Happy summer! I hope everyone had a wonderful spring and has lots of grand plans for the warmer weather ahead. And, hopefully, those grand plans include registering for the annual meeting. Registration and the hotel block open on June 21st (a little birthday treat for me!). Beth and your meetings hosts, Dan and Vanessa, are providing updates related to the meeting, so I won’t say too much about it, except for this - Make sure you check out the announcement about the President’s Masquerade Ball; CC did an amazing job in bringing my vision to life. I would love to see many of you lean into the theme with formal attire (think floor length gowns, tuxes, fancy suits) and extravagant masks. Who doesn’t love an excuse to dress up?! We last had a masquerade theme in Phoenix in 2008, and I thought after 15 years it was time to bring it back.

Beyond the annual meeting, I wanted to share with you some highlights of the Board’s activities from the last few months:

We received more than 20 applications for the Diversity Task Force. We worked with Dr. Victor Vandell, Task Force Chair, to finalize appointments and the committee is meeting bimonthly to move forward towards their goal of increasing diversity in our organization, starting with outreach to young scientists.

We did a thorough review of the By-laws and identified areas for update. Keep an eye out in the next issue of ToxTalk for a redline version showing the edits. We will be voting on these changes at the annual business meeting in Denver.

Speaking of the annual business meeting, big news here! To allow more access to committee reports, as well as to stay within the time constraints for the business meeting, committee reports will no longer be given at the annual business meeting. Instead, we are going to hold virtual open meetings twice a year where committee chairs will provide their reports to the membership. With this change, it also negates the need for the Board of Directors to meet at the annual business meeting.

INSIDE THIS ISSUE

PRESIDENT’S MESSAGE .............................................. 1-2
FROM THE EXECUTIVE DIRECTOR’S DESK .............. 2
TREASURER’S REPORT ............................................... 3-4
2023 ANNUAL MEETING UPDATE .............................. 5-15
YFT COMMITTEE .................................................. 16
RTL UPDATE .......................................................... 17
IN MEMORIAM ...................................................... 18
PROFESSIONAL MENTORING PROGRAM ................... 19

AAFS UPDATES AND NEWS ........................................... 21
DRUGS & DRIVING SPECIAL SESSION ...................... 21-24
DFC SNAPSHOT - ALPRAZOLAM ............................... 24-26
FRANKENSTEIN OPIOID ........................................... 27-31
SOFT MEMBERSHIP ............................................... 32
ORAL FLUID DUID CASES - 2023 UPDATE ............... 33-34
VALERYLFENTANYL ................................................. 35-39
SOFT INFORMATION ................................................ 40
Director open sessions at SOFT and AAFS, so only closed session Board meetings will be held.

Also related to committees, the Board has set aside funding specifically for committee work, so we can provide these groups with the resources they need to accomplish their missions.

Lastly, I would be remiss if I didn’t address the untimely passing of SOFT member, annual meeting Exhibitor Liaison, and my friend, Liz Kiely. For those of you that didn’t know her, Liz was a true ray of sunshine. She had a great personality, an infectious laugh, and was simply just really fun to be around. She cared deeply about SOFT and successfully worked hard to get involved in the organization. Her deepest devotion was to her family, particularly her son, Noah. I want to thank each of you that took the time to send in a photo or memory that could be shared with her family. I am sure they truly appreciated it. In honor of Liz and in recognition of her work as the Exhibitor Liaison, I am thrilled to announce that we will be naming the Exhibit Hall after her this year.

Best wishes,
Erin A Spargo

FROM THE EXECUTIVE DIRECTOR’S DESK

BETH OLSON
SOFT EXECUTIVE DIRECTOR

I just returned from the Gaylord Rockies Resort & Convention Center in Denver, where CC and I, along with Meeting Hosts Dan Anderson and Vanessa Beall, AV Coordinator Frank Wallace, and F&B Coordinators Ann Marie Gordon and Denise Teem, met with staff at the hotel to begin the final stages of planning for SOFT’s 2023 Annual Meeting. As we toured the property, I could picture our SOFT attendees everywhere – meeting in the convention center, dining at bars and restaurants, playing lawn games on the grand lawn, keeping warm at the fire pits, hanging out in the (heated!) water park, playing pickleball, and riding bikes (offered free to guests!) around the property. There is even an escape room onsite! This year’s meeting is definitely going to be one to remember.

While meeting planning is ongoing, the SOFT office, Board of Directors, and committees continue to plan throughout the year. Check out the SOFT calendar on the website HERE for webinars, SOFTopics, the SOFT Summer Book Club, committee meetings, and more that will be held over the summer.

In a continued effort to increase engagement in SOFT and improve transparency, members will see more changes in the structure of SOFT committees and their activities.

The Board will be instituting term limits for committee members, and restricting committee participation to one committee per member at a time. There is a plan to roll this out over the next three years, so as to stagger the ending of terms. As you probably already know, committees are utilizing an open application process to branch out possible committee membership to all members of SOFT. Please participate in our virtual open committee meetings, as well. This is a great way to get involved in SOFT! All of those meetings for the year can be found HERE.

I also wanted to take just a moment to remember Liz Kiely. I’m not sure that anyone other than myself and CC knew how much time, energy, and passion that Liz put into her role as Exhibitor Liaison. This year’s meeting planning doesn’t feel the same without her. That being said, I am so glad that I had the opportunity to get to know her over the past six years, and had the pleasure of meeting her mom and Noah for the first time in Cleveland. Like many of you, I miss her both personally and professionally.
First, I would like to say thank you to all SOFT members for placing your trust in me to oversee the financial soundness of SOFT as your new Treasurer. Tate Yeatman, Beth Olson, CC Watson, and all the SOFT Board have been absolutely remarkable in bringing me in on all the financial responsibilities and processes to ensure I am ready to serve. I cannot believe we are already in our second quarter with many meetings and budget reviews behind us!

We are beginning 2023 with some great accomplishments achieved in 2022 with our Treasurer, Tate Yeatman, leading the charge! A recap of 2022 noteworthy accomplishments include: 1) Conversions to a 501c3 which allow us to benefit from significant tax breaks and the opportunity to solicit for tax deductible donations — implemented for our 2023 meeting in Cleveland; 2) Finalized an investment policy — approved by the Board; 3) Selected an investment firm — contract signed; and 4) Completion of the Biennial external auditor, Metz Accounting — no findings were identified.

We hit the ground running and the Treasurer transition is complete; I am now a representative on banking and investments accounts, and I have honed my QuickBooks aptitude. Some additional financial goals we have for 2023 include: 1) Establish investment accounts with new portfolio manager, Fiducient Advisors; 2) Complete quarterly finance reviews and development of 2024 budget; and 3) Investigate a potential donation campaign on the new SOFT website; 4) Review of investment policy after first year of implementation to document needed revisions based on actual processes and findings.

SOFT remains in a strong financial position. As of April 13, 2023, SOFT’s bank account balances totaled $1,544,585. At the interim board meeting held during the AAFS meeting, the board unanimously approved the 2023 budget.

The Finance Committee consisting of myself, Tate Yeatman, Robert Sears, Russell (Rusty) Lewis, Steven Fleming, Chris Heartsill, and Ayana Chan-Hosokawa convened right on schedule. The committee helps provide financial oversight for the organization and provides guidance and recommendations to the Board on financial matters. The committee completed the Q1 Audit and review of the financials through April 30, 2023.

In full transparency to its membership, SOFT provides the approved budget for your review and input annually in ToxTalk. I encourage you to review the included budget spreadsheet which includes budget vs. actuals since 2021 and the approved budget for 2023. If you have any questions, please don’t hesitate to contact me.

Jeri Ropero-Miller

2023 GOALS

1. ESTABLISH INVESTMENT ACCOUNTS WITH NEW PORTFOLIO MANAGER.
2. COMPLETE QUARTERLY FINANCE REVIEWS AND DEVELOPMENT OF 2024 BUDGET.
3. INVESTIGATE A POTENTIAL DONATION CAMPAIGN ON THE NEW SOFT WEBSITE.
4. REVIEW OF INVESTMENT POLICY AFTER FIRST YEAR OF IMPLEMENTATION.
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At the time of writing this update, it’s the middle of May and Colorado’s version of Spring is upon us. The mountain snow is melting, temperatures are rising, and flowers and trees are finally blooming. Spring also means we are about five months from our annual meeting, and we continue to prepare for this exciting event.

At the end of April, we participated in a site visit at the Gaylord of the Rockies Hotel. We were joined by SOFT’s own Beth Olson and CC Watson, Food and Beverage Coordinators Ann Marie Gordon and Denice TeEm, AV Coordinator Frank Wallace, and Volunteer Coordinators Stephanie Olofson and Jenny Beckstrom. The site visit allowed us to gather more information for a continued, successful planning and we can see why the Gaylord of the Rockies Hotel and Convention Center was selected as the venue for the annual meeting. Notably missing from this visit was Exhibitor Liaison, Liz Kiely whose untimely passing was felt by all. Duties of this position were transferred to the SOFT office and Allison Vietenheimer, who participated in this role in the past and has graciously agreed to serve again as the Liaison while on site.

The Workshop Coordinators, Donna Papsun and Lisa Reidy, were successful in soliciting many diverse workshops. Additionally, this year, a new format of all half-day workshops will give attendees several options and flexibility for both Monday and Tuesday. The Scientific Program Coordinators, Luke Rodda and Sara Schreiber, were busy evaluating a new platform for submission and review of abstracts. JAT’s Special Issue Editor, Sandy Bishop-Freeman is working hard to create an issue filled with excellent scientific content. The Karla Moore Memorial Fun Run Coordinator, Aria McCall is working on a creative design for the Fun Run shirt. YFT Coordinator, Marissa Finkelstein is working with her committee to prepare a successful Sunday evening event, and the Student Enrichment Program (SEP) to include local high school students. The mobile application folks, Rusty Lewis, Roxane Ritter, and Sunday Hickerson, have also successfully evaluated a new mobile platform for the Denver meeting.

We are very excited to see the program come together. One last piece of exciting news. We are pleased to offer something new to the SOFT attendees—puppies! During lunch on both Wednesday and Thursday in the exhibit hall area, Lifeline Puppy Rescue will offer “puppy playtime” where attendees can interact with the puppies and enjoy some downtime.

Overall, planning has ramped up and we are looking forward to a successful annual meeting. Please start making your plans to attend. We look forward to seeing you soon in Denver, CO. Thank you!

See the next page for important information regarding SOFT 2023.

Dan and Vanessa
President Spargo's
MASQUERADE BALL
Enjoy an Evening with Dinner, Dancing and Masquerading!
Formal Attire and Masquerade Masks are Requested

NOV 2 2023
GAYLORD ROCKIES RESORT
DENVER, CO
Thu 7:00 PM

Soft 2023
What to expect at the Masquerade Ball

Attendees may bring their own mask or use one provided by SOFT. You are encouraged to be fancy with your mask and attire!
ANNUAL MEETING UPDATE - DENVER, CO

REGISTRATION
Registration Opens June 21
Late Registration Begins: September 1
Onsite Registration Begins: October 11
Download the 2023 Rate Sheet Here!

2023 HOSTS

DAN ANDERSON
SCIENTIFIC PROGRAM COORDINATORS
LUKE RODDA
SARA SCHREIBER

WORKSHOP COORDINATOR
DONNA PAPSUN
LISA REIDY

VOLUNTEER COORDINATOR
STEPHANIE OLOFSON
JENNIFER BECKSTORM

SOCIAL COORDINATOR
DENICE TEEM

FUN RUN COORDINATOR
ARIA MCCALL

JAT SPECIAL ISSUE EDITOR
SANDRA BISHOP-FREEMAN

MOBILE APP
RUSTY LEWIS
ROXANE RITTER
SUNDAY HICKERSON

AV COORDINATOR
FRANK WALLACE

FOOD & BEVERAGE
ANN MARIE GORDON
DENICE TEEM
DELISA DOWNEY

YOUNG FORENSIC TOXICOLOGISTS
MARISSA FINKELSTEIN

ELMER GORDON FORUM COORDINATOR
DANI MATA

INTERIM EXHIBITOR COORDINATOR
ALLISON VIETENHEIMER

EXHIBITOR LIAISON (2018-2023)
THE LATE LIZ KIELY

REGISTRATION FEES

<table>
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<tr>
<th></th>
<th>Early Bird (June 1 - Aug 31)</th>
<th>Late (Begins Sept 1)</th>
<th>Onsite (Begins Oct 11)</th>
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REGISTRATION INCLUSIONS

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<th>Breakfasts &amp; Refreshment Breaks (W,Th,F)</th>
<th>Lunch (W,Th)</th>
<th>Social Events (T,W,TH)</th>
<th>Abstract/Program Book</th>
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Download the 2023 Rate Sheet Here!

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Download the 2023 Rate Sheet Here!
SCIENTIFIC PROGRAM

DEADLINES
Final Decision and Schedule to Authors: July 31
Presentations Due: October 2

Abstract submissions for SOFT 2023 closed on June 8. Scientific Program Coordinators will begin their review and final decisions will be sent on July 31. Platform and Poster Presentations will be held Wednesday, November 1 through Friday, November 3, 2023, in Denver, CO at the Gaylord Rockies Resort & Convention Center.

QUESTIONS?

SCIENTIFIC PROGRAM COORDINATORS

LUKE RODDA  SARA SCHREIBER

WORKSHOPS

We are happy to announce that Workshop Program Coordinators, Donna Papsun and Lisa Reidy have selected 16 workshops for SOFT 2023. Workshops are offered on Monday, October 30 and Tuesday, October 31 from 8:00 am - 5:30 pm.

This year’s program is focusing on half-day workshops or full days divided into two parts: for example, beginner knowledge in the morning and advanced concepts in the afternoon. We hope attendees will be able to find more flexibility with additional workshop options.

2023 WORKSHOP RATES
Early Bird (June 21 - Aug 31)
Member: $150, Non-Member $200
Late (Begins Sept 1)
Member: $175, Non-Member $225
Onsite (Begins Oct 11)
Member: $200, Non-member $250

DEADLINES
Presentations and Handouts Due to Coordinators: September 29
Handouts Provided to Registrants: October 16

2023 HOSTS

DAN ANDERSON  VANESSA BEALL

SCIENTIFIC PROGRAM COORDINATORS
LUKE RODDA
SARA SCHREIBER

WORKSHOP COORDINATOR
DONNA PAPSUN
LISA REIDY

VOLUNTEER COORDINATOR
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INTERIM EXHIBITOR COORDINATOR
ALLISON VIETENHEIMER

EXHIBITOR LIAISON (2018-2023)
THE LATE LIZ KIELY

2023 PLANNING COMMITTEE MEMBERS

OCTOBER 29–NOVEMBER 3, 2023
### Monday, October 30
#### AM Workshops, 8:00 AM - 12:00 PM

**Workshop 1:** Pharmacology, Detection, and Control Actions of Synthetic Drugs  
Chairs: Jonna Berry/Joe Kahl  
Audience Knowledge: Intermediate

**Workshop 2:** The Human Brain and Factors Affecting the Neurobiological Development from Adolescent to Adulthood Exploring the Intersection of Mental Illness, Addiction, and the role of Laboratory Science  
Chairs: Michael Wagner/Tom Kupiec  
Audience Knowledge: Intermediate

**Workshop 3:** QTOF 101: A Guide to Successful Development and Validation (Part I)  
Chairs: Kaitlyn Palmquist/Christina R. Smith  
Audience Knowledge: Basic/Intermediate

**Workshop 4:** Pediatric Toxicology Part I: From Bottle to Backpack - Introduction to Pediatric Toxicology (Part I)  
Chairs: Jennifer Swatek/Kari Midthun  
Audience Knowledge: Basic

### Monday, October 30
#### PM Workshops, 1:30-5:00 PM

**Workshop 5:** Lessons Learned from Implementing QTOF Analysis into Routine Workflow (Part II)  
Chairs: Dani Mata/Brittney Casey  
Audience Knowledge: Basic/Intermediate

**Workshop 6:** Pediatric Toxicology Part II: From Bassinet to Body Bag - Postmortem Challenges and Considerations in the Investigative Process (Part II)  
Chairs: Jennifer Swatek/Kari Midthun  
Audience Knowledge: Basic

**Workshop 7:** Cannabis Testimony in Today’s Environment  
Chairs: Jennifer Limoges/Stephanie Olofson  
Audience Knowledge: Intermediate

**Workshop 8:** beMUsed by Measurement Uncertainty? Let’s Talk  
Chairs: Sue Pearring/Dustin Yeatman  
Audience Knowledge: Basic

### Tuesday, October 31
#### AM Workshops, 8:00 AM - 12:00 PM

**Workshop 9:** Win. Lose or Withdrawal: The Pharmacology, Management, and Interpretation of Drug Withdrawal  
Chairs: Aaron Shapiro/Nathalie Desrosiers  
Audience Knowledge: Advanced

**Workshop 10:** “Steady as She Goes”: Mastering Stability in Forensic Toxicology  
Chairs: Karen Scott/Lorna Nisbet  
Audience Knowledge: Intermediate

**Workshop 11:** Forensic Interpretation of Novel Psychoactive Substances in Challenging Cases  
Chairs: Alex Krotulski/Dani Mata  
Audience Knowledge: Intermediate

**Workshop 12:** Drug-Facilitated Crimes (DFC) Analytical Methods and Statistics (Part I)  
Chairs: Laureen Marinetti/Celeste Wareing  
Audience Knowledge: Basic

### Tuesday, October 31
#### PM Workshops, 1:30-5:00 PM

**Workshop 13:** Drug-Facilitated Crimes (DFC) Case Presentations (Part II)  
Chairs: Laureen Marinetti/Celeste Wareing  
Audience Knowledge: Basic

**Workshop 14:** Principles of Lean Six Sigma and Their Application to Forensic Toxicology Laboratories  
Chairs: Marissa Finkelstein/Joe Kahl  
Audience Knowledge: Basic

**Workshop 15:** Oral Fluid Testing: An Automatic Answer?  
Chairs: Robert Lockwood/Kristin Tidwell  
Audience Knowledge: Intermediate

**Workshop 16:** Career Development and Leadership Techniques for the Forensic Toxicologist  
Chairs: Kristen Kahl/Erin Strickland  
Audience Knowledge: Basic

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**2023 WORKSHOP TITLES**

The following workshops are offered in two parts, a morning workshop (Part I) and an afternoon workshop (Part II) on a related topic. Participants can register for Part I or Part II or both Part I and Part II.

- Workshops 3 & 5
- Workshops 4 & 6
- Workshops 12 & 13

**VIEW THE 2023 WORKSHOP SCHEDULE, ABSTRACTS, AND REGISTRATION RATES HERE!**
2023 HOSTS

DAN ANDERSON    VANESSA BEALL
SCIENTIFIC PROGRAM COORDINATORS
LUKE RODDA
SARA SCHREIBER

WORKSHOP COORDINATOR
DONNA PAPSUN
LISA REIDY

VOLUNTEER COORDINATOR
STEPHANIE OLOFSON
JENNIFER BECKSTORM

SOCIAL COORDINATOR
DENICE TEEM

FUN RUN COORDINATOR
ARIA MCCALL

JAT SPECIAL ISSUE EDITOR
SANDRA BISHOP-FREEMAN

MOBILE APP
RUSTY LEWIS
ROXANE RITTER
SUNDAY HICKERSON

AV COORDINATOR
FRANK WALLACE

FOOD & BEVERAGE
ANN MARIE GORDON
DENICE TEEM
DELISA DOWNEY

YOUNG FORENSIC TOXICOLOGISTS
MARISSA FINKELSTEIN

ELMER GORDON FORUM COORDINATOR
DANI MATA

INTERIM EXHIBITOR COORDINATOR
ALLISON VIETENHEIMER

EXHIBITOR LIAISON (2018-2023)
THE LATE LIZ KIELY

HOTEL
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6700 N Gaylord Rockies Blvd
Aurora, CO 80019
Room Block Opens June 21!
Room Rate: $239

2023 PLANNING COMMITTEE MEMBERS
ANNUAL MEETING UPDATE - DENVER, CO

PAGE 11

OCTOBER 29–NOVEMBER 3, 2023
ELMER GORDON FORUM

We are excited to announce that the SOFTopics Team will take up the mantle of moderating the Elmer Gordon Forum! As the Team has experience moderating discussions throughout the year on a variety of forensic toxicology topics, they are the perfect fit to assume this role at the upcoming meeting. Please see below for an announcement from the SOFTopics Team.

- Erin Spargo

SOFTopics and the Elmer Gordon Forum are teaming up this year at the 2023 SOFT Meeting in Denver, CO! Join us on Tuesday night after walking through the Welcome Reception and meet some of the people you’ve gotten to know over our virtual discussions. Check the app or program for exact time and location.

Like previous years, don’t be shy in asking your fellow toxicologists in the room your burning questions or feel free to share interesting observations from your laboratory. A slight change to the format will be instituted this year by taking your suggestions for topics and/or questions you’d like to submit for discussion during the forum. Please submit your topic or question below. We look forward to seeing you in Denver!

With this transition, we want to give a BIG thank you to Chip Walls and his various co-moderators from over the years for all their hard work with the Elmer Gordon Forum. We are deeply appreciative of all you did to make this a meaningful and beneficial event for SOFT attendees.

The SOFTopics Team,
Dani Mata
Vanesssa Meneses
Alanna de Korompay

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The SOFTopics Team,
Dani Mata
Vanesssa Meneses
Alanna de Korompay
IMPORTANT DATES & DEADLINES

- Registration and Room Block Open: June 21
- Late Registration Begins: September 1
- ToxTalk Publication: September 8
- Onsite Registration Begins: October 11
- SOFT 2023: October 29 – November 3, 2023

EXHIBITING

Interested in exhibiting at SOFT 2023? We still have room in the SOFT 2023 Exhibit Hall!

We invite you to join us for SOFT 2023 in Denver, CO from October 29 - November 3, 2023! Please review the 2023 Prospectus for pricing and sponsorship opportunities. We look forward to seeing you and your team in Denver, CO.

QUESTIONS?

Booths reservations for SOFT are still being accepted. Reserve your space today!

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- 41,730 sq Feet of Exhibit Hall Space
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2023 HOSTS

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SCIENTIFIC PROGRAM COORDINATORS
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WORKSHOP COORDINATOR
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EXHIBITOR LIAISON (2018-2023)
THE LATE LIZ KIELY

2023 PLANNING COMMITTEE MEMBERS

2023 PROSPECTUS

BOOTHS RESERVATIONS FOR SOFT ARE STILL BEING ACCEPTED. RESERVE YOUR SPACE TODAY!
Thank you to our 2023 Sponsors, we appreciate your support of SOFT!

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Pure Chromatography
The original Tox ‘N Purge run was created by Dr. Karla Moore in 1997 for the Salt Lake City meeting. In addition to her involvement in the field of toxicology and participation in SOFT, she was an officer in the United States Air Force.

After her passing in 2008, the run was memorialized in her honor. The proceeds from the run are donated to the American Cancer Society in Dr. Moore’s memory and expenses for the event are supported by our SOFT exhibitors. Please help us thank them for their support of Dr. Moore’s vision!

2023 Fun Run Coordinator
Aria McCall
Hello fellow SOFT members!

The Young Forensic Toxicologist committee is hard at work preparing for the SOFT annual meeting in Denver!

We are excited to announce that one of last year’s award winners, Joseph Kahl (Poster), will be at the YFT Symposium on Sunday, October 29, to update us on what he has been working on. The symposium will also include a panel discussion about different forensic toxicology careers.

The webinar we co-hosted with the Membership Committee in February titled “How to Promote Yourself in SOFT and in Your Career” was well received with a great turn out! We look forward to putting together more webinars and workshops to help young toxicologists as they are beginning their journey into this field. If anyone has a topic they would like covered during a webinar, do not hesitate to reach out by emailing us at YFT@soft-tox.org We are always open to suggestions!

We want to thank everyone who attended our open meeting in May and appreciate the continued support from this community.

Look for more details about YFT events in the next issue of ToxTalk!

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**YFT 2023 PROGRAM SUMMARY**

**Symposium and Professional Development Fair (PDF)**
*Sunday, October 29, 4:30-9:00 PM*

The symposium is an opportunity for younger toxicologists to come together for a night of professional networking. Attendees must be 41 years of age or under to participate in the Symposium. Drinks and hors d’oeuvres are provided to attendees.

For the PDF, representatives from various accreditation/certifying agencies, graduate programs and laboratories will be available to discuss continuing education, professional training, board certification, academic and career opportunities including scientific writing.

**Student Enrichment Program (SEP)**
*Monday, October 30, 8:00 AM – 5:00 PM*

A day-long program focused on introducing high school students to the world of Forensic Toxicology. Lunch will be provided to participating students. Local high school students are eligible to participate with an accepted application. Please check back for the application!

**Leo Dal Cortivo Award**
*Thursday, November 2*

The winners of the SOFT 2023 Leo Dal Cortivo Best Poster Award and Best Platform Presentation Award will be presented at the President’s Banquet on Thursday, November 2, 2023.
For the last few months, the RTLs have planned and scheduled free testimony training for the laboratories in NHTSA regions 5, 7, and 9. As of this update, seven training events are on the calendar, with a few more in the scheduling phase. The RTLs are working to combine as many labs into one training as possible to maximize everyone’s time and expertise. The training is completely customizable and some of the topics include:

- ASB Best Practice Recommendations 037 Guidelines for Opinions and Testimony in Forensic Toxicology
- Drug Evaluation and Classification Program (DRE)
- Alcohol and Drug Pharmacology
- Toxicology-Poly Drug Use
- Challenging Drug(s) Cases
- Testifying to Impairment
- Case Approaches for Direct and Redirect Questions

The training will incorporate local representatives from the courts and DREs. Most trainings are scheduled for one day; however, a few have requested more time. Again, the training is customizable to your laboratory’s needs. The training is approved by ABFT for continuing education credits. If you are in NHTSA regions 5, 7, or 9, please contact your RTL for more information. If your laboratory is outside the NHTSA regions currently covered by the RTL program, please contact the Project Manager, Amy Miles, to discuss further.

The next training the RTLs will create will be focused on method development and validation. Stay tuned for announcements as the curriculum is developed. If you have any suggestions for a training topic you would like to see, please contact the RTLs or Project Manager Amy Miles.

In addition to planning testimony training, the RTLs have continued the laboratory visits and attended highway safety meetings and working groups. NHTSA has contracted with ToXcel (http://toxcel.com/) to hold statewide toxicology meetings, and RTLs Sabra Jones (region 5) and Chris Heartsill (region 7) were involved in the meetings held in Wisconsin and Kansas. Both meetings allowed toxicology laboratories, State Highway Safety Offices (SHSO), Traffic Safety Resource Prosecutors, DREs, and other partners to learn more about their forensic toxicology laboratories. Outcomes from those meetings have produced better communication amongst attendees and partners and a path to create a more sustainable future and comprehensive testing outlook for the laboratories. Several other states have been selected for the statewide toxicology meetings and are in the planning stages. If you are wondering if your state is one of them, reach out to the RTLs or your SHSO for more information.

Amy Miles, Project Manager
amy.miles@slh.wisc.edu

Sabra Jones, Region 5
sabra@soft-tox.org

Chris Heartsill, Region 7
chris@soft-tox.org

Kristen Burke, Region 9
kristen@soft-tox.org
The SOFT family experienced a great loss when Liz Kiely unexpectedly passed away on February 21st. Liz began working in Toxicology in 2002 upon her graduation from Eastern Kentucky University’s Forensic Science program. Not only was Liz a valued member of the Montgomery County Coroner’s Office and Crime Lab, but of the entire forensic science community.

Liz was a member of the Society of Forensic Toxicologists (SOFT). In addition to serving on several SOFT committees through the years, she was currently serving as their exhibitor liaison. She was also a member of the Midwest Association for Toxicology and Therapeutic Drug Monitoring (MATT) where she served as the annual meeting co-chair (twice!) and their treasurer for eight years.

Over her career, Liz published and presented numerous papers and case studies on a range of topics including Topiramate Toxicity, Analysis of Opiates in Hair, Drug-Facilitated Sexual Assault Cases Involving Lorazepam and Oxycodone, Oral Ingestion of Methamphetamine, and Fentanyl, Acetylfentanyl, and Carfentanil in Impaired Driving Cases.

Liz actively facilitated process mapping to uncover inefficiencies in processes and assisted in determining and implementing solutions to those hindrances. She thrived in this task and helped several disciplines in multiple agencies reduce turnaround time as a result.

Those that worked with her daily will remember Liz as she rolled into work each day late, just knowing that it was Liz- and she would be late! And volunteering with the Board of Elections for every election, rain, sleet, and snow. And chatting with her in the elevator about how her frozen lunch smelled wonderful but would not taste that way. And her books….and books….and books….

Liz is survived by her mom, brother, and son, Noah. Words cannot express how saddened we are by her passing. We will continue to keep her family in our thoughts and prayers, and her memory alive. We hope that with any luck, one day, Noah will become a scientist like his Mom!

If you would like to support Noah's 529 College savings plan in honor of his Mom, you can make a donation using this link: https://gifting-529.accessportals.com/contribute/XNPCO

-Montgomery County Coroner’s Office Toxicology Family
Leadership in Action

In March, participants in the Mentoring Program took part in a webinar that explored a TED Talk by Scott Schwefel: Your Personality and Your Brain and then discussed which color(s) we felt most aptly described our personality. This exercise uses the DISC (dominance, influence, steadiness and compliance) assessment tool and builds from the foundational work of William Marston’s book Emotions of Normal People (1928), where these personality quadrants are represented by colors.

During our group discussions, we shared our assessed color(s) and explored how these colors/personality-types are perceived (good and bad) and then discussed how understanding how we are perceived and how we communicate with peers or family of similar or different personalities can help how we show up and lead. The graphic above illustrates how each personality type may take on roles and make contributions and the graphic below provides a glimpse into these same traits when we are at our best and how we may behave when overwhelmed or stressed.

Below is an activity that a committee member created to incorporate this topic as a team building exercise in their agency. We encourage you to use this as a blueprint for a “leadership in action” exercise at your workplace.

**Goal:** To have staff think about their communication style of how they receive and give information to their co-workers. You can also have individuals watch the Ted Talk and discuss along with the color wheels. The charts are a great visual to relate to communication styles as well as show some of the assets a color energy may bring to a teamwork approach.

**Example email to staff:** We will take the first 10-15 minutes of our next staff meeting to do an activity on communicate styles. Review the charts prior to the meeting and think about the following questions:

- What color do you most relate to?
- How can that color be perceived by others?
- How could knowing a person’s color energy help improve communication?
- What types of improvements can be made with how you communicate based on this exercise?

As in life, one tool alone is not likely to get the desired outcome. This type of assessment can certainly promote self-awareness, improve collaboration, and strengthen emotional intelligence, but it should be used to support a multifaceted approach to being an integral part of and building high performing teams. As further discussed in Pierre and Gigliotti (2021), human behavior and thus relationships, are complex and certainly context specific. These innate personality and leadership assessment tools are valuable but have their limitations; as a result, attention should be exercised to limit oversimplification of personal traits that could negatively bias an individual’s perceived behavior that extends to their leadership potential. As with all great experimentation, data derived from multiple sources, over time and in context, drives the most meaningful discoveries.

**References**


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* Tube Size - 10ML
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* Closure - Rubber
* Closure Color - Gray
* Additive Concentration
  Sodium Fluoride - 100mg
  Potassium Oxalate - 20mg
First, on behalf of the AAFS Toxicology Section, I would like to thank everyone who joined us in Orlando for an incredible meeting! It was nice to have everyone in-person, and we look forward to seeing you all next year in Denver. We like to extend a big thank you to all of the sponsors who supported our receptions, and of course, tons of appreciation for our workshop chairs, presenters, program chairs, moderators, abstract reviewers, and everyone who helped facilitate the outstanding meeting – we couldn’t have done it without you!

We have an exciting year ahead, so I wanted to get things rolling. As Section Chair, I am pleased to announce that Toxicology Section leadership will include Diane Moore (Secretary), Dayong Lee (Program Chair), and Erin Karschner (Program Co-Chair). While we await scientific program deadlines, now is the time to get your workshop proposals and abstract ideas together. If you are thinking of a workshop, please reach out to Dayong Lee (dlee@hfsctx.gov) to let us know your plans. We would also like to start gathering abstract reviewers now. If you are willing to help out (and get service that counts towards your membership promotion application), then please email Dayong to serve as an abstract reviewer (dlee@hfsctx.gov).

Now is also a great time to think about nominating some of our colleagues for AAFS Toxicology Section awards and scholarships. Nominations and supporting documents are due August 1, 2023 to the Awards & Scholarships Committee Chair Jennifer Colby (jennifermcolby@outlook.com). A full list of awards and descriptions are linked here.

Are you thinking about promoting your membership status or applying to become a member? AAFS membership is a great way to serve on committees, network, join mentor-ship programs, apply for grants/scholarships/awards, and serve on Toxicology Section Leadership. You can read about our membership categories and promotion requirements here. If you are looking to promote, there are Academy and Section requirements which include attendance at business meetings, conference attendance, and service to the field. Some ways to advance within the Section for promotion include presenting abstracts, moderating, serving as a workshop presenter or an abstract reviewer, etc.

Stay tuned for more information on the 76th Annual AAFS meeting in Denver, CO, February 19-24, 2024 themed “Justice for All”!

Submitted by: Jennifer Limoges, MS and Tim Rohrig, PhD

The SOFT/AAFS Drugs and Driving Committee sponsored a special session during the 2023 AAFS Meeting in Orlando, FL. Highlights of the presentations prepared by the authors are included below. The email address is listed for the author that can be contacted if there are additional questions or requests for more information.

**Acute Psychotic Episodes in Impaired Driving Cases Involving Tetrahydrocannabinols (Δ8 and Δ9)**

Nicholas Tiscione*, Palm Beach County Sheriff’s Office, West Palm Beach, FL

TiscioneN@pbso.org

- In the majority of impaired driving cases involving cannabis, characteristic impairment is observed such as impaired ability to perform divided attention tasks, impaired memory, poor dexterity, eyelid tremors, impaired balance, and sedation.
Recently there has been an influx of atypical acute psychotic episodes involving cannabinoids including delusions and visual disturbances.

Two impaired driving cases, one involving Δ8 and one Δ9, were presented in detail.

Three additional cases involving psychosis with Δ9, one impaired driving and two suspected homicides, have also been observed in Palm Beach County, FL.

Common themes in these cases seem to involve “speaking in tongues”, other spiritual themes, delusions, and chemical restraint utilized (with ketamine) to avoid injury to the subject and first responders.

Drug Testing and Traffic Safety: What You Need to Know

Amy Berning, MA, PhD*, National Highway Traffic Safety Administration, Fairfax, VA; Ryan Smith, PhD, National Transportation Safety Board, Washington, DC; Kathryn Wochinger, United States Department of Transportation/National Highway Traffic Safety Administration, Washington, DC; Morgan Drexler, MPH, American Medical Group Association, Arlington, VA

Amy.Berning@dot.gov

- The National Highway Traffic Safety Administration’s (NHTSA) Fatality Analysis Reporting System (FARS) is a national census of fatal crashes in the United States. A crash must include a motor vehicle that was traveling on a public road, and at least one person died within 30 days as a result of the crash. This data is a cornerstone of NHTSA’s data collection systems and is relied upon by Federal and State agencies, legislators, advocacy groups, and researchers to provide key data about crashes across all road user types. Data on alcohol-impaired driving has been a foundation for national- and State-level planning, research, and policy making for decades.

- Collecting data on drug-positive road users is far more complicated than for alcohol and procedures are still evolving. This discussion presented limitations with the drug data, including information on toxicology drug testing and reporting to FARS.

- Whereas for other research areas with missing or incomplete data, there is often a skew in one direction and estimates may still be useful. This is not the case with FARS drug data. Some of the issues illustrate how statistical analyses using drug prevalence results lead to underestimates (such as limited drug test panels and drugs not being detected when they really are present) and, conversely, other issues that may lead to overestimates – such as using results from drugs screening tests, which may contain false positive results.

- These limitations constrain interpretation of the drug data, including examining trends across years, or comparing States. NHTSA is working on efforts to improve the quantity and quality of the data.

https://rosap.ntl.bts.gov/view/dot/60969

1,1-Difluoroethane in Driving Under the Influence (DUI) Cases: A Comparison of Interference Data on the Intoximeter® DMT and Draeger Alcotest 7110 Versus Toxicology Blood Results

Jasmine Maxwell, MSFS*, Greg Turner, PhD, Curt Harper, PhD, Alabama Department of Forensic Sciences, Hoover, AL

jasmine.maxwell@adfs.alabama.gov

- DFE has an IR response on the Draeger 7110 and Intoximeter DMT Dual Sensor that causes an interference-
ence error
- The DMT is more sensitive to interfering substances due to the nature of the detector (≈3.4µ wavelength, C-H region)
- DFE remains prevalent in Alabama casework with 16 DUI DFE cases and 24 DFE death cases between 2019-2022
- Officers should ask if the subject is diabetic (ketoacidosis) or abused inhalants (DustOff, spray paint, gasoline) when an interference message occurs
- Officers should be encouraged to collect blood in a timely fashion and denote on submission form inhalant case

A Standardized Method for Analyzing Toxicology Data in Drugged Driving Research

Ryan Smith, PhD*, Mary Pat McKay, MD, MPH, Jana Price, PhD, National Transportation Safety Board, Washington, DC
ryan.smith@ntsb.gov

- The NTSB recently completed a safety research report on Alcohol, Other Drug, and Multiple Drug Use Among Drivers
- The report addressed significant gaps with common drug data and analysis approaches
- A standardized approach to analyzing toxicology data was developed and applied to toxicology data from four prominent laboratories
- Results indicated approximately half of drivers arrested for impaired driving had more than one category of drug in their system
- Alcohol was the most commonly detected drug followed by cannabis
- Alcohol was most commonly detected on its own; whereas cannabis was most commonly detected in combination with alcohol and/or other drugs
- NTSB made several new safety recommendations to promote ANSI/ASB Standard 120 and the necessary resources to help labs meet this standard

Impaired Driving Drug Trends and Stop Limit Testing Evaluation

Grace Cieri, BS*, Amanda Mohr, MS, Melissa Fogarty, MSFS, Barry Logan, PhD, The Center for Forensic Science Research and Education, Willow Grove, PA
grace.cieri@cfsre.org

- THC (48.8%), Methamphetamine (15.5%), fentanyl (13.8%), and amphetamine (13.8%), were the most common Tier I drugs detected (n=2,514).
- The most common poly drug combination detected was ethanol and THC together in 359 cases.
- Some of the most frequently seen NPS were 8-aminoclonazolam (3.2%), fluorofentanyl (2.8%) and etizolam (1.8%).
  - Novel benzodiazepines, in particular 8-aminoclonazolam, was seen with almost equivalent frequency to traditional benzodiazepines like alprazolam (3.5%).
- 19% of samples at or above the most common stop limit testing threshold, 0.10 g/100 mL, contain a Tier I and/or Tier II drug.
- The NSC-ADID's recommendations for Tier I and Tier II drugs are supported with the most frequently detected drugs captured in Tier I.
α-Pyrrolidinoisohexanophenone (α-PiHP) in Driving Under the Influence (DUI) Cases

Kristin Kahl, MS*, University of Miami Toxicology Laboratory, Miami, FL; Lisa Reidy, PhD, University of Miami, Miami, FL

kwkahl@miami.edu

- Synthetic cathinones, which are classed as central nervous system stimulants, have been reported in human performance toxicology cases in Miami-Dade and Broward Counties, Florida over the past several years.
- A current trend is the detection of α-Pyrrolidinoisohexanophenone (α-PiHP) in DUI in cases from Broward County, FL, but none have yet to be reported in Miami-Dade County, FL.
- α-PiHP was detected in 2% of the Broward County, FL DUI cases that underwent drug testing, from suspects who were between 26-35 years of age and were predominately male.
- α-PiHP was the only drug detected in 1 case, but in all other cases α-PiHP was detected with other drugs, including cannabinoids, novel benzodiazepines, opioids, and cocaine.
- Minimal pharmacological information is known about α-PiHP, and human performance observations should always be used in conjunction with toxicological results.

Drug Facilitated Crime Snapshot - Alprazolam

By Joseph J. Saady, Ph.D., F-ABFT for the SOFT DFC Committee

SOFT-DFC Snapshots are short reports of critical information about the more common drugs associated with drug-facilitated crimes (DFCs). They are not complete literature reviews about the drug or drug class. One key aspect is their focus on the ability to detect a drug after a single-dose administration, as is often the situation in DFC investigations. As such, these summaries also point out instances in which available data is limited, hoping this will encourage further research studies. Finally, SOFT-DFC Snapshots point to the use of these drugs in actual DFC cases, as cited in the medical and open literature.

Alprazolam is a triazolo analog of the 1,4-benzodiazepine class of central nervous system depressant compounds. The chemical name is 8-chloro-1-methyl-6-phenyl-4H-s-triazolo [4,3-α] [1,4] benzodiazepine. The drug is widely prescribed in the United States, ranging from 30 million prescriptions (2014) to 16.7 million in 2020.¹ A recent global study² found alprazolam to be the third most reported drug in Drug Facilitated Crime cases.

Drug Class: Benzodiazepines

Generic Name: Alprazolam

Brand Name(s): Xanax®, Xanax XR®, Niravam®

Dosage Forms: Oral concentrate (1 mg/mL); oral tablet (0.25 mg; 0.5 mg; 1 mg; 2 mg); oral tablet, disintegrating (0.25 mg; 0.5 mg; 1 mg; 2 mg); oral tablet, extended-release (0.5 mg; 1 mg; 2 mg; 3 mg)

FDA Approval: Alprazolam can be prescribed to treat anxiety disorders and panic disorder (sudden, unexpected attacks of extreme fear and worry about these attacks). It works by decreasing abnormal excitement in the brain.

Metabolism/Elimination: Alprazolam is extensively metabolized in humans, primarily by cytochrome P450 3A4 (CYP3A4), to two major metabolites in the plasma: 4-hydroxy alprazolam and α-hydroxyalprazolam. The pharmacologically active
metabolites have half-lives like alprazolam of approx. 12 hrs. (range 6-27 hr.). Compared to the parent alprazolam concentrations, the plasma concentrations of 4-hydroxy alprazolam and α-hydroxyalprazolam were consistently less than 4%. The reported relative potencies in benzodiazepine receptor binding experiments and animal models of induced seizure inhibition are 0.20 and 0.66, respectively, for 4-hydroxy alprazolam and α-hydroxyalprazolam. Such low concentrations and the lesser potencies of 4-hydroxyalprazolam and α-hydroxyalprazolam suggest they are unlikely to contribute much to the pharmacological effects of alprazolam. Alprazolam and its metabolites are excreted primarily in the urine.

It should be noted that adsorption, metabolism, and excretion changes can occur in various populations, such as individuals with impaired hepatic function, alcoholism, and geriatric patients.

**Single Dose Studies:**

**Urine:**

The SOFT DFC Committee and the AAFS Standards Board have established the importance of testing urine samples from alleged victims of drug-facilitated crimes for alprazolam’s primary urinary metabolite, α-hydroxyalprazolam, at a decision point concentration of 5 ng/mL or lower. Urine is easily collected, straightforward to analyze, and provides a longer window of detection of alprazolam ingestion compared to blood.

Literature on single-dose studies of alprazolam generally pre-date the year 2000; there are few single-dose studies for such a frequently prescribed drug.

One recent study evaluated eleven healthy volunteers who ingested 10 mg diazepam at the start of the study and 0.5 mg alprazolam on Day 3 of the study. A total of 10 oral fluid samples and 17 urine samples were collected from each participant. Tmax values were 11 hours. Drug detection times in urine ranged from 0-27 hrs. for alprazolam (median 12) and 26-61 (median 36) for hydroxyalprazolam in urine.

**Blood/Plasma/Serum:**

A plasma concentration range between 20-40 ng/mL has been proposed for targeting symptoms of panic disorder; higher concentrations correlate with significant central nervous system depression. Twelve volunteers were administered 1 mg of alprazolam, and plasma was collected at various times, demonstrating a Cmax of 16.5 mg/mL with a Tmax of 1.25 hours.

Twelve healthy adolescent volunteers (13–17 years) and 12 adult healthy volunteers (20–45 years) received single Xanax XR 1 mg or 3 mg tablets. Cmax for the 1 and 3 mg groups were 7 – 9 ng/mL and 23 – 24 ng/mL, respectively. Tmax values for both groups were 8 – 10 hours.

Twelve healthy male volunteers received 1 mg of alprazolam or a placebo on three occasions in a double-blind, randomized, single-dose, three-way crossover study. The three trials were: (a) oral alprazolam and sublingual placebo; (b) an oral placebo and sublingual alprazolam; (c) a placebo by both routes. Cmax for oral and sublingual administration was 12 and 11.3 ng/mL, respectively, and the Tmax was 1.8 and 2.8 hours, respectively.

**Hair:**

Hair analysis allows for the longest detection window of alprazolam compared to blood and urine. Generally, hair analysis is more complex and less routine for toxicology laboratories. In addition, determining the time of ingestion is far less sensitive and specific than blood or urine. Studies show, however, that following a 0.5 mg oral alprazolam dose, alprazolam was not detected in a hair sample.

That said, hair analysis has been useful in some instances. For example, alprazolam was found in hair segments in two drug-facilitated crimes examined by Kintz. Alprazolam was detected at 4.9 and 3.1 pg/mg, which was concluded through repeated doing of alprazolam.

**DFC Cases:** A large study examining 1000 sexual assault cases listed alprazolam as identified in 9.3% of urine cases and 7.4% of blood cases. There are limited case-specific reports involving alprazolam. This may be due to the difficulty of determining drug exposure and suspected DFC.
References:


Recent media reports have warned the public about ‘Frankenstein Opioids’. This is a non-descript and colloquial term for a group of novel synthetic opioids (NSO)—namely the benzimidazole opioids—which are also referred to in shorthand as the “nitazenes”. Originally, nitazenes were developed in the 1950s by Ciba AG, a chemical company based in Switzerland, with the intent of becoming analgesic alternatives to morphine. However, due to the increased risk for adverse health effects, these compounds were never approved for medical use. More recently, the nitazene subclass emerged after domestic and international scheduling efforts reduced the prevalence of fentanyl analogues, such as 2-furanylfentanyl and cyclopropylfentanyl. They are structurally distinct from fentanyl, are potent μ(μ)-opioid receptor agonists, and some exceed the potency of fentanyl. Due to their unique structure and potent μ-opioid receptor agonism, these properties made the nitazene subclass of NSO prime targets for repurposing as replacement for heroin and/or fentanyl in the illicit opioid market.

Protonitazene is one of the most recent emerging nitazene compounds, although it was first identified in May 2021 by NPS Discovery. Protonitazene likely made its way to the drug market as a replacement for previously scheduled nitazenes. Isotonitazene was amongst the first in this class to hit the recreational drug market in 2019. Discovered in casework in late 2019, isotonitazene remained popular until late 2020 when the US Drug Enforcement Administration (DEA) promptly announced the drug would be placed as a Schedule 1 substance under the Controlled Substances Act (CSA). This federal intervention quickly and negatively impacted isotonitazene’s popularity. It also paved the way for other NSOs to take its place as drug manufacturers raced to create substitutes. Shortly after isotonitazene’s scheduling, other nitazenes such as metonitazene and etodesnitazene began to proliferate. By April 2022, these compounds were also scheduled. This cycle continues to create significant challenges for laboratories aiming to keep up with ever-evolving drug trends.

Similar to other nitazenes, protonitazene produces euphoria, analgesia, respiratory depression and profound sedation that can progress to coma and ultimately death. Protonitazene is estimated to be roughly three times more potent than fentanyl. The μ-opioid receptor antagonist, naloxone, may be able to combat the effects of protonitazene, but given the latter’s increased potency, larger or repeated doses of naloxone may be required.

Protonitazene is commonly sold in pill or powder form, sometimes under the pretense of being another substance, such as another opioid. A public health alert in Australia has also warned of it being marketed as ketamine. It is frequently mixed into the illicit drug supply with other opioids such as fentanyl, potentially for the purposes of increasing profits or producing a better high from a product. Adding new compounds to the drug supply, especially those with unknown toxicity, poses serious risks to drug consumers who may be unaware of what they are ingesting, and likely resulting in unintentional overdoses.

At NMS Labs, drug screening for protonitazene, in addition to other specified nitazene compounds, was performed using liquid chromatography time-of-flight mass spectrometry (LC-TOF/MS) and a surveillance library containing a number of different NPS compounds, including NSOs, designer benzodiazepines, and novel stimulants like N,N-dimethylpentylone. Presumptive positive identification was determined by evaluating retention time, chromatography, mass accuracy and area response relative to a set threshold. If these criteria were met, additional testing was recommended and if approved, confirmation testing using liquid chromatography tandem mass spectrometry (LC-MS/MS) was performed. Quantitation was achieved using three levels of standard addition with a reporting limit of 0.50 ng/mL.

By May 2021, protonitazene (along with N-pyrolidino etonitazene) was beginning to appear in toxicological casework. At NMS Labs, 42 blood samples were quantitatively reported for protonitazene between November 2021 and March 2023. These samples were obtained during death investigations originating from 18 states in the US (31 cases) and 3 provinces in Canada (11 cases). Figure 1 represents the geographical distribution of these reported cases across the US. The range of concentrations reported were 0.53 - 48 ng/mL. The mean and median concentrations reported were 3.8 ± 7.3 ng/mL and 1.8 ng/mL, respectively. As seen in the histogram in Figure 2, the majority of blood results for protonitazene were reported with concentrations between 0.50 and 3.0 ng/mL. This is consistent with other concentrations seen in the literature, with the exception of a 1400 ng/mL protonitazene cardiac blood concentration in a case of mixed drug toxicity. A limitation of the data is that the reported results are from casework submitted to the reporting laboratory and elected for confirmatory testing for protonitazene. Given this, the prevalence of protonitazene is most likely under-reported.
From the dataset described, 39 of the above 42 cases underwent comprehensive drug screening. In 2 of these cases, protonitazene was the sole finding with concentrations of 0.59 and 5.6 ng/mL. In the case of the blood concentration reported as 0.59 ng/mL, the case history was listed as “suspected overdose”. Five cases (~13%) were also positive for one or more nitazene(s), namely N-pyrrolidino etonitazene, metonitazene, and isotonitazene. Twelve cases (~31%) were also positive for one or more designer benzodiazepine(s), specifically 8-aminoclonazolam, bromazolam, etizolam, and flubromazepam. In roughly 44% of cases, fentanyl was also detected.

Protonitazene presents two analytical challenges. The first challenge involves the issue of differentiating isomers. Protonitazene is an isomer of isotonitazene (see Figure 3), therefore differentiating the two isomers is highly recommended since both compounds have been reported in authentic casework. Having the capability to differentiate allows for more accurate reporting and assessment of each compound’s prevalence. The second analytical challenge involves the sensitivity of instrumentation due to low concentrations of nitazenes being observed. Recent drug trends suggest that the prevalence of NSOs is at least holding steady, if not increasing with the variety of nitazenes still detected in casework in low concentrations. Therefore, it is recommended that analytical techniques employ chromatographic separation of known isomers as well as appropriate sensitivity (i.e., lower reporting limits). The Center for Forensic Science Research and Education (CFSRE) and SOFT NPS Committee recommend reporting limits of less than 1 ng/mL for most nitazene compounds.12

As of April 2022, new legislation went into effect making protonitazene a Schedule 1 substance under the DEA’s ruling along with several other nitazene compounds, including metonitazene and N-pyrrolidino etonitazene.4 Protonitazene continues to appear in casework along with other nitazenes, despite the fact that drug scheduling efforts typically drive a decline in popularity with a subsequent surge of a replacement compound. Two new nitazene compounds, N-desethyl isotonitazene and N-pyrrolidino protonitazene, have started to appear in toxicology casework, but it is too soon to tell if they are replacement compounds or merely expanding the group. Labs should continue to monitor for protonitazene and other nitazenes.

Dubbing ‘nitazenes’ as ‘Frankenstein Opioids’ may have been an effective soundbite, but the term does not have any scientific basis. Maybe the thought behind ‘Frankenstein opioids’ was the potency comparison to fentanyl or the structural differences compared to fentanyl. Frankenstein was technically the creator of the “monster” and potentially this is where the term is applicable. Legislative efforts to schedule protonitazene may ban one “monster” in order to limit its life span but will very likely give life to new ones.

**Figure 1: Heat Map of confirmed protonitazene cases in The United States of America**
Figure 2: Histogram showing frequency of reported protonitazene concentrations between November 2021 and March 2023

![Frequency of Reported Concentrations](image)

Figure 3: Structure of Protonitazene (left) and Isotonitazene (right)

**Synonyms:** Pronitazene, Propoxynitazene,

**Formal Name:** N,N-diethyl-2-[5-nitro-2-[(4-propoxyphenyl)methyl]benzimidazol-1-yl]ethanamine

**Molecular Formula:** \( C_{23}H_{30}N_4O_3 \)

**Molecular Weight:** 410.51 g/mol

\([M+H]^+\): 411.2391

**GC/MS Spectrum:**
“IT’S ALIVE!”: PROTONITAZENE, THE LATEST ‘FRANKENSTEIN OPIOID’

Pharmacological Drug Class: Opioid agonist
References


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Submitted by: Christine Moore, Cindy Coulter, and Kristin Tidwell on behalf of the SOFT/AAFS Oral Fluid Committee

**Introduction:** Drugs in oral fluid generally reflect free drug in blood, therefore is a viable specimen for use in DUID cases. The time for blood collection after a traffic stop averages 1.5 – 2 hours while a warrant and medical personnel are located, time during which drugs are dissipating from the blood. Oral fluid can be collected easily proximate to the incident, maintaining the integrity of drug concentrations.

**Annual Survey:** To assess the utility of oral fluid in DUID cases, in August of 2022 the 4th annual survey was sent to laboratories in the USA and one in Canada; 42 laboratories responded (38%).

**Laboratory (Evidentiary) testing:** While 26% of respondents indicated that their state statute allows for oral fluid evidentiary drug testing in DUID cases, only one state (Alabama) responded that oral fluid is actually tested. Somewhat encouragingly, four jurisdictions (Louisiana, New York, New Jersey, California – Orange County) are working on validating oral fluid confirmation procedures, and three other laboratories (Wisconsin State Laboratory of Hygiene, Forensic Fluids, Ohio – Montgomery County) have fully validated methods. No laboratories reported outsourcing of specimens to private reference facilities, although there are some private labs that offer this service (e.g., Forensic Fluids, NMS Labs).

Which evidentiary specimen(s) do you typically test in DUID cases?

- Blood: 52.5% (N=21)
- Urine: 15.0% (N=6)
- Oral Fluid: 0% (N=0)
- Blood and Urine: 40.0% (N=16)
- Blood and Oral Fluid: 2.5% (N=1)

**Roadside screening:**

- 24% of respondents affirmed that their state statute allows for oral fluid roadside screening by law enforcement.
- 19% indicated their state/jurisdiction had conducted and completed an oral fluid pilot project.
- 7% indicated such a project was in process and a further 7% said a project was in the planning stages.
- Almost 40% of completed projects were conducted in conjunction with representatives from the Drug Recognition Expert (DRE) program, and 26% in conjunction with their Traffic Safety Resource Prosecutor (TSRP).
- One respondent indicated the use of the Draeger DT5000, five use the Abbott SoToxa (formerly known as the Alere DDS2), and one uses the Randox Multistat for oral fluid roadside screening.
- As of this survey, no states have had a Daubert or Frye hearing related to roadside oral fluid testing for probable cause or for oral fluid evidentiary (confirmation) testing, but one agency has testified in oral fluid DUID cases. (However, in 2015 a Draeger DT5000 result was allowed to be used as evidence after showing it is a valid scientific test.)
Summary: Overall, since the first survey was performed in 2018 the number of laboratories implementing or even considering oral fluid testing for DUID cases has not grown. The stalled growth of oral fluid testing given the somewhat higher percentages of completed pilot studies show there is an interest in conducting oral fluid testing, but laboratories may not have the resources needed to fully validate the program. The number of states allowing for oral fluid DUID testing has steadily increased from 2018. To help promote oral fluid testing we may need to survey what resources laboratories lack, and in what areas collaboration and assistance can be provided.
UTILIZING STANDARD ADDITION IN THE QUANTITATION OF THE RARE FENTANYL ANALOG: VALERYLFENTANYL

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Wisconsin State Laboratory of Hygiene – Forensic Toxicology Section
University of Wisconsin – Madison, School of Medicine and Public Health

Introduction

Fentanyl is an opiate of high potency and short duration of action capable of achieving high levels of respiratory depression, muscle rigidity, seizures, coma, and hypertension\(^1\). Although initially synthesized as a pharmaceutical anesthetic, illicitly manufactured fentanyl has caused an increase of overdose deaths since the mid-2000’s\(^2\). Fentanyl analogs were created shortly after the synthesis of pharmaceutical fentanyl for therapeutic and illicit use. Following the introduction of the analogs alpha-methyl fentanyl and methyl fentanyl, the US Controlled Substances Act regulated any substance structurally similar to compounds listed in a schedule\(^2\).

The novel fentanyl analog valerylfentanyl was reviewed by the World Health Organization and is known to be manufactured clandestinely for illicit purposes\(^3\). Valerylfentanyl is less potent than fentanyl and has no known therapeutic purpose. Like fentanyl, valerylfentanyl is a CNS depressant and acts as an agonist to the μ-opioid receptor producing similar, typical opioid effects and has been associated with several documented deaths\(^3\). In documented cases, valerylfentanyl has mostly been found in combination with fentanyl and other CNS depressants and, although it exists on its own, is only prevalent through poly drug use\(^4,5\). In a specific case study completed by the New York City Office of the Chief Medical Examiner (NY OCME), valerylfentanyl concentrations are compared to fentanyl concentrations within samples. In the majority of cases, the fentanyl concentration was shown to be higher than the concentration of valerylfentanyl\(^5\). This might suggest that in instances with higher fentanyl concentrations, the presence of valerylfentanyl may be a byproduct of illicit fentanyl synthesis. In instances where the valerylfentanyl concentration is higher, this could indicate deliberate addition of the compound\(^5\).

Due to the changing landscape of fentanyl analogs, it is difficult for publicly funded forensic toxicology laboratories to identify and quantify these compounds. The Wisconsin State Laboratory of Hygiene – Forensic Toxicology Section (WSLH) receives over 20,000 samples yearly for impaired driving and Medical Examiner casework. Developing and validating quantitative methods for emergent fentanyl analogs is a constant challenge. The WSLH provides an opportunity to use an established method, standard addition, to quantify valerylfentanyl in an interesting case.

Method

General Drug Screen via Quadrupole Time of Flight (QTOF)

Whole Blood samples, collected for suspected Operating While Intoxicated (OWI) investigations, are submitted to the WSLH for ethanol and drug analysis. Suspected impaired driving samples are delivered to the lab in grey top tubes containing sodium fluoride and potassium oxalate for preservation and anti-coagulation, respectively. Samples that fall within the criteria for drug testing are primarily screened via QTOF using a Waters I-Class HPLC with Xevo G2-XS QToF. Each specimen may require separate, additional qualitative or quantitative tests, dictated by the presence of additional analytes in the QTOF screen. Valerylfentanyl, per the WSLH Standard Operating Procedure, does not have a validated quantitative method and is reported qualitatively by its presence in the QTOF screen and a separate confirmatory test.

Additional Semi-Quantitation

A single blood sample containing valerylfentanyl was tested multiple times to assess the drug’s stability and to gain a semi-quantitative value using the Waters I-Class HPLC with Xevo G2-XX QToF. One hundred microliters of sample was analyzed and compared against known valerylfentanyl standards, obtained from CDC - Traceable Opioid Material® (TOM) Kits, with known concentrations 4, 10, 20 and 40 ng/ml.

Quantitation through Standard Addition

One hundred microliters of the whole blood sample of interest was pipetted five separate times into the supported liquid extraction plate used in the QTOF drug screen analysis. A standard of valerylfentanyl was created which was used to spike each well with known concentrations. The first well contained the unfortified sample with no spike. The remaining four wells were then spiked with known concentrations of valerylfentanyl standards (2.5, 5.0, 10.0, 15.0 ng/ml) to build an internal calibration. Using the internal calibration, the estimated concentration of the valerylfentanyl in the highlight-
ed sample was 9 ng/ml. The ASB054 document, “Standard for a Quality Control Program in Forensic Toxicology Laboratories”, was used as a reference for the standard addition. ASB-054 states that a minimum, three standards should be used at 50%, 100% and 150% of the expected drug concentration. In this instance, four standards were used to widen the detection range as it was uncertain how accurate the estimated value would be. A simple linear regression was created to accommodate the five sample levels.

Case Notes

A 36-year old male was arrested on an OWI charge. Officers responded to the scene after reports of a white sedan driving erratically through a residential area. According to witnesses, the operator of the vehicle was driving through front yards, weaving in and out of trees. After being tased and apprehended, the subject was brought to the hospital where blood was drawn with a warrant. En route to the hospital, the subject had slurred speech, was lethargic and uncooperative, had “extremely constricted” pupils, and could not follow a train of thought.

The subject, while in custody at the medical center, fell asleep and was unable to be awoken. One of the doctors mentioned to law enforcement “the subject had cocaine in his system”. The subject was kept at the hospital as medical staff stated it was in his best interest to keep him under observation for the night. It was noted that 3-4 doses of naloxone were administered while at the hospital.

According to the extensive case reports provided by law enforcement, the subject was a known distributor of illicit drugs. Approximately six days before this OWI arrest, officers responded to the scene of an abandoned car found in a cornfield. One witness stated two males were seen throwing items from the car into the rows of corn and then evacuating the scene. Items recovered were a scale, approximately 500 g of methamphetamine, 85 blue pills with markings of 30 mg Oxycodone, green plant material (suspected marijuana), and a brown powder that field tested positive for heroin & fentanyl. An additional 44 blue pills were recovered through a K-9 search. A search warrant was issued for the subject’s residence. Evidence recovered from the residence included cocaine, methamphetamine, sertraline, gabapentin, MDMA, alprazolam, lorazepam, counterfeit oxycodone pills, marijuana, and a series of bags of powder. Four bags, each holding 5 bags of powder within each larger bag, were individually tested and were positive for methamphetamine and fentanyl. Housed in the same container as the 4 larger bags were counterfeit oxycodone pills. The results of any chemistry testing performed on the recovered evidence was not made available to the WSLH.

Results

**Drug Screen & Semi Quantitation**

Upon examination of the screen results, a series of drugs were detected in the whole blood sample. These drugs can be seen in Table 1.

<table>
<thead>
<tr>
<th>Detected Analytes</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>52 ng/ml</td>
</tr>
<tr>
<td>Benzoylcegonine</td>
<td>571 ng/ml</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>150 ng/ml</td>
</tr>
<tr>
<td>4-ANPP</td>
<td>**</td>
</tr>
<tr>
<td>2-Fluorofentanyl (o-FF)</td>
<td>**</td>
</tr>
<tr>
<td>3-Fluorofentanyl (m-FF)</td>
<td>**</td>
</tr>
<tr>
<td>4-Fluorofentanyl (p-FF)</td>
<td>**</td>
</tr>
<tr>
<td>Valerylfentanyl</td>
<td>9 ng/ml*</td>
</tr>
<tr>
<td>Naloxone</td>
<td>**</td>
</tr>
<tr>
<td>Xylazine</td>
<td>**</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>**</td>
</tr>
</tbody>
</table>
Notable results include Fentanyl at 150 ng/ml and the presence of fentanyl analogs, xylazine, and naloxone. Fentanyl analogs that are restricted controlled substances by statute in Wisconsin are not usually quantitatively reported but are qualitatively confirmed and reported as present. Due to the interest in valerylfentanyl, the response was compared to known concentrations of valerylfentanyl standards producing an estimated value of 9 ng/ml.

**Standard Addition Result**

Standard addition can be utilized as an alternative method to obtain a quantitated value of an analyte that does not have a specific validated method optimized for the analyte. This method is being considered in laboratories due to its minimal need for validation and ability to validate within its own matrix. Standard addition is being utilized in postmortem laboratories as there is much variability in matrix effects between samples. In light of the recent discussion of Standard Addition being utilized in forensic laboratories, a point of reference is ASB-054. The method of standard addition used in this case is an adapted version of the method stated in ASB-054. As stated before, five levels were included (one, zero level non fortified sample level, and four spiked levels) as opposed to the four minimum levels recommended by ASB-054. The calibration range was also widened to better suit the target analyte, in the event of unknown drug stability in the sample. Although the majority of samples tested by WSLH are properly preserved whole blood samples, the interest lies within the ability to target a quantitative result without validating a method for an analyte that is rarely included in production work. It was of interest to achieve a concentration through standard addition because of the rarity of the analyte and the severity of the case report. By obtaining area ratios and plotting them against known spiked concentrations of the target analyte, valerylfentanyl, a simple linear regression was created to produce a quantitative value of 7.7 ng/ml.

**Table 2: Calculated Area Ratios from Valerylfentanyl Injections**

<table>
<thead>
<tr>
<th>Calibration Level</th>
<th>Added Conc.</th>
<th>ISTD Peak Area</th>
<th>Analyte Peak Area</th>
<th>Area Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>L0 (Unspiked)</td>
<td>0.000</td>
<td>1039329</td>
<td>201291</td>
<td>0.194</td>
</tr>
<tr>
<td>L1</td>
<td>2.500</td>
<td>951034</td>
<td>249785</td>
<td>0.263</td>
</tr>
<tr>
<td>L2</td>
<td>5.000</td>
<td>947470</td>
<td>341262</td>
<td>0.360</td>
</tr>
<tr>
<td>L3</td>
<td>10.000</td>
<td>864750</td>
<td>363027</td>
<td>0.420</td>
</tr>
<tr>
<td>L4</td>
<td>15.000</td>
<td>514319</td>
<td>311020</td>
<td>0.605</td>
</tr>
</tbody>
</table>

**Graph 1: Standard Addition - Concentration/Plotted Area Ratios**
Discussion

There is interest in studying this case due to the presence of the rare fentanyl analog valerylfentanyl. It is unknown whether the presence of valerylfentanyl in the sample is an isolated incident or present in illicit drugs that are distributed locally. Although the annual submission volume for WSLH exceeds 20,000 samples, valerylfentanyl has only been reported in 37 samples from 2019-2021. The last time the drug was reported was September of 2021.

Of the 20,000 cases submitted annually to the WSLH, approximately 85% are impaired driving offenses. The remaining 15% of sample submissions are from Coroners and Medical Examiners (C/ME) across the state. Outside of impaired driving and C/ME cases, the WSLH is involved in a program monitoring fentanyl analogs appearing in non-fatal overdose urine samples from emergency departments in northern Wisconsin. Primarily, hydroxyfentanyl analogs and acetylfentanyl analogs are being seen in these urine samples. Valerylfentanyl has not yet been observed.

The presence of valerylfentanyl, and its connection to the user, can produce information regarding the adulterants present in illicitly produced fentanyl. As stated previously, it is difficult to distinguish whether valerylfentanyl is an additive or a byproduct of illicit fentanyl production. Other analytes found within the sample are known signatures, or compounds that appear only as a direct result of a specific synthesis route. For instance, 4-ANPP is encountered as a fentanyl precursor of illicit synthesis. In 2017, 4-ANPP, along with NPP, were placed under international control as they are signatures to methods of illicit synthesis. Fluorofentanyl is a modified fentanyl analog fluorinated at the para, meta, or ortho position of the aniline ring, also known as the 2, 3, 4 positions. Xylazine is a known, non-opiate sedative approved for veterinary use and has been recently used as an adulterant of fentanyl. Although fentanyl alone is not considered a Schedule 1 drug, it is still a fast-acting synthetic agonist creating severe respiratory depression and euphoric feeling.

The presence of analogs, precursors, and adulterants, such as those found in this sample, are indicative of illicit production of fentanyl. Valerylfentanyl and 2,3,4-Fluorofentanyl are Schedule 1 drugs because of their relation to illicit fentanyl production. 4-ANPP is registered as a Schedule II drug but is also related to illicit fentanyl production.

The subject’s ability to safely operate a motor vehicle while intoxicated with extremely high concentrations of illicit drugs (fentanyl & cocaine) also draws an interest to this case. In the thirteen case postmortem review conducted by Ton et al. a quantitative valerylfentanyl range of 0.22-0.85 ng/ml with a standard deviation of 0.21 ng/ml was reported. The authors further noted uncertainty of this range was an accurate representation of valerylfentanyl postmortem concentrations. In postmortem samples collected by NY OCME, the range of valerylfentanyl concentrations was <0.10-21 ng/ml. It is uncertain whether a concentration of 7.7 ng/ml is a high or low concentration for valerylfentanyl in comparison to these published studies and the lack of research regarding therapeutic ranges.

Initially, it was of interest to establish a quantitative value of valerylfentanyl out of curiosity of the analyte itself. However, it was made clear that using different methods of quantitation in the process of this study could better prepare the laboratory for instances where an analyte needs to be quantitated outside of the existing methods. Comparing the two modes of quantitation, the calculated values (9 ng/ml: Semi Quant Value; 7.7 ng/ml: Standard Addition Value) were within 15% of each other. This variation could be due to degradation of analyte over the span of time between tests or could be due to the variation in methodologies. It should be noted that the plotted area ratio curve had a $R^2$ value of 0.97225 which is below the generally accepted $\geq 0.99$ for deuterated internal standards and $\geq 0.98$ for non-deuterated internal standards. An $R^2$ value of 0.99 is also referenced in ASB-054. It is possible the high amount of methanol utilized in the procedure caused extraction issues in the supported liquid extraction plate at the higher end of the calibration curve.

Conclusion

The presence of valerylfentanyl in the analyzed sample raises the concern of the prevalence of fentanyl analogs, understanding illicit fentanyl synthesis, and quantitation of analytes that have not previously been validated. Valerylfentanyl is recognized as a fentanyl analog with known effects similar to fentanyl and its other analogs. Illicit products used recreationally may effect the route of administration, dose, and composition. Fentanyl analogs are a risk because their presence in illicit fentanyl product creates more variability in the safety of the product. Little is known of the overall...
increase or decrease in toxicity with the presence of valerylfnentany in an illicit sample compared to other analogs. It is a challenge to determine the origination of the fentanyl analogs, like valerylfnentany, in a sample. As studies show, analogs like valerylfnentany, can be an adulterant or a byproduct of production. It is unknown what effect the isolated drug may have. More research on specific analogs would be of benefit to understand each drug’s effects.

The utilization of Standard Addition in the quantitation of analytes was beneficial. As previously stated, the Standard Addition method is proving to be a valuable tool in postmortem toxicology laboratories as a way to manage and mitigate matrix effect. The additional benefit lies within the ability to standardize a method that can quantitate a single analyte, such as a novel psychoactive substance, that is of interest to the lab. It may not be cost or time effective to validate a method for a single analyte that may not have consistent occurrence in received samples. Standard addition can be a validated, generalized tool that may be used when necessary.

Citations:


