recalled. The study was a Phase I clinical trial. It was not clear how many people were taking part in the study.

Later reports from the French Health Ministry stated that they faulted the laboratory in charge of the clinical drug trial for continuing to administer the pharmaceutical to other participants after the first volunteer was hospitalized. In a preliminary report on the clinical trial, the Health Ministry found the lab, Biotrial, failed to swiftly suspend the trial on Jan. 10, when the first person was hospitalized with serious injuries from the drug. Biotrial injected (earlier articles said the drug was given orally) other healthy volunteers a day later with the drug, the report said. Four of those volunteers were subsequently hospitalized with neurological disorders. The ministry said Biotrial could continue carrying out drug trials. "The way the trial was conducted was not the cause of the accident," Biotrial Chief Executive François Peaucelle said in an interview. The French Health Ministry's report did not shed light on the causes behind the volunteer's death. A full report on the incident isn't due to be published until late March.

The trial began on July 9 in the northwestern French city of Rennes. In January, Biotrial began administering the drug at a higher dosage, according to the French Health Ministry. Mr. Peaucelle of Biotrial said the volunteer who eventually died was hospitalized on Jan. 10 with a headache and blurry vision after taking the higher dosage. At 8 a.m. local time the following day, five more volunteers received the same dosage. An hour later, the hospital informed Biotrial that the hospitalized volunteer had been sent for an MRI scan after his condition worsened, Mr. Peaucelle said. Later that day, the volunteer was declared brain dead and the trial was suspended. On Jan. 13, Biotrial began sending the other volunteers to the hospital

DRUGS IN THE NEWS (CONTINUED)

and informed authorities of the situation a day later, according to the ministry and Mr. Peaucelle. Ms. Touraine of the French Health Ministry said the remaining volunteers were now home and their health was improving, but it was too early to determine if they would make a full recovery.

Clinical trials typically have three phases to assess a new drug or device for safety and effectiveness. Phase one entails a small group of volunteers, and focuses only on safety. Phase two and three are progressively larger trials to assess the drug's effectiveness, although safety remains paramount. Human participation in such trials and scrutiny by outside watchdogs are essential for getting market authorization. Every year thousands of volunteers, often students looking to make extra money, take part in such clinical trials that are seen as safe. Mishaps are relatively rare, but in 2006 six men were hospitalized in London after taking part in a clinical trial into a drug developed to fight autoimmune disease and leukemia. In gene therapy, setbacks have included the 1999 death of an 18-year-old US volunteer, Jesse Gelsinger, and the development of cancer among two French children treated for "bubble baby" syndrome, a chronic lack of immune defenses.

Did the drug contain cannabinoids or not? I think not, see the additional information below.

A visit to Bial's website identified the drug in the trial as a f**atty acid amide hydrolase** (FAAH) inhibitor. FAAH is an integral membrane **enzyme** that hydrolyzes the fatty acid amide class of lipid transmitters. According to information posted by Pfizer, FAAH inhibition results in higher intracellular levels of endocannabinoids, such as anandamide and palmitoylethanolamide. In a recent paper related to the function of FAAH related to the endocannabinoid tone, the following remark is important:

Data from the literature, however, caution on a global inhibition of FAAH or other endocannabinoid-metabolizing enzymes in the brain, as it has been demonstrated that endocannabinoids regulate neuronal activity in certain cerebral regions in a selective, subtle manner. (Losonczy et al, 2004; Hentges et al, 2005).

Furthermore, the reported constitutively action of endocannabinoids could be compromised as a result of FAAH inhibition, with unpredictable consequences.

And:

…recent data warn against the prolonged blockade of FAAH in astrocytes. We have tested the influence of the genetic inactivation of FAAH (FAAH-knock outs) on the response of primary cortical mouse astrocytes cultures when exposed to synthetic fibrils of amyloid 1-42 (Benito et al., submitted). As expected, the addition of this peptide to the cells led to profound changes in the cytokine secretion profile, with increases in selected molecules, such as IL1b, IL6, TNFalpha, CCL2 and CCL5. In addition, the expression of several enzymes known to be involved in neuroinflammation, such as COX-2 and iNOS, were also augmented.

Was the drug injected or administered orally? I think this depends upon what type of inhibitor was used. Several FAAH inhibitors have been described, including trifluoromethyl ketones, a-keto heterocycles, sulfonyl fluorides, fluorophosphonates and carbamates. For additional information on FAAH see; Cravatt, B.F. and Lichtman, A.H. Fatty acid amide hydrolase: an emerging therapeutic target in the endocannabinoid system. Current Opinion in Chemical Biology 2003, 7:469–475.

The 22nd IACP Training Conference on Drugs, Alcohol, and Impaired Driving

Registration is now open for the 22nd IACP Training Conference on Drugs, Alcohol, and Impaired Driving in Denver, Colorado from August 13-15, 2016. Every year, the IACP DRE Section hosts the nation's largest gathering of drug recognition experts and other professionals who come together to learn about and discuss the latest developments in the drug recognition field. Register for the conference, view the schedule, and book lodging at www.theiacp.org/DREconference. We look forward to seeing you in Denver.

SOFT 2016 Annual Meeting Update
October 16-21, 2016 in Dallas, TX
Committee Co-Chairs: **Erin Spargo** and **Chris Heartsill**

We are deep in the midst of planning what will surely be a memorable meeting here in Dallas! Our 20+ committee members are hard at work to bring you the best meeting possible. In an effort to make sure you are aware of key dates associated with our meeting, we have compiled a list of "SOFT 2016 Important Dates and Deadlines", located on the Annual Meeting portion of the SOFT website. Be sure to check it out!

One of the upcoming important dates is April 15th, when both on-line registration and the hotel room block open. Registration and workshop fees are unchanged from last year:

Meeting Registration: $499 for members and $675 for non-members
Workshops: $125 for half-day and $200 for full-day for members (non-members pay an additional $50)

The conference will be held at the Dallas Sheraton (www.sheratondallashotel.com), with a room rate of $174/night, which includes complimentary Wi-Fi. Be sure to book early as the room block does tend to fill up.

Our annual meetings are so great because of participation of you, the members. We hope that many of you will become involved through scientific session presentations, attendance at and chairing of workshops, and by volunteering at the meeting itself. Please visit the website to find additional information about each of these areas.

Hope to see y'all in October! *Erin and Chris*

CALL FOR ABSTRACTS, MODERATORS AND REVIEWERS FOR THE SOFT 2016 ANNUAL MEETING IN DALLAS, TX OCTOBER 16-21, 2016

ABSTRACT SUBMISSION DEADLINE IS MAY 2nd, 2016

The SOFT 2016 Scientific Program Committee is requesting abstracts on all topics related to forensic toxicology. The Committee will select appropriate abstracts to be presented as either a 15-minute platform presentation or poster presentation. Please refer to the SOFT website for additional information on abstract requirements and submission (http://www.soft-tox.org/scientific-sessions).

In addition, the Leo Dal Cortivo Memorial Fund is allowing the Young Forensic Toxicologists Committee to present two awards to young forensic toxicologists at the SOFT 2016 Annual Meeting. The best platform presentation and the best poster presentation will be chosen from among the eligible entries, and the presenting author will be awarded a cash stipend of $1000 in addition to a free registration for a future SOFT meeting. The judging takes place from October 19-21, 2016. For eligibility requirements and instructions on how to apply, go to the Young Forensic Toxicologists tab on the SOFT website (www.soft-tox.org/yft).

If you would like to serve as an abstract reviewer or moderate a session at the meeting, please contact the Scientific Program Committee Chairs at SOFTScience2016@gmail.com.

The SOFT 2016 Scientific Program Committee Chairs are:
Sabra Botch-Jones Karen Scott

DRUG FACILITATED CRIME (DFC) COMMITTEE SPECIAL SESSION

The DFC Committee will once again be hosting a platform special session at this year's SOFT meeting. Please submit your cases, methods etc… related to drug facilitated crimes and check off the appropriate category box on the abstract submission form.

Thanks in advance!!!!

Summary of the 68th Annual, American Academy of Forensic Sciences Meeting

Submitted By **Dan Anderson, AAFS** Toxicology Section Chair

We had a wonderful 68th Annual AAFS conference in Las Vegas! A big thanks to Section Program Chairs, Fiona Couper and Nikolas Lemos for their work and dedication. As always a successful meeting would not be possible without our vendors. We want to thank: Aegis, Randox, Agilent, Cerilliant, Immunalysis, Waters, Lipomed, RTI and NMS Labs for their wonderful support of the Toxicology section.

The Toxicology section hosted three workshops and one breakfast: "Advanced Mass Spectrometry (MS) techniques for Forensic Analysis: What does the Future Hold?" chaired by Sherri Kacinko and Kenyon Evans-Nguyen, "Vaping: What you didn't know about Electronic Cigarettes-And why you should care" chaired by Michelle Peace and Justin Poklis, "Diversity and Inclusion at the Forensic Science Workplace" chaired by Nikolas Lemos and Daniel Isenschmid, and "A Primer on the Structure and Activity of the National Institute of Standards and Technology's (NIST's) Organization of Scientific Area Committees (OSAC) chaired by Barry Logan. All three workshops and breakfast were excellent and very well attended. We also want to thank Phil Kemp for his continued contribution to the student academy. There were approximately 100 high school students who were exposed to the different disciplines for the day as they gathered information to "solve a case".

The general scientific session started on Wednesday evening and consisted of 49 poster and 34 oral presentations including a multidisciplinary session with Pathology/ Biology and the annual Postmortem Pediatric Toxicology coordinated by Robert Middleberg and Nikolas Lemos. Thank you to all of the reviewers, moderators, and judges who volunteered their time to make this year's program a success. Congratulations to Melissa Friscia, recipient of the 2016 Best Poster Award and $1,000 prize (supported by RTI) for her poster titled: Development and Validation of a Confirmatory Method for Six Novel Psychoactive Substances (NPS) in Whole Blood Using Ultra Performance Liquid Chromatography/ Tandem mass Spectrometry (UPLC/MS/MS).

The annual Toxicology Luncheon continued its success with the attendance of about 120 participants. During the luncheon Marina Stajic was honored with life presentations from Yale Caplan, Daniel Isenschmid, and Robert Middleberg and Life Facilitator Cathy Tobin presented "Find your Zen" and five techniques for catching your breath and de-stressing. We recognized Mahmoud ElSohly (Alexander O. Gettler Award), Rod McCutcheon (Rolla N. Harger Award), Robert Kronstrand (Ray Abernathy Award), and Erin Spargo (Irvine Sunshine Award At our Toxicology Awardees Reception).

Last but certainly not least, thank you to my good friend, colleague, and mentor, outgoing Section Chair Sarah Kerrigan for all of her hard work and leadership this year and for making this journey a wonderful one. The 2017 AAFS meeting will be in New Orleans. This year's Section Program Chair Nikolas Lemos and Co-Chair Bill Johnson are busy preparing for another terrific program with the meeting theme of "Our Future Reflects Our Past: The Evolution of Forensic Science." Hope to see you there.

SOFT Continuing Education Workshop:
Forensic Toxicology Testimony: How to Effectively Communicate our Science to the Courts
May 23, 2016, Houston, TX

The workshop will provide tools for communicating to the court accurate, clear, and unbiased explanations of how samples are processed and analyzed, the results of any testing performed, and the relevance of their findings based on the scientist's education, training, and knowledge of the scientific literature. Workshop faculty will include both toxicologists and attorneys who will use their experiences in the courtroom to illustrate the topics discussed. The attorneys will discuss basic courtroom etiquette and terminology as well as their expectations for an expert witness. The toxicologists will share their approaches to meeting the needs of the court and communicating complex scientific concepts to non-scientists. The workshop will conclude with a question and answer session where participants can have any remaining questions addressed by the attorneys and/or toxicologists.

Instructors:

Ashraf Mozayani, Ph.D.
Texas Southern University

Richard Alpert, J.D.
Tarrant County District Attorney's Office

Taylor Flood, J.D.
Taylor Flood & Associates, Inc.

Teresa Gray, Ph.D.
Harris County Institute of Forensic Sciences

Training Venue:
Texas Southern University
Barbara Jordon-Mickey Leland School of Public Affairs
Dept. Of Administration of Justice 402 AH
3100 Cleburne Street
Houston, TX 77004

Registration Deadline: **May 9, 2016**

Registration Fee:

SOFT Member:	$80
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Are you a SOFT Member? NO YES

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TOXTALK® **Deadlines** for Contributions:

February 1 for March Issue

May 1 for June Issue

August 1 for September Issue

November 1 for December Issue

Future SOFT Meeting Destinations:

2016:	Dallas, TX	Oct. 16-21st, 2016 — Chris Heartsill/Erin Spargo
2017:	Boca Raton, FL	Sept. 10-15th, 2017 — Ruth Winecker/Dan Anderson
2018:	Minneapolis, MN	Oct. 7-12th, 2018 — Loralie Langman
2019:	San Antonio, TX	Oct. 13-18th, 2019 — Veronica Hargrove/Brad Hall
2020:	San Diego, CA	Sept. 20-25th, 2020 — TBD

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