



# ORAL

FLUID ANALYSIS:  
**AN EXPLODING AREA  
OF DRUG TESTING**

Have you ever wondered if the guy or gal driving in the fast lane is “on something”?

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For years, impaired driving has been assessed by the analysis of blood for alcohol and drugs, simply because it is the biological fluid most likely to reflect recent intake. Today, with the major improvements in oral fluid testing technology, including better collection devices, more information on drug recovery from oral pads, and increasing amounts of data on drug stability during transportation and storage, oral fluid is poised to become the next major specimen being used for drug testing in many fields of toxicology including DUID.

While workplace drug testing, school programs, and the criminal justice system have embraced oral fluid as a testing matrix due to its easy, rapid collection; its non-invasiveness compared to urine or blood; the convenience of collecting a specimen anywhere, anytime, and the difficulty of adulteration, the main advantage of saliva remains its innate suitability for post-accident or “for-cause” testing since the presence of a parent drug can assist in the determination of an individual being “under the influence”.

The number of laboratories now offering oral fluid analysis routinely has increased from a small handful of laboratories in 2002 to over 50 laboratories today demonstrating the acceptance of oral fluid as an accurate and effective alternative to urine. While there are several point-of-care devices commercially available for oral fluid testing, to date none of these are able to attain the required sensitivity for the detection of marijuana in oral fluid, probably the major disadvantage of rapid tests. In addition, due to the commercial availability of immunoassays screens and confirmation equipment, laboratory testing offers a much larger drug test panel than point-of care devices, so more potential markets can be targeted using a laboratory-based test.

Further interest in testing oral fluid is evidenced when one considers the number of papers presented at the Society of Forensic Toxicologists (SOFT) annual meeting over the last five years. In 2004 only 4% of the papers were concerned with this matrix; by 2009 almost 20% of the presentations provided information on oral fluid.

The use of oral fluid in various drug-testing programs is expanding rapidly due to its accessibility, rapid easy collection, difficulty of adulteration and ability to reflect recent drug intake.

Oral fluid loses nothing to urine when the overall positivity rates are compared. As far back as 2002, Cone et al. reported that the prevalence rates of drug positives in oral fluid in a workplace setting were remarkably similar to those in urine, even though the samples were not paired<sup>1</sup>. In 2004, for the purpose of workplace drug testing in the USA, the Federal Government proposed the determination of five drug classes in oral fluid: cocaine; opiates; amphetamines; phencyclidine; and cannabinoids.

As with all specimens there are certain drawbacks to oral fluid testing in today's environment: non-standardization of collection devices; low sample volume compared to urine; limited information on drug recovery and stability during storage and transportation; and the inability of some subjects to provide a valid sample—"dry-mouth syndrome". However, manufacturers of saliva collection devices as well as instrumentation and immunoassay

screening companies have begun to address these challenges.

First, the adoption of devices which give a clear indication that adequate sample has been collected has been a major advancement in the testing of drugs in oral fluid. A known volume provides a basis for a valid quantitative analytical result. The most widely used collection devices are those that incorporate a pad and a buffer rather than the collection of neat oral fluid via expectoration, which has obvious problems with viscosity, stability, and frothing of the saliva. The use of a pad allows the sample to be collected more quickly, and on some devices indicates when adequate volume has been absorbed. The buffer stabilizes drugs during transportation, helps remove analytes from the pad, and prevents bacterial growth in biological specimens.

Second, improvements in both screening and confirmation technology have allowed reliable assays to be easily implemented into drug test laboratories. A broader menu of assays for illicit drugs and prescription medications is now available making oral fluid a good choice for pain management testing and therapeutic drug monitoring programs in addition to workplace, criminal justice/court ordered and school testing.

Third, many of the published articles on oral fluid testing now include information about the percentage drug recovery from a collection pad (also known as extraction efficiency referring to the ability to remove the drug from the pad) as well as stability data and recommendations for storage. Laboratory based oral fluid analysis generally requires the collected specimen to be transported overnight to a testing facility; therefore the stability of the analytes under these conditions and in long-term storage is an important issue.

In 2009, Ventura et al. noted, "*As the stability of drugs of abuse in oral fluid can affect drug testing results, it is essential to test collection devices for this parameter,*

*together with drug recovery before they are routinely applied*"<sup>2</sup>.

Not all collection devices are created equal, and not all drugs react the same way. In general, oral fluid specimens collected into a buffer may be stored at room temperature for a few days, refrigerated up to 30 days, and frozen (-20°C) for long-term storage. The main culprit for adherence to surfaces is marijuana (THC): its average loss has been reported to be approximately 1.6% per month, calculated after 9 months of storage at -20°C (presented at SOFT 2008).

However, the least stable of the major drug classes during storage is cocaine. Since both cocaine (COC) and its main metabolite benzoylecgonine (BZE) are detectable in oral fluid, the conversion of COC to BZE over time is important. In 2009, cocaine in proficiency specimens was shown to completely degrade over a period of 18 months, with significant amounts of BZE being produced in its place. While the positivity of the sample remains unchanged, the interpretation of the result will be affected. The presence of parent drug in an oral fluid sample indicates recent use, and potentially a determination of being "under the influence." The presence of a metabolite only may indicate use was further back in the metabolic cycle, and the individual may no longer be feeling the effects of the drug. Such differences may have legal consequences and are not trivial matters.

An interpretation of an oral fluid result, for example, by a Medical Review Officer (MRO), may be helped by knowledge of the ratio of the concentration of drug between the oral fluid and the plasma, commonly referred to the saliva: plasma (S:P) ratio. Drugs that exhibit a high S:P ratio will be more easily detected in oral fluid than those with a ratio <1. Generally, the more basic drugs will tend to accumulate to a greater extent in the saliva than acidic drugs. Further, drugs that are strongly protein bound (e.g., benzodiazepines) do not easily accumulate in saliva. Apart from the protein binding,

benzodiazepines also have one of the lowest S:P ratios so are therefore more difficult to detect in oral fluid. Conversely, Ecstasy (MDMA) is found easily in saliva.

While only morphine, codeine, and 6-acetylmorphine (6-AM) are suggested as Federal workplace target analytes, many other opioids have been detected in oral fluid, including the commonly abused pain medications hydrocodone (Vicodin®) and oxycodone (Oxycontin®). The treatment of pain, compliance testing and the management of pain medications is currently an area of substantial laboratory testing using urine. Oral fluid is now being increasingly investigated for this market segment due predominantly to its ability to detect parent drug, and identify recent intake. The interpretation of drug concentrations in urine is problematic because of individual variation in creatinine amounts, specific gravity etc., whereas with oral fluid, the interpretation in such programs is simplified.

Many pain medications including propoxyphene, meperidine, buprenorphine, tramadol and methadone are all easily detectable in oral fluid since their concentration in saliva compared to plasma (S:P ratio) is significantly higher than 1. Of the main prescription pain medications, only carisoprodol (Soma®) has an S:P ratio significantly <1. Fortunately, it is an older drug, the dosage given is also high, so both

carisoprodol and its main metabolite, meprobamate can be detected in oral fluid.

Perhaps the widest ranging study confirming the utility of oral fluid was the National Roadside Survey (NRS) in 2007, funded by the National Highway Traffic Safety Administration (NHTSA). For the first time in its history the NRS included measures to estimate the use of potentially impairing drugs, other than alcohol, in traffic safety. The research provided the first nationally representative estimate of the prevalence of drugs in drivers in various geographical locations in the USA. The project involved the collection of over 7,000 oral fluid samples and over 3,000 corresponding blood specimens. The drivers were stopped randomly, not for cause, mostly between the hours of 11 p.m. and 1 a.m. on Friday and/or Saturday evenings. Twenty drug classes incorporating over 50 analytes (plus alcohol) were tested from a single specimen of one-milliliter (1mL) neat oral fluid collected with the Quantisal™ device, demonstrating the flexibility and range of a laboratory-based program. Overall 16.3% of drivers were positive for drugs, with approximately half of those showing the presence of marijuana in their oral fluid and/or blood; and multiple positives in some specimens were reported. The full report is available at [www.nhtsa.gov](http://www.nhtsa.gov).

## Summary

The use of oral fluid in various drug-testing programs is expanding rapidly due to its accessibility, rapid easy collection, difficulty of adulteration and ability to reflect recent drug intake. The disadvantages, such as limited sample size and low drug concentrations have largely been overcome with continual improvements in the technology of collection and laboratory analysis. ■

## Footnotes

<sup>1</sup>Cone EJ et al. J Anal Toxicol 2002; 26(8): 541-6

<sup>2</sup>Ventura et al. Ther Drug Monit 2009; 31(2): 277-80



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