thermo scientific

PROMISES AND PITFALLS OF ALTERNATIVE MATRICES:

Capture the drug traces you need

ThermoFisher SCIENTIFIC

INTRODUCTION

Sample backlogs, delayed casework, and increasing numbers of substance abuse cases present serious challenges for forensic, clinical research, and sports antidoping labs. Traditional biological matrices, such as blood and urine, continue to be useful, but have limitations that affect their ability to answer important questions. For example, labs not only encounter traditional drugs, but also many new psychoactive substances (NPS), drug combinations, and an expanding list of illicit or prohibited compounds, such as synthetic cannabinoids and opioids, which may be difficult to detect using traditional matrices and approaches.

The high potency and low blood concentrations of NPS, and rapid decreases in other drug concentrations due to distribution, metabolism and excretion pose additional challenges. Even if performed with sensitive and specific analytical methods, drug-detection windows are short in some sample matrices. The time required to collect a blood sample, for example for a drug-impaired driving case, may result in the un-metabolized (parent) drug being undetectable. Blood collection is invasive and requires a medical professional. Urine collection cannot be readily performed in the field. Sample substitution and adulteration are additional concerns with urine samples.

Many labs now analyze fit-for-purpose alternative sample matrices such as oral fluid, hair, and exhaled breath to detect a growing list of drugs faster and with more certainty, and to make sample collection as convenient, noninvasive, and reliable as possible. Advancements in toxicokinetics (TKS) research and new analytical technologies are making these analyses routinely practical.

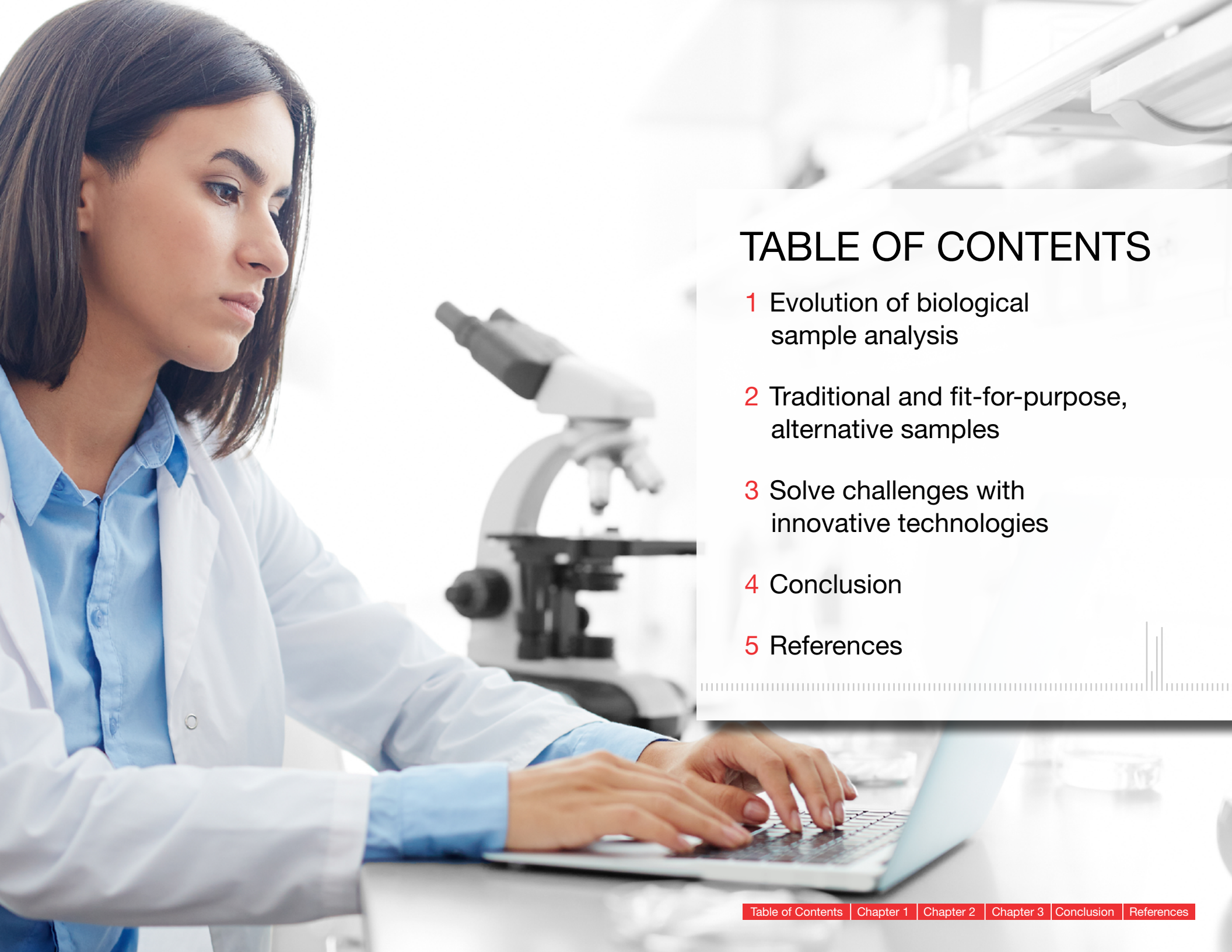


TABLE OF CONTENTS

1 Evolution of biological sample analysis

2 Traditional and fit-for-purpose, alternative samples

3 Solve challenges with innovative technologies

4 Conclusion

5 References

Chapter 1
EVOLUTION OF BIOLOGICAL SAMPLE ANALYSIS

Throughout history, the application of new science and technology to the analysis of biological samples has played a key role in improving scientists' ability to identify exposure to an expanding list of drugs and toxins faster, cost-effectively, and with more certainty.

Emergence of forensics

In ancient times, interest in forensics began with poisons. However, poisoning convictions were based on circumstantial evidence instead of compound identification. True scientific study of toxins did not begin until the 19th century, and the introduction and adoption of methods did not grow substantially until the second half of the 20th century. With the emergence of new methods and technologies, specialized police crime labs were introduced in France and the U.S. in the early 1900s.

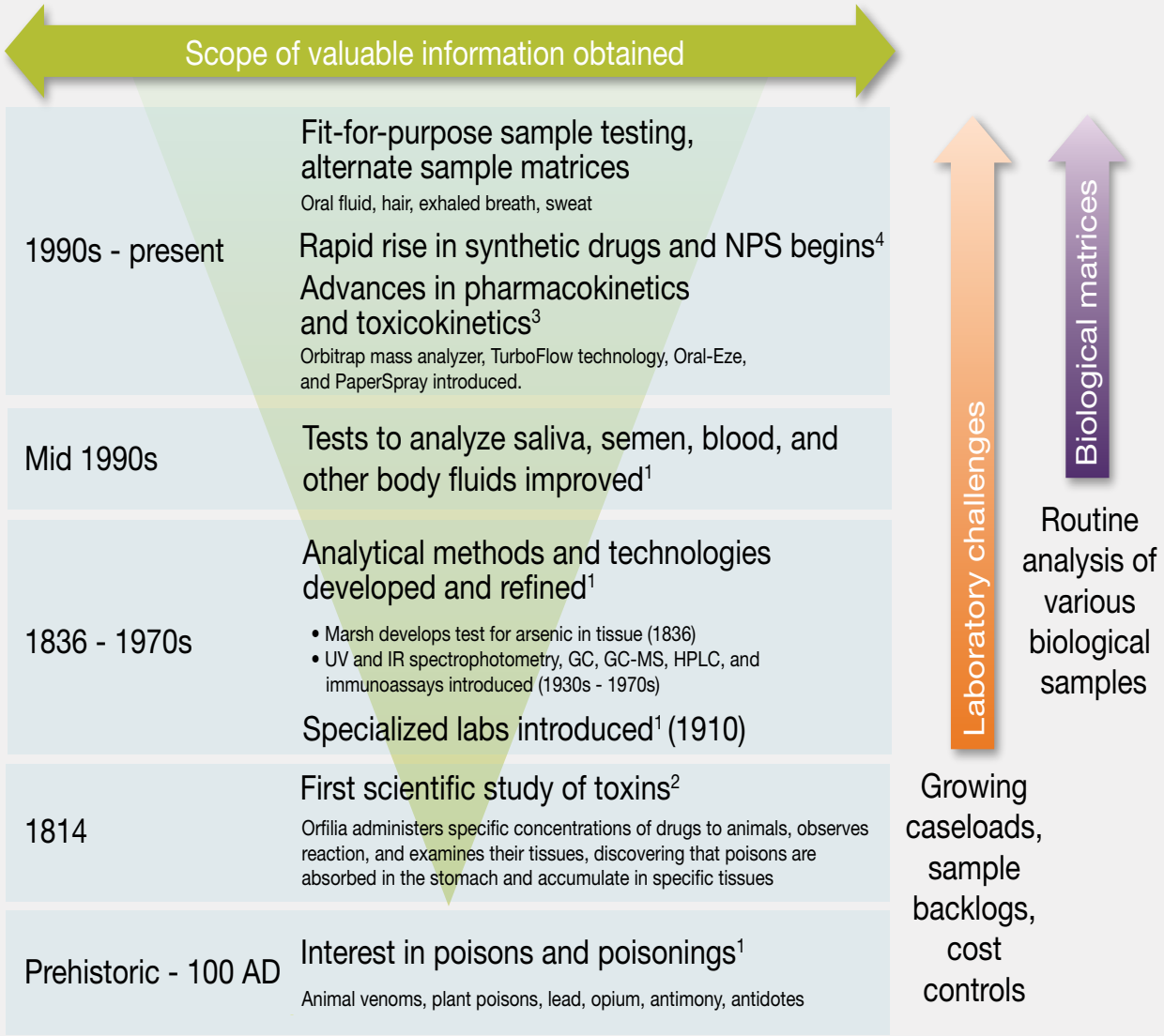
Research advances, new drugs

By the end of the 20th century, scientists had numerous technologies to apply in their work including chromatography and mass spectrometry (MS). Researchers used this new toolkit to advance our understanding of pharmacokinetics (PKS)—how compounds enter the body and are distributed, metabolized, and excreted—and toxicokinetics (TKS)—the relationship of exposure to a compound and its toxic effects. On the streets, law enforcement witnessed a rapid rise in synthetic drugs and NPS. Advances in PKS and TKS have quickly shown the value of alternative sample matrices in addressing the growing drug problem.

Challenges, future needs

Today, specialized forensic, clinical research, and sports antidoping labs must accurately detect and quantify numerous compounds in biological matrices to correlate concentrations with impairment at time of death or crime, and exposure or use. Because justice and health are on the line, rock solid results beyond reproach are required. Maintaining chain of custody is also paramount. Faced with the challenges of growing caseloads, sample backlogs, and cost controls, labs are looking for ways to work faster and better including making sample collection as convenient, tamper-proof, and reliable as possible, and reducing time-consuming analytical steps such as sample preparation.

EVOLUTION OF IDENTIFICATION OF EXPOSURE TO DRUGS AND TOXINS IN BIOLOGICAL SAMPLES



Pharmacokinetics and Toxicokinetics

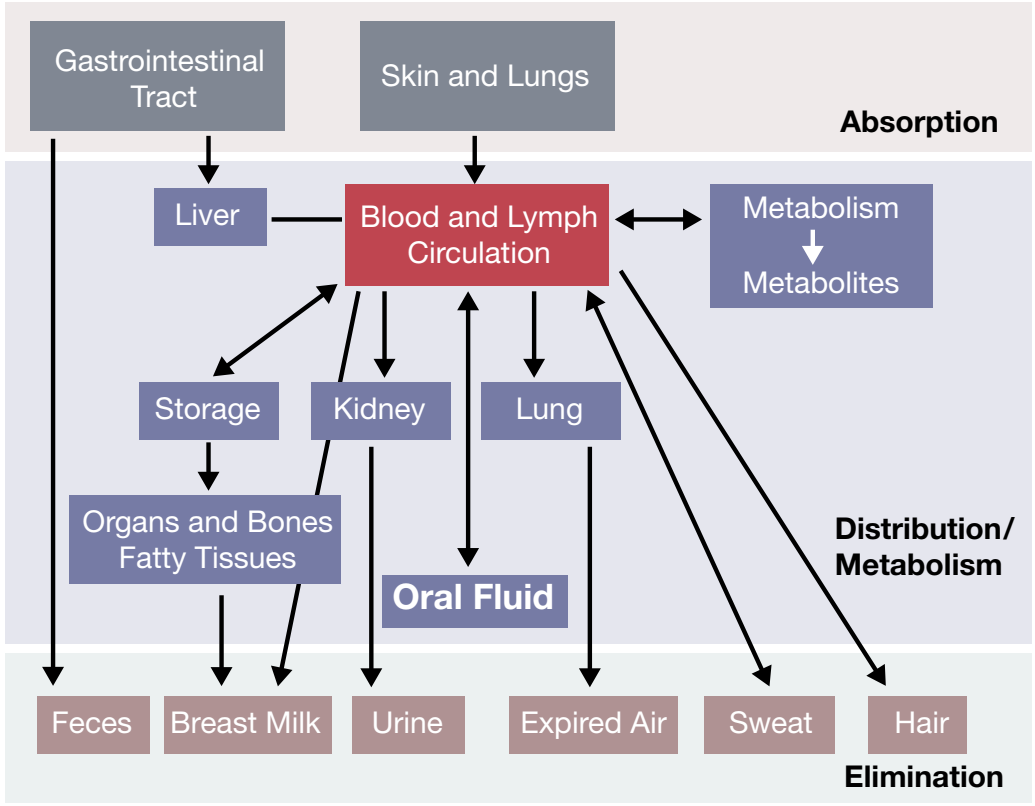
Pharmacokinetics (PKS) is the study of the rate at which a compound enters the body and how it is distributed, metabolized, and excreted. Controlled drug administration studies can determine the onset, peak and duration of effects, as well as correlate drug metabolites with these effects. Toxicokinetics (TKS) is the application of PKS to determine the relationship of exposure to a compound and its toxic effects such as impairment or death. Both PKS and TKS research influence evidence-based drug policy, identification of new NPS metabolic pathways and target metabolites, and drug monitoring research to deter drug use.

For scientists, PKS means that the compounds detected can be quite different depending on the sample matrix and the timeframe in which it is analyzed. Together, PKS and TKS thus determine the choice of analytes—that is parent-drug, metabolites, or both—monitored in different sample matrices.

A drug's PKS varies by its route of administration. Drugs that are smoked, vaporized, insufflated (snorted), or taken orally are found in high concentrations in oral fluid because they are directly deposited in the oral mucosa. Drugs also distribute to oral fluid from blood.

Chronic drug use can also impact its TKS. Concentrations of THC, the primary psychoactive compound in cannabis, in blood are affected by the frequency and chronicity of use. In occasional (less than daily) cannabis users, THC is generally detected in blood for about six hours, while THC may be measureable in chronic users' blood for more than 30 days.[5] This makes data interpretation difficult when trying to establish drug impairment. Because the window of THC detection may be long in chronic cannabis users, one cannot presume impairment from the presence of THC alone.

Interrelated Processes of Absorption, Distribution, Biotransformation, and Elimination



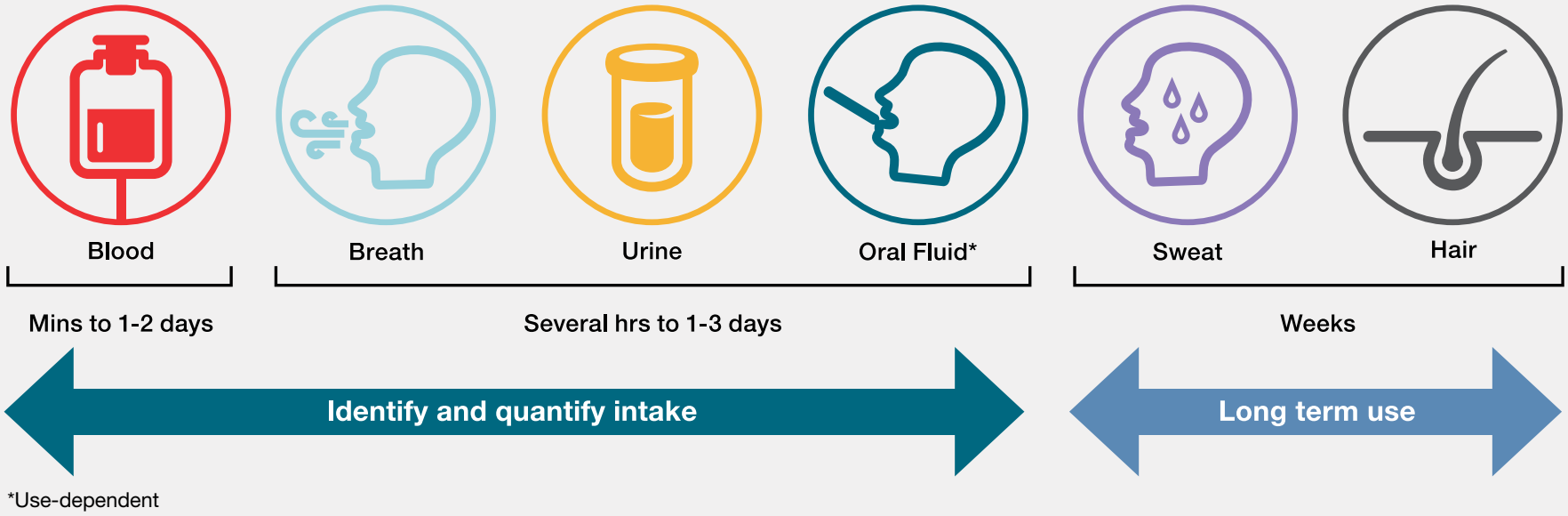
Window of detection

A key concept related to PKS and TKS is the "detection window" for a drug and its metabolites in various biological matrices. In order to identify a drug, its window of detection must be long enough for sampling to occur.

In the U.S., blood is the matrix most often analyzed in DUID cases. However, because samples are typically taken at a hospital or a police station rather than in the field, it takes time. Studies document that THC concentrations in blood drop 74% in 30 minutes, and 90% in 1.4 hours, while the average time to get blood drawn in the U.S. is between 1.4 and 4 hours.[7] An individual can be highly impaired at the time of a motor vehicle crash or when stopped by law enforcement, but by the time the sample is taken, the blood THC concentration may be low or test negative.

Learn more [Mitigating the Key Growing Pains of Legalized Marijuana]

Detection Window for Drugs in Biological Matrices



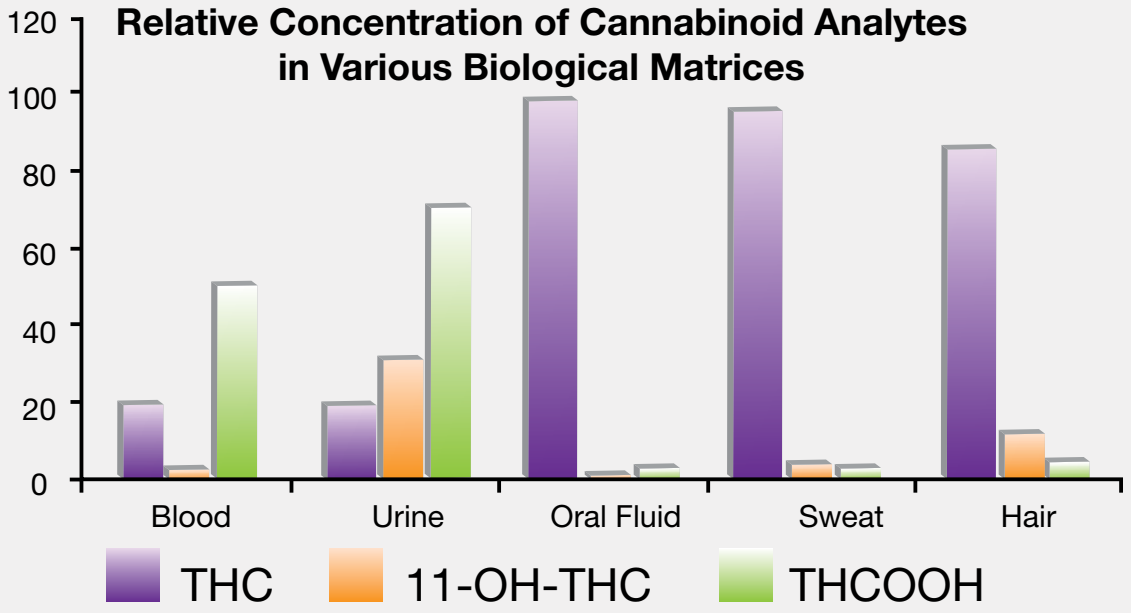
Chapter 2
FIT-FOR-PURPOSE: TRADITIONAL AND ALTERNATIVE SAMPLES

Fit-for-purpose samples

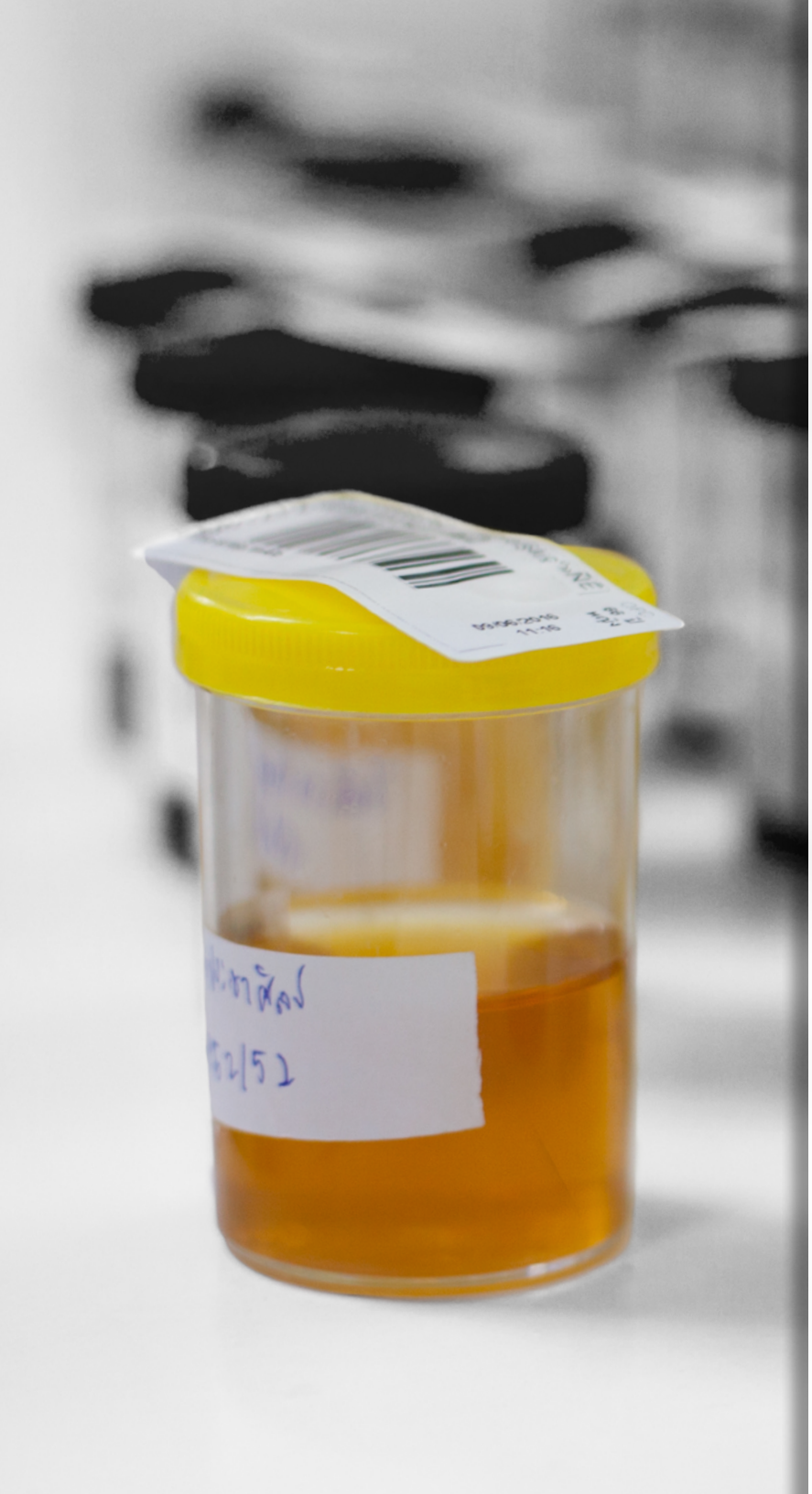
The trend today is toward analyzing the best sample matrix for the application. Whether it's urine, blood, hair, oral fluid, breath, or sweat, each matrix offers advantages and disadvantages, and provides unique information which can be used to interpret drug use, and cause of impairment or death. One consideration is window of detection—how long evidence of drug use can be detected in a particular matrix. For example, depending on hair length, analysts can determine use days, weeks, and even months in the past. Urine and blood provide information about drug use over a much shorter period of time.

Why consider an alternative sample matrix?

- Appropriate window of detection
- Easier, less invasive sample collection
- Less potential for adulteration
- Greater analyte stability
- Cleaner matrices
- Easier or complementary data interpretation, greater insight



Relative proportions of analytes can be quite different depending on the sample type. THC (parent drug), 11-OH-THC (active metabolite) and THCCOOH (inactive metabolite).[5]



Urine

Historically, urine has been the sample of choice for monitoring drug intake in criminal justice, pain management research, sports antidoping, and drug testing research because relatively high concentrations of drugs and metabolites are generally present in it after use. Urine offers a wide window of drug detection and it's less invasive than a blood draw. More than 55% of current tests use urine.[8]

Most urine testing focuses on detecting metabolites rather than the parent drug, which may indicate drug use weeks after consumption. Metabolites of THC such as 11-nor-9-carboxy-THC (THC-COOH) are routinely quantified in urine of chronic, frequent users to determine marijuana use up to 30 days in the past.[9] For sports anti-doping, only urine and blood samples are currently considered acceptable.

However, urine results do not correlate well with impairment because its window of detection can extend for days, especially in the case of cannabis. Further, only same-gender officials can collect a urine sample, which adds additional expense and time for witnessed specimen collection.

Advantages

- Widely accepted, established methods
- Broad detection window
- Sufficient volume
- High concentration of metabolites
- Easy to automate analysis

Disadvantages

- Long detection windows can exceed impairment windows
- Moderately intrusive, costly, and time-consuming collection
- Ease of sample adulteration

Blood

Blood, the second most commonly tested matrix, is generally considered the “gold standard” because it measures drugs in circulation and thus results reflect recent use. Blood tests generally target the parent drug, making interpretation of results easier than matrices with a high proportion of metabolites. In the U.S, blood is commonly analyzed in DUID cases—mostly for blood alcohol concentration (BAC) testing.

While blood testing is widely accepted for many drugs, recent studies measuring THC levels in blood indicate there may be better sample matrices to correlate recent cannabis use with acute impairment. For example, THC detected in blood can indicate recent use and acute impairment. However, THC may also be detected in blood of chronic, frequent cannabis users for much longer after last use. As regulations for recreational cannabis use evolve, testing for cannabis-related impairment may change as well.

Because collection can result in infection, only medically trained professionals may collect blood samples, adding expense and time waiting for proper sample collection to occur. Blood collection is also not easily repeatable. Other issues, such as storage conditions, biohazards, and multiple parties handling samples, necessitate strict chain-of-custody procedures for blood samples.

Advantages

- Widely accepted, established methods
- Useful for Identification of parent drugs in circulation and ideally recent use
- Enables quantification of parent drugs and metabolites

Disadvantages

- Requires medical personnel for sample collection
- Invasive, potentially delayed collection
- Fast drug clearance, short detection windows
- Sensitive detection methods required

Hair

Hair is useful for investigating drug use history, days or even months before sample collection. Seven to ten days after last use, hair containing a drug first emerges from the scalp. In drug-facilitated crimes, especially sexual assault, authorities recommended collecting hair four to six weeks after alleged use so the time window of the event is viewed in the hair segments analyzed.[10] Drug concentrations decrease along the hair shaft such that, at 12-15 cm from the root hair retains only about 4% of a drug.[10] For this reason, hair analysis requires very sensitive detection.

Scalp hair is easy to collect, even by non-medical personnel in a non-medical setting, and is minimally invasive. Slow drug decomposition in hair allows collection of fresh, essentially equivalent hair samples when there is a claim of specimen mix-up or breach in the chain of custody. In addition, the possibility of substitution and adulteration during sample collection is lower than other sample matrices, because drugs and metabolites are captured within hair, while adulterants can be washed away during sample processing. Factors affecting drug incorporation and elimination from hair are melanin content (hair color), cosmetic treatments (bleaching and straightening), and ultraviolet damage.

There are multiple mechanisms of drug incorporation into hair, including from the blood supplying the hair follicle and deposition from sweat and sebum.[11] Basic drugs such as cocaine, nicotine, and amphetamines accumulate in hair to a much greater extent than more acidic drugs, such as GHB or THCCOOH. In addition, there can be lower drug concentrations of opioids, methadone, cocaine, methamphetamine and cannabinoids in scalp hair compared to beard, pubic, and other hair. These differences should be considered when interpreting results. Recently, hair analysis has been useful for identifying emerging NPS.

Advantages

- Useful for determining drug use history and not yet known NPS
- Simple, minimally invasive, observable, gender-neutral collection
- Low chance of adulteration
- Duplicates easily collected
- Easy to store

Disadvantages

- Potential for environmental contamination
- Hair source, color, cosmetic treatments, external conditions, and distance from the root may impact drug concentration
- Requires highly sensitive detection

Watch the video to learn more

Oral fluid

Oral fluid testing is new compared to blood and urine testing, and currently represents less than 10% of the matrices tested, but it's growing nearly twice as fast.[8] Because it's easy to collect, oral fluid is now the matrix of choice for testing programs in many areas of the world. Since 2004 in Australia, and shortly thereafter in Europe,[8] oral fluid testing is the norm for DUID cases, because it can be collected at the roadside at the time the individual is judged to be impaired. Today, countries including Australia, Belgium, UK, Germany, France, Switzerland, Canada, and selected states in the US, now collect oral fluid for drug testing, particularly at the roadside. Oral fluid testing is also used in drug monitoring research.

Oral fluid collection is noninvasive, gender-neutral, and easily performed. Roadside oral fluid testing technology for DUID applications is already available. Compared to blood and urine, a small volume is collected, which allows repeat collections if necessary.

Active forms of drugs that are smoked, snorted, or taken orally are directly deposited in high concentrations in the oral mucosa and oral fluid. For this reason, bystanders may passively inhale a drug if it's in high concentration in nearby smoke. Like hair, basic drugs such as cocaine, amphetamines, and opiates concentrate in oral fluid at higher concentrations than in blood. Like blood, more parent drug tends to accumulate or partition into oral fluid than metabolites. However, recent studies show that, with highly selective detection systems, oral fluid can be used to target low concentration metabolites. For cannabis testing, THC metabolites such as tetrahydrocannabivarin (THCV) and cannabigerol (CBG) may be better markers for recent cannabis use than THC.

Advantages

- Simple, noninvasive, gender-neutral collection
- Fast, on-site collection technology exists
- Duplicates can be collected
- More difficult to adulterate, easier witnessed collection
- Reflects recent drug use
- Useful for detecting parent drug and metabolites

Disadvantages

- Limited specimen volume, especially after stimulant use, high-sensitivity detection needed
- Potential for passive exposure
- Elution buffer can interfere with LC-MS/MS detection
- Drug administration route impacts results and interpretation
- Short window of detection

Learn more Oral Fluid: Is It the "Magic Loogie" of Drug Testing?

Exhaled breath

To address the shortcomings of testing blood and urine, researchers are exploring breath testing. Breath reflects the composition of the alveolar lining, which is fed by the blood supply. Breath alcohol testing is commonly used, and studies show that cocaine and cannabinoids can be measured in breath with a short window of detection that is similar to the window of impairment. For law enforcement, breath testing for cannabis could be better than blood and urine testing, because it could be done in the field, is noninvasive, and relatively inexpensive. However, to date, no cannabis or cocaine roadside-breath-testing device has published data that evaluate its performance using a controlled drug administration study.

Advantages

- Noninvasive
- Allows measurement of parent drug
- Allows frequent and easier witnessed collection
- Fast

Disadvantages

- More studies needed to expand use
- Limited number of analytical tests
- Limited TKS understanding

Watch the webinar to learn more

Sweat

Researchers have analyzed many drugs and their metabolites in sweat, including methadone, phenobarbital, morphine, cocaine, THC, and methamphetamine. Sweat analysis is currently limited because the correlation between amount of drug taken and concentration in sweat is not well established. The mechanism by which drugs are incorporated into sweat is not fully clarified; however, the excretion of basic drugs into sweat is greater than for acidic drugs.

Several collection methods have been proposed for sweat including gauze, pads, cotton swabs, perspiration stains from clothing, drug wipes, and Band-Aid-like devices. In some studies, sweating was boosted by heat or other stimuli prior to collection.

Advantages

- Noninvasive
- Sweat patches can be used for monitoring applications

Disadvantages

- Few labs testing sweat
- Few data to inform results

Chapter 3
SOLVE CHALLENGES WITH INNOVATIVE TECHNOLOGIES

While each testing technique has some limitation, the factors most labs consider when choosing methods are cost, accuracy, speed, operator skill needed, and robustness. Historically, drug tests have used immunoassay (IA) screens followed by GC-MS confirmation. However commercial IAs are only available for a limited portion of the growing number of analytes, and time-consuming derivatization is often required for confirming GC-MS tests. LC-MS represents a complementary and potentially future replacement to IAs by offering greater specificity, speed, analyte range, throughput and multichannel capabilities.

Learn more

Around the world, labs are investigating the latest technologies to quickly and cost-effectively advance their science, while reducing the risks inherent to optimized workflows. Recent innovations in sample preparation, chromatography, and MS technology are helping labs overcome the obstacles to adopting analysis of alternative sample matrices. Sample preparation method automation, and high-resolution accurate-mass (HRAM) Thermo Scientific™ Orbitrap™-based MS systems are providing the necessary sensitivity and specificity to identify all sorts of drugs in alternative sample matrices.

Sample collection

Ideally, sample collection should be, fast, non-invasive, unadulteratable, safe, and easy to perform anywhere. The collection method should also account for the matrix, metabolism, target analytes, and test that will be used. In addition, collection and storage must maintain sample integrity and continuous chain of custody.

Many tests continue to rely on blood or urine samples collected in a sanctioned facility. This method of collection is intrusive, time consuming, and expensive. Field-based sample collection is highly desired. Recent innovations in sample collection devices, such as the Thermo Scientific™ Oral-Eze™ Oral Fluid Collection System, are making this desire a reality.

Technology Spotlight

SIMPLIFIED SAMPLE COLLECTION

Collection of oral fluid samples requires tools that are simple and easy to use yet collect enough sample for analysis. The Oral-Eze Oral Fluid Collection System is the solution. The System's unique indicator window turns blue when collection is complete, taking the guesswork out of the process and reducing repeat collections. Sample collection typically takes about three to five minutes, and the specimen and any drugs in it are stable for 21 days after collection. Specimens stored frozen are stable for at least one year.

Sample preparation

Interferences such as proteins, salts, and phospholipids often make biological samples incompatible with GC-MS and LC-MS techniques. Even cleaner matrices such as oral fluid require some sort of sample cleanup prior to analysis.

Common cleanup methods include liquid-liquid phase extraction (LLE) and solid-phase extraction (SPE). SPE methods are generally preferred over LLE, because they are easier to automate and generally produce cleaner samples. Protein precipitation (PPT) by "salting out" is an additional step needed for samples such as blood, which contain high concentrations of proteins. For GC-MS analysis, time-consuming derivatization is often performed to make analytes volatile and thermally stable. To avoid these derivatization steps, LC-MS is becoming the technique of choice.

Liquid-Liquid Extraction (LLE)

1. Aliquot of sample
2. Spike with IS
3. Add buffer
4. Add MTBE
5. Shake 10 min
6. Centrifuge
7. Remove organic
8. Evaporate to dryness
9. Reconstitute
10. Transfer to plate
11. Inject onto column

Solid Phase Extraction (SPE)

1. Aliquot of sample
2. Spike with IS
3. Add 0.1N HCL
4. Condition sorbent
5. Add sample to sorbent
6. Wash
7. Evaporate
8. Reconstitute
9. Transfer
10. Inject onto column

Protien Precipitation (PPT)

1. Aliquot of sample
2. Spike with IS
3. Add acetonitrile
4. Centrifuge
5. Remove supernatant
6. Reconstitute
7. Evaporate
8. Transfer to plate
9. Inject onto column

Common methods used to prepare biological samples for LC-MS analysis involve many time-consuming error-prone steps.

The recovery and selectivity of the cleanup method used affects detection of target analytes and thus analytical results. Each method requires trade-offs between selectivity and versatility. The major drawback of any sample prep method is the cost and time to perform it. For this reason, labs are looking to new technologies, such as Thermo Scientific™ TurboFlow™ online sample preparation technology, to capture analytes of interest while eliminating unwanted interferences. Other innovations such as the Prosolia Velox 360™ PaperSpray™ ion source, are sidestepping sample preparation entirely.

Technology Spotlight
FAST ONLINE SAMPLE PREP

TurboFlow technology automatically eliminates matrix interferences such as proteins, salts, and phospholipids using online diffusion, chemistry, and size exclusion, prior to LC-MS analysis. In addition to improving sensitivity for target analytes, the technology reduces the amount of time a lab would spend on preparing biological samples by up to 95%. Because TurboFlow technology eliminates manual steps, it also minimizes errors.

The Thermo Scientific™ Transcend™ II system combines TurboFlow technology with multi-channel HPLC to bring the productivity of up to four separate, parallel UHPLC channels to a single mass spectrometer. This increases sample throughput by up to four times, maximizing MS productivity and return on investment. Multiplexing also allows different methods to be run simultaneously, reducing cross-contamination and the time it takes to switch between methods.

Technology Spotlight
NO SAMPLE PREP

The Prosolia Velox 360™ PaperSpray™ system fully automates sample extraction from biological samples. For many sample types, it completely eliminates time-consuming, error-prone sample preparation, including extraction and centrifugation.

Because PaperSpray does away with chromatography, there are no columns needed. An MS-based workflow with PaperSpray uses small solvent volumes and produces little solvent waste. Significantly simpler than HPLC, analysis involves depositing only 5-12 µL of sample onto a paper cartridge, where it's absorbed and allowed to dry. It is then inserted into the Velox 360 system, which loads the cartridge, deposits a small amount of solvent on the cartridge, and positions the cartridge in front of the mass spectrometer inlet. A high voltage is applied, which vaporizes and ionizes the analytes for MS analysis.

Detection and measurement

Analyzing samples for known drugs uses a variety of techniques to screen for substances, followed by a selective assay to confirm compound identity, and to quantify its concentration if needed. Screening and quantification of known substances requires reference material and can take two or three days. If unknown or multiple drugs are involved, more analysis steps are needed because traditional screens can't detect unknowns.

Samples are analyzed using a combination of IA, GC, LC, and GC-MS, LC-MS and MS/MS hyphenated-techniques. Due to the need to analyze biological sample matrices, LC-MS based techniques are increasingly favored. LC-MS methods are sensitive and specific, do not require derivatization, and are fast and reliable. Advanced triple quadrupole LC-MS/MS and HRAM Orbitrap-MS based methods provide the substantial advantage of being able to simultaneously screen and identify a broad panel of drugs and metabolites in a single analysis. High-resolution MS (HRMS), including HRAM Orbitrap-MS based analysis, is becoming popular for unknown or untargeted drug identification due to its ability to generate more complete information that allows scientists to re-review data for new substances as they appear, without re-running samples.

While IA methods continue to be used for screening, compared to MS methods they can lack adequate sensitivity to detect low drug concentrations, and the specificity to deal with the drug-to-metabolite ratios present in alternative matrices.

Targeted and Untargeted Drug Identification

	Targeted Screening	Confirm	Quantify	Untargeted screening	Retrospective Analysis
Immunoassay	XX				
GC/LC	XXX	X	X		
GC/LC-MS/MS	XXX	XXX	XXX		
HRMS-QTOF	XXX	XX	X	XX	XX
HRMS-Orbitrap	XXX	XXX	XXX	XXX	XXX

Number of Xs represent relative performance.

PUBLICATION SPOTLIGHTS
DISTINGUISHING PASSIVE VERSUS DELIBERATE CANNIBIS USE

Detection of the metabolite THCCOOH in a sample points to deliberate cannabis use, because the metabolite is not present in smoke. Analysis for THCCOOH versus THC is therefore a hot topic to obtain evidence of deliberate consumption and dispel any doubt of passive exposure. However, analysis is challenging due to the low concentrations of THCCOOH found in hair and oral fluid, and the small amount of sample typically collected for analysis. Chemical background in the sample matrix can also make it difficult to attain required detection levels.

GC-MS/MS analysis of THCCOOH in hair

THC can be adsorbed onto hair during exposure to cannabis smoke. This can lead to low-level THC detection due to non-intentional exposure. Able to quantify THCCOOH in hair down to 0.05 pg, the Thermo Scientific™ TSQ™ 8000 Evo GC-MS/MS makes it possible to easily distinguish between deliberate ingestion and non-intentional contamination.

Learn more Sensitive Determination of THCCOOH in Hair to Regulatory Requirements Using Triple Quadrupole GC-MS/MS (Application note 10493)

LC-MS/MS analysis of THCCOOH in oral fluid

THC has also been detected in the oral fluid of non-smokers passively exposed to cannabis smoke, causing data interpretation issues. LC-MS/MS methods to detect THCCOOH require derivatization or time-consuming SPE approaches to achieve the desired sensitivity levels of 10 or 15 pg/mL. Using the Thermo Scientific™ SOLAμ™ SAX SPE plate, THC and THCOOH can be extracted from oral fluid using a simple and fast SPE method without preconditioning, evaporation, or reconstitution. The Thermo Scientific™ TSQ Series triple quadrupole mass spectrometers allow simultaneous determination of THC and THCCOOH with high sensitivity down to 10 pg/mL.

Learn more A Sensitive and Efficient Method to Analyze THC and THCCOOH in Oral Fluid Using LC-MS/MS in Forensic Toxicology Laboratories (Application note 641)

Concheiro et al.[12] also described a method for simultaneous quantification of THC, THCCOOH, CBD and CBN Thermo Scientific™ UtliMate™ 3000 RSLCnano system coupled to a Thermo Scientific™ Q Exactive™ mass spectrometer. Oral fluid collected with the Oral-Eze Oral Fluid Collection System.

Chapter 4

CONCLUSION: IMPACT OF ALTERNATIVE MATRICES AND WHAT IT MEANS

Alternative, fit-for-purpose sample matrices are of intense interest because they have the potential to make sample collection more convenient, noninvasive, and reliable. Analysis of drugs and metabolites in alternative matrices also provides insight into drug metabolism, differentiation of active drug use versus passive exposure, and better correlation with recent cannabis use and acute impairment. As a result, labs can now quickly and confidently detect an expanding list of drugs and metabolites in matrices best suited to the reason for the test.

Though interpretation of the concentrations of drugs in alternate sample matrices is still a hot research topic, advancements in analytical technologies are now making testing of alternative, fit-for-purpose sample matrices a practical reality. When alternate matrices were introduced, few detection methods were sensitive enough to quantify the target drugs and metabolites at the levels needed. Today, state-of-the-art HRAM Orbitrap-based and LC-MS/MS triple quadrupole instruments provide the selectivity and sensitivity needed to quantify compounds in hair, oral fluid, breath, and sweat at pg/mL levels. In addition, workflow improvements in automation, sample preparation, and interfaces that eliminate complex workflow steps are helping labs overcome the remaining obstacles to analysis of alternative, as well as traditional, sample matrices.

Though technology advances are providing practical solutions, with new capabilities comes the need to train or obtain highly qualified staff and to validate new procedures. Likewise, before alternative matrices are universally adopted, complex legal issues must be considered such as, “How will it be determined if oral fluid, breath, or sweat testing are ready for field use?” and, “When should policymakers begin considering legislation authorizing the use of alternative samples and the technologies used to collect and analyze them?”

REFERENCES

1. Pappas, A. A.; et al. Toxicology: Past, Present, and Future. *Annual of Clinical and Laboratory Science.* 1999. Vol. 29, No. 4, 253-262.

2. Handbook of Forensic Medicine, First Edition. John Wiley & Sons Ltd., Part 1. Duties of Forensic Medicine in Modern Societies. 2014. 1-14.

3. Welling, P. G. Differences between pharmacokinetics and toxicokinetics. *Toxicol Pathol*. 1995, Mar-Apr;23(2):143-7.

4. CAPTURE TRACES OF TOMORROW'S DRUGS TODAY Identify rapidly evolving novel psychoactive drug substances faster. Ebook. Thermo Scientific. 2017.

5. Huestis, M. Advances, Benefits and Challenges of Oral Fluid Testing in Forensic Toxicology. Webinar. *Forensic Science Magazine.* November 2017.

6. Meyer, M. R. and Maurer, H. H. Handbook of Forensic Medicine, First Edition. John Wiley & Sons, Ltd. Toxicokinetics and Toxicgenetics. 2014. 879- 899.

7. Expert outlook: Addressing current trends and challenges in clinical research with mass spectrometry. WHITE PAPER 65121. Thermo Scientific. 2018.

8. Thomas, L. Analyte Guru. Oral Fluid: Is It the "Magic Loogie" of Drug Testing? March 24, 2016. Accessed December 10, 2017. http://analyteguru.com/oral-fluid-is-it-the-magic-loogie-of-drug-testing/

9. California NORML. Marijuana Drug Detection Times. Accessed December 10, 2017. http://www.canorml.org/healthfacts/drugtestguide/drugtestdetection.html

10. UNODC. Laboratory and Scientific Section. UNITED NATIONS OFFICE ON DRUGS AND CRIME. Guidelines for Testing Drugs under International Control in Hair, Sweat and Oral Fluid. 2014.

11. Henderson, G. L. Mechanisms of drug incorporation into hair. *Forensic Science International*. 1993. 63, 19-29.

12. Concheiro, M.; et al. Simultaneous quantification of Δ(9)-tetrahydrocannabinol, 11-nor-9-carboxy-tetrahydrocannabinol, cannabidiol and cannabinol in oral fluid by microflow-liquid chromatography-high resolution mass spectrometry. *J. Chromatogr. A*. 2013 Jul 5;1297:123-30

ADDITIONAL RESOURCES

Advances, Benefits and Challenges of Oral Fluid Testing in Forensic Toxicology. Webinar.	Learn more
Exhaled Breath Analysis Becomes Easier for more Reliable Drugs of Abuse Testing. Webinar.	Learn more
Forensics Learning Center	Learn more
High Confidence, Non-Targeted Screening for Drugs of Abuse in Urine. Application note 10495.	Learn more
Should LC-MS Replace Immunoassay.	Learn more
Forensic Toxicology Workflow Solution Utilizing LC-MS. Video	Learn more

EVERYTHING LEAVES A TRACE

When results can mean the difference between life and death, or innocence and guilt, accurate results are essential. Thermo Scientific offers both law enforcement and labs a comprehensive set of reliable, cost-effective solutions for every step of the analytical workflow to help reveal the truth hidden in the growing load of forensic toxicology, clinical research, and sports antidoping samples. Whether you're focused on meeting today's caseloads or anticipating future emerging drugs, we can help. Because when justice and health are on the line, so is your reputation. Find the truth.

Join our forensic community

Join our Clinical Research community

thermo scientific

www.thermofisher.com/FindtheTruth

BR65157EN-0218S

ThermoFisher SCIENTIFIC