

**Editorial**

**Introduction to Clinical Toxicology Laboratories Testing Control Pharmaceuticals**

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**Introduction**

Drug abuse is a serious challenge in US. According to the report of the Drug Abuse Warning Network, more than 50% of the patients involved the abuse of control pharmaceuticals such as taking more than the prescribed dose of a prescription [1]. A more serious concern is that the control pharmaceuticals was taken by healthy individuals. This challenge is more specific in pain management with opioids such as morphine, oxycodone, oxymorphone, hydrocodone, hydromorphone, dihydrocodeine, methadone, meperidine, fentanyl, and buprenorphine. It is reported by the Centers for Disease Control and Prevention (CDC) that in 2014, more Americans died of drug overdose than any other year on record: more than 47,000 deaths in 2014, which is more than the deaths to car crashes, gun violence, and AIDS [2]. Therefore, it is important to physicians to monitor the drugs in their patients to avoid the above risks. This necessity created an increased burden on clinical toxicology laboratories and many new labs or called LLCs providing measurement of control pharmaceuticals services were launched in recent years. For example, there are at least 5 labs or called LLC launched in Houston Areas in the past 3 years.

**Function of a Clinical Toxicology Laboratories**

A typical toxicology lab or LLC can support the testing control pharmaceuticals using biological fluids collected from patients with methods that are highly sensitive, rapid and economical without compromising precision accuracy. The services usually include presumptive screening with immunoassay (IA) and confirming with Liquid chromatography-mass spectrometry (LC-MS). Screening with IA can test the presence or absence of certain drugs or drug classes with good sensitivity and specificity, while confirming with LC-MS can not only test the presence of a specific drug but also quantify its content. Due to relatively low cost, easy to collect and reasonable detection windows, urine and saliva are the most commonly samples for clinical toxicology test although other type of samples, such as blood, hair, are also available. Antidepressants, Depressants / Sedatives / Hypnotics, Stimulants, Narcotics / Opioids, Anticonvulsants, Cannabinoids, Esoterics, and Hallucinogens are usually the tested drug classes.

A toxicology lab or LLC runs with time line manner. When samples are collected from the doctor offices and shipped to the lab by express, a partition of the collected samples is processed with a standard extraction procedure and another partition is saved for repeat in case of needed. Urine samples are usually incubated with

$\beta$ -glucuronidases and sulfatases to hydrolyze the metabolites (i.e., glucuronides and sulfates) of those drug before extraction. This step is necessary because parent drug could be totally metabolized into conjugates in some patients. Hydrolysis could release the parent drug. Saliva samples are extract directly because the chance of glucuronides or sulfates excreting into saliva is low due to distribution of drug efflux transporters. After initial screening for presumptive positives by IA, quantitative/qualitative confirmation can be performed by LC-MS based on the order from the doctor. Finally the results are certified by at least two technical person before being released to the doctor. The whole processing is usually taken 48-72 hours. All of the procedures are accredited by COLA, a physician-directed organization whose purpose is to promote excellence in laboratory medicine and patient care through a program of voluntary education, consultation, and accreditation.

**Challenges and Concerns**

Clinical toxicology labs or LLCs provide useful information helping the physician to test drug of abuse. However, challenges and concerns remain. For IA, a common challenge is specificity due to the lack of specific enzymes to distinguish certain drugs. For example, when a patients take hydrocodone, a positive of MS-Contin may show positive as the anti-body could not distinguish these two drugs. Therefore, a conformation tested with LC-MS is needed in most of the cases. More specific antibody needs to be developed.

The LC-MS is more specific, but, the challenge for LC-MS is more serious. A typical LC-MS method in such as lab usually can detect and quantify 60-80 drugs with similar number of internal standard in a short period of time (e.g., 5 min), which equals to quantify more

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than 100 analytes in about 5 min. To make the instrument running efficiently, usually two LCs are hooked with one MS running 24/7 manner [3]. The instrument is easy to be contaminated, which could generate false positive results. Experienced processers and technical expert are needed to process the results from LC-MS and maintain the instrument, which increase the processing time and the cost of the testing.

Other than the concerns of the instruments or methods, another important concern is polymorphism of metabolism. The glucuronides and sulfates can be hydrolyzed back to the parent drugs for urine samples for analysis, therefore, no matter how much of the drug molecules are metabolized, only parent drugs are tested after conversion. However, some of the drug can undergo other metabolism pathways such as phase 1 metabolism. For example, phencyclidine could be metabolized by CYPs into 1-(1-phenylcyclohexyl)-4-hydroxypiperidine, 5-(N-[19-phenylcyclohexyl] amino) pentanoic acid, or other hydroxylates [4]. These potential metabolites usually could not be detected in both screening and confirming tests or the test of these potential metabolites will highly increase the cost. In case the drug is totally metabolized through these pathways, false negative will be reported. More server issue is the drug-drug interaction could also affect the metabolism of some of the drugs, which increase the chance of false negative results [5]. Guidances to regulate this issue are needed.

More concerns is that the report either from IA or LC-MS is actually a negative/positive report although actual concentrations are detected. In other word, physicians only interested in or only know whether the patient take the prescribed medication or not. The dose accuracy or call precision medicine could not be reflected even if the actual concentration in the urine is known as only one time point is tested. More studies are needed at scientific level to determine how to reflect the dose from urine sample testing.

## Conclusion

It is reported by USA Today News that physicians wrote 259 million prescriptions for opioid painkillers, enough to give a bottle of pills to every adult in the country, in 2012 in US and it is estimated that not all of these drug end up in patients' hand, instead proliferating to black markets. Governments began to go after doctors who prescribe these drugs too leniently. Physicians have to pay increasing attention on the testing of control pharmaceuticals to avoid incarceration or loss of their medical licenses. The revenue of toxicology test will continuously increase in the near future and more labs or LLCs will be launched. However, more studies are needed to make the testing more specific, more accurate, and more economy. In addition, more guidance is needed to regulate the test.

## References

1. Services USDoHaH (2012) highlights of the 2009 Drug Abuse Warning Network (DAWN) findings on drug-related emergency department visits.
2. Rose A, Rudd NA, Jon E, Zibbell, Matthew Gladden, et al. (2015) Increases in Drug and Opioid Overdose Deaths-United States, 2000-2014. Centers for Disease Control and Prevention Morbidity and Mortality Weekly report Dec 18.
3. Wang J, Yang Z, Lechago J (2013) Rapid and simultaneous determination of multiple classes of abused drugs and metabolites in human urine by a robust LC-MS/MS method - application to urine drug testing in pain clinics. Biomedical chromatography BMC 27(11): 1463-1480.
4. Laurenzana EM, Owens SM (1997) Metabolism of phencyclidine by human liver microsomes. Drug metabolism and disposition the biological fate of chemicals 25(5): 557-563.
5. Hustveit O, Maurset A, Oye I (1995) Interaction of the chiral forms of ketamine with opioid, phencyclidine, sigma and muscarinic receptors. Pharmacology & toxicology 77(6): 355-359.