SureScreen Diagnostics

Best Practice Bulletin 2
Retention Times and Cut-off Levels

Modern screening for drugs is now so simple and accurate that we tend to take the technology for granted. And in fact the majority of screening really is a simple matter of collecting urine or oral fluid and testing it there and then to screen out all the negatives, then put the few positives through a confirmatory laboratory process.

But while most screening is routine, some customers are now asking much more from our screening processes, requiring a greater understanding or interpretation of the results. That is where SureScreen's free telephone Medical Review Process can help you with:

- The effect of any prescribed or over-the-counter medication
- The possible interactions between one drug and another
- How long the detected drugs stay in the body
- Whether any drugs taken recently would have already been lost from the body

In Issue 1 we showed that the half life of a drug is often linked to its psychoactive period, and its addictive quality. But in drug screening we are not usually concerned with the psychoactive performance, we simply want to detect drugs that are still present in the system.

However, it is wrong to assume that a drug which has a short half life will be lost from the body quickly. Even a drug like cocaine that has a very short half-life will stay in the body for an extended period, leading to different Retention Times for each drug group. This is because the body metabolises drugs into other compounds, called metabolites and some stay in the body for a longer time than others after drug consumption. The retention times of drugs and metabolites is of particular interest to physicians, drug workers and forensic scientists working in drug screening and harm minimisation because they need to know when a drug user will start to test negative after coming off drugs. And this is linked with drug test cut off levels - in other words, test accuracy.

To explain accuracy in testing we have to consider different factors that affect the test results:

Oxazepam is safer than many other Benzodiazepines

- The metabolism of the drug. This usually occurs in two stages. Phase 1 occurs mainly by the action of enzymes in the liver, so anyone with liver function problems may retain drugs for longer. Phase 2 is called conjugation, which increases water solubility so that the drug can be flushed out of the system.
- The excretion of the metabolites, usually through urine via the kidneys, but also in faeces, in breast milk, sweat, hair sebum and in semen. Volatile substances like alcohol also excrete in the breath.
- The binding ability of the drug to combine with fatty deposits in the body and other lipids.
- The test medium that is used is important because different drugs are detected at different levels in different media. Drugs typically only stay in oral fluid for 24 hours maximum.
- The sensitivity of the test is crucial in providing the right level of detection without risking possible accidental detection through contamination issues.
- The drug test cut off level which is different in different countries, or for different applications.

Phase 1 metabolism is a detoxification process that occurs in the liver but it can be slowed down by prescribed drugs that compete for liver enzymes. These drugs include cimetidine, fluoxetine, diltiazem and verapamil.

Most Phase 2 reactions involve a reaction to form glucuronides. Mostly these compounds are psychotropically inactive, but a notable exception is the metabolism of morphine into morphine-6 -glucuronide, which has a much greater analgesic quality than morphine itself.

Oxazepam, a metabolite of many benzodiazepines, is itself a potent antidepressant, but when oxazepam is prescribed it moves straight into Phase 2 metabolism without delay. Oxazepam is therefore safer than many other benzodiazepines in patients with impaired liver function as it is simply metabolized via glucuronidation. This means that oxazepam is less likely to accumulate and cause adverse reactions in the elderly or people with liver disease.

EXAMPLES OF PHASE 1 METABOLISM

PROCESS	DRUG
N-dealkylation	amitriptyline, TCA's
O-dealkylation	codeine
Ester hydrolysis	cocaine
De-acetylation	heroin
De-amination	chlordiazepoxide, Librium
Nitro-reduction	flunitrazepam
Reduction	chloral hydrate
Hydroxylation	THC, cannabinoids

EXAMPLES OF PHASE 2 METABOLISM

Glucuronidation	oxazepam,
Sulphate formation	morphine
Glutathionation	paracetamol
Methylation	theophylline
Carboxylation	THC, cannabinoids

The conjugation of paracetamol has been studied extensively because it is converted to an epoxide that is then detoxified by glutathionation. But in a paracetamol overdose there is insufficient glutathione available, so the epoxide attacks the liver cells, causing a lingering death by liver failure. This would not happen if a trace of glutathione was added to paracetamol tablets but the extra few pence cost per packet has been seen as an unacceptable price to pay.

Most screening uses urine or oral fluid, but SureScreen's laboratory has worked with faeces and semen, and has handled cases where breast milk from a cocaine user has resulted in positive hair samples in a young baby. More than 65% of cannabis is excreted in faeces, though we would not appreciate further samples of this medium for testing, thank you.

Cannabis is the most commonly quoted drug that binds to fats, and this considerably slows its passage through the body. Excretion of benzodiazepines is also slowed because many are virtually insoluble in water. Both of these drug types have represented the greatest challenges in drug testing.

DRUG RETENTION TIMES

These factors make it impossible to predict just when a drug will leave the system. It not only depends on excretion and metabolism, but on the amount consumed, body weight, and exactly which drug or drug cocktail was used. And some people become 'fast metabolisers' as their drug habit develops because the liver adjusts to the demands put upon it by producing more of the enzymes needed to promote Phase 1 metabolism.

The following Table can therefore only be used as a guide.

Type	Retention Times—Urine	Oral fluid
Amphetamines	1 - 4 days	72 hours
Barbiturates	3 - 8 days (Phenobarbital 14 days+)	
Benzodiazepines	3 days – 6 weeks	6 – 48 hours
Buprenorphine	3 – 6 days	
Cannabis	7 - 30 days	14 hours
Cocaine	2 – 5 days	24 hours
Methadone	1 – 7 days	48 hours
Methamphetamines	1 – 4 days	72 hours
Opiates	1 - 4 days	48 – 72 hours
PCP	3 - 8 days	24 hours
Propoxyphene	1 – 4 days	
TCA	1 – 9 days	

RETENTION TIMES OF SOME DRUG TYPES

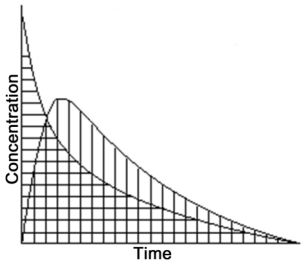
Many of the drugs in this Table which we highlighted in Issue 1 as fast acting with a short half life and therefore very addictive, nevertheless stay in the body for some considerable time after consumption. This seems to be counter intuitive, but it happens because the metabolic process is the rate-controlling process in what scientists call 'drug clearance'.

The psychotropic function of the drug usually ceases once it has been through Stage 1 metabolism, forcing the body to deal with clearance through metabolic pathways. For this reason, products sold to speed up drug clearance rarely have much effect on retention times. Those with greatest success have a liver stimulating effect and are traditionally used in body detox formulations, though even this is not significant.

Clearance of benzodiazepines is much more complex because this is a large group of structurally related compounds. Over 2,000 different benzodiazepines have been synthesized. Generally, the half-life for benzodiazepines is between 6- 28 hours. Dalmane has a much longer half-life (100 hours), while Verstan is about 200 hours. Moreover, their stage 1 metabolism varies too.

This makes prediction of benzodiazepine clearance difficult, especially so if the user has taken a benzo cocktail. These drugs are also problematic in oral fluid because their acidic base does not partition well in oral fluid, with a partition ratio of typically 1:0.03. For this reason, oral tests have to be very sensitive, typically around 10ng/ml in the neat oral fluid. Any higher, and the drug will not usually be detected.

Metabolic route For Stage 1	Drug	Metabolite
Dealkylation	Diazepam	Nordiazepam
	Temazepam	Oxazepam
	Flurazepam	N-1-desalkylflurazepam
De-amination	Librium	Demoxepam
Hydroxylation	Alprazolam	alpha-hydroxyalprazolam
	Diazepam	Temazepam
	Nordiazepam	Oxazepam
Reduction	Clonazepam	7-Aminoconazepam



WHAT IS THE CUT OFF LEVEL OF A DRUG TEST?

The rate of clearance of most drugs follows a curve that is known as asymptotic, or parabola shaped. Recent use peaks and then reduces, while frequent use followed by abstinence follows a constantly reducing curve.

A point in time is reached where a person should be deemed drug-free. Authorities such as SAMHSA, TOLL, and EWDTS issue recommended sensitivity levels for drug testing. This is achieved by controlling the drug test cut off level. These values harmonise the sensitivities of screening products so that all products in a market work at similar sensitivities. These 'cut off levels' are the detection levels for individual drugs, and serve a number of purposes.

- Set a standard for products from different manufacturers
- Ensure traces of drugs will not give a false positive
- Define when a positive person becomes technically 'negative'
- Provide a basis for quality control and audit.

Unfortunately these factors are rather arbitrary instead of being scientifically based. For this reason different countries and different markets have somewhat arbitrarily chosen their own cut off levels.

The best way to explain cut off levels is to compare them with speed limits on the road. Above the limit and the specimen is deemed positive, below the limit and the specimen is deemed negative.

Cut off levels can be compared to a speed camera

Drug cut off values are chosen to make sure only the true positives are recorded by the test, so anyone who is exposed to environmental drug exposure need not worry about being wrongly accused of drug taking. Just like speed cameras which should not hold any fear for a responsible motorist.

TYPICAL CUT OFF LEVELS (Popular UK cut off in Bold)

Code	Drug	Cut off level (ng/ml) Urine	Oral fluid
AMP	Amphetamines	**1000**/500/300	**50**
BAR	barbiturates	300	-
BZO	Benzodiazepines	**300** / 200	**10**
THC	Cannabis (Parent)	-	100
THC	Cannabis (Metabolite)	20/**50**/75/100/120	**12**
COC	Cocaine	100/**300**	20/**30**
PPX	Dextropropoxyphene	**300**	-
EDDP	(Methadone metabolite)	300	-
KET	Ketamine	1000	
MAMP	Methamphetamines	**1000**/500/300	**50**
MDMA	(Ecstasy)	1000/**500**/300	
MTD	Methadone	**300**	10
MOP	Opiates	**300 / 2000**	30/**50**
OXY	Oxycodone	**300**	-
PCP	Phencyclidine	**25**	**10**
PPX	Propoxyphene	**300**	-
Tram	Tramadol	**100**	-
TCA	Tricyclics	**1000**	-

HOW IS THE CUT OFF LEVEL CONTROLLED?

The cut off level of rapid tests is carefully adjusted by controlling the number of antibody binding sites on the membrane. Antibodies are just complex proteins, made originally by the immune system of an animal but manufactured in a bioreactor thereafter. The antibody concentration on a test is very accurate, however because these tests are read visually there is always some hysteresis around the actual cut off point, when the line changes from absent to present as someone is coming off drugs. There will always be a point in time where the person's sample reaches the cut off level, and the line will begin to appear, very faintly at first. In fact faint lines on rapid tests often indicate the remnants of prior drug use, but any line is a negative, however faint it is. But, as we have seen, this cut off level is itself rather arbitrary.

SO HOW IMPORTANT IS CUT OFF LEVEL?

The cut off level is like a speed limit. The speed camera is really there to stop people driving irresponsibly, for example travelling at 50 mph in a 30 mph zone. Drug cut off levels are there to avoid wrongly accusing someone of drug abuse.

These limits can change too, just like cut off levels. Pretty annoying if yesterday you were caught doing 34 mph in a 30 mph limit only to find that today the road has been reclassified to a 40 mph limit.

A couple of years ago SAMHSA changed the opiates cut off from 300 ng/ml to 2000 ng/ml because some tests were being triggered by the traces of opiates in poppy seeds used to decorate some bread products.

But although the cut off level is an arbitrary value that has been set to avoid falsely accusing someone of drug use, it is important that rapid tests match the results from laboratories, whose business it is to provide accurate quantitative results. To them, a result of 1450 ng/ml is just as important as a result of 1460 ng/ml, even though this level of accuracy is not needed in screening processes, where we just need to know whether someone is positive or negative.

SCREENING VERSUS LABORATORY ANALYSIS

So screening and laboratory confirmation analysis has to work in harmony with each other. Screening needs to be quick, inexpensive and accurate in screening out all the negatives, and identifying the positives. These positives are then analysed by a laboratory to confirm the result. Each technology has its own place in screening.

This is a powerful safeguard against an incorrect accusation

Sometimes this can go wrong, not because the products or the systems are at fault, but because the laboratory has to focus on detecting different compounds. The gas chromatography mass spectrometry (GC/MS) in the laboratory quantifies drugs and metabolites individually. These metabolites will generally form only a small part of the total drug derivatives in the body. The rapid test detects them all, but the laboratory just picks out one or two. And both technologies use control standards for their calibration but these standards are made from different drugs in different solution matrices. For this reason the cut off values shown by the laboratory for confirmation are often lower than they are for screening.

This should not be seen as a shortcoming of the whole system, it is simply a feature of the technology. Having two systems is a powerful safeguard against an incorrect accusation of drug taking. But occasionally the rapid test result and the lab result may not match for the reasons given.

FALSE POSITIVES OR FALSE NEGATIVES?

Continuing with our speed camera analogy, we can summarise as follows:

- Assume a speed camera is set to trigger at 32 mph. If a camera detects someone who is travelling at 31 mph and records them falsely at 33 mph, that is a FALSE POSITIVE. The motorist is recorded as positive when they were negative.
- If the camera fails to record someone when they were travelling at 34 mph, that is a FALSE NEGATIVE. The motorist was over the limit but the camera failed to detect them.

The principle for false positives and negatives in drug screening is similar. In an ideal world rapid test results should exactly match lab results, but due to the uncertainty of rapid tests right at the cut off level, manufacturers tend to err slightly on the side of false negatives, so as to avoid wrongly accusing someone.

Drug Class	Oral S	Oral C	Urine S	Urine C
Amphetamine	25	16	300	200
Barbiturates	25	20	200	200
Benzodiazepines	10	8	200	100
Buprenorphine	2	2	5	5
Cannabinoids	2	2	50	15
Cocaine metabolite	10	4	300	150
Methadone/EDDP	25	12	100	100
Methamphetamine	25	20	300	200
Opiates	20	12	300	300
Mono Acetyl Morphine	2	2	10	10
Phencyclidine	5	4	25	25
Propoxyphene	20	16	300	300

S = Screen by immunoassay in laboratory, cut off levels ng/ml
C = Confirmation by GC/MS in laboratory, cut off levels ng/ml

SUMMARY

To summarise on cut off levels, rapid tests work just like a speed camera:

- Most people will have zero drugs in their system, and they have no cause for any concern when performing a drug test.
- A few people will be exposed to environmental drug exposure perhaps because of their job or because of the friends they keep. The cut off level will prevent them from producing positive results.
- Those who used drugs in the last few days (or cannabis in the last few weeks) but have abstained since will have a reducing drug level. At some point they will have a substance level around the cut off level. Statistically the number of people in this group will be very small indeed.
- People who use drugs will be detected accurately and reliably.

CONCLUSIONS

To avoid falsely accusing someone of drug use, products should screen close to the cut off level and just above it, rather than close to the cut off and below it. This ensures that a high proportion of the people tested and found positive will be positively confirmed in the laboratory, while people right at the cut off level will be given the benefit of the doubt.

Drug screening is a complex and involved process because the drugs undergo several changes in the body and all of these compounds develop at different rates in each individual.

Next issue: Pharmacokinetics of Alcohol.

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How Drugs of Abuse are Handled in the Body

Drug Type	Calibrator	Cut-off (ng/ml)
Amphetamine (AMP)	d-Amphetamine	1,000
Amphetamine (AMP 500)	d-Amphetamine	500
Amphetamine (AMP 300)	d-Amphetamine	300
Barbiturates (BAR)	Secobarbital	300
Benzodiazepines (BZO 300)	Oxazepam	300
Benzodiazepines (BZO 200)	Oxazepam	200
Buprenorphine (BUP)	Buprenorphine	10
Cocaine (COC)	Benzoylecgonine	300
Cocaine (COC 150)	Benzoylecgonine	150
Clonazepam (ACL)	7-Aminoclonazepam	100
Cotinine (COT)	Norfentanyl	20
Ketamine (KET)	Ketamine	1,000
Marijuana (THC)	11-nor-Δ^9-THC-9 COOH	50
Marijuana 20 (THC 20)	11-nor-Δ^9-THC-9 COOH	20
Marijuana 150 (THC 150)	11-nor-Δ^9-THC-9 COOH	150
Methadone (MTD)	Methadone	300
EDDP 300 (EDDP)	EDDP	300
EDDP 100 (EDDP 100)	EDDP	100
Methamphetamine (MET)	d-Methamphetamine	1,000
Methamphetamine (MET 500)	d-Methamphetamine	500
Methamphetamine (MET 300)	d-Methamphetamine	300
MDMA (MDMA)	d,l-MDMA	500
Morphine (MOP)	Morphine	300
Opiate (OPI)	Morphine	2,000
Oxycodone (OXY)	Oxycodone	100
Phencyclidine (PCP)	Phencyclidine	25
Propoxyphene (PPX)	Propoxyphene	300
Tramadol (TRA)	Tramadol	100
Tricyclic Antidepressants (TCA)	Nortriptyline	1,000

N.B. EDDP is 2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine and MDMA is Methylenedioxymethamphetamine.

Amphetamines
Common cross-reactants: Prescription appetite suppressants such as Phentermine, other amphetamine-like prescription drugs; Ecstasy-like club drug called MDA (which is a metabolite of MDMA). In addition, there are several therapeutic agents, such as Benzphetamine, that metabolize to amphetamine (and methamphetamine) in the body and will produce positive drug test results. It is also important to note that amphetamine is a metabolite of methamphetamine and will appear in the urine of a person who has taken methamphetamine. The current GC/MS industry standard confirmation cutoff is 500 ng/ml. Proposed changes in SAMHSA are to lower the screening cutoff to 500 ng/ml, change target drug from D-amphetamine (historical) to D-methamphetamine and hange the GC/MS confirmation to 250 ng/ml. Outside USA, amphetamine screening cutoffs may be 300 ng/ml.

Barbiturates
Barbiturates are drugs that act as central nervous system depressants and can therefore produce a wide spectrum of effects, from mild sedation to total anesthesia. They have potential for both physical and psychological addiction. Recreational users report that a barbiturate high gives them feelings of relaxed contentment and euphoria. Physical and psychological dependence may also develop with repeated use. Other effects of barbiturate intoxication include drowsiness, slurred speech and ataxia, decreased anxiety and a loss of inhibitions. Barbiturates are also used to alleviate the adverse or withdrawal effects of illicit drug use, in a manner similar to long-acting benzodiazepines such as diazepam and clonazepam. Drug users tend to prefer short-acting and intermediate-acting barbiturates. The most commonly abused are amobarbital (Amytal), pentobarbital (Nembutal), and secobarbital (Seconal). A combination of amobarbital and secobarbital (called Tuinal) is also highly abused. Short-acting and intermediate-acting barbiturates are usually prescribed as sedatives and sleeping pills. These pills begin acting fifteen to forty minutes after they are swallowed, and their effects last from five to six hours. Slang terms for barbiturates include barbs, bluebirds, dolls, wallbangers, yellows, downers, goofballs, sleepers, 'reds and blues' and tooties.

Benzodiazepines
Benzodiazepines are a large "class" of drugs used primarily for sedation and anxiety relief. Group includes diazepam (Valium), chlordiazepoxide Librium), alprazolam (Xanax), and clonazepam (Klonopin). Most benzodiazepines are prescription use, but some benzodiazepines are diverted for illegal consumption. Common cross-reactants: Sertraline (Zoloft). NOTE, given the large number of benzodiazepine drugs (35+), be aware that GC/MS labs will not be able confirm for all of them, but SureScreen's test will find them all. NOT A SAMHSA-regulated drug, screening cutoff: 300 ng/ml or 200 ng/ml while GC/MS confirmation cutoffs vary but usually range from 100-200 ng/ml. Again, GC/MS labs are limited by the number of benzodiazepines they identify on their GC/MS analyses, usually looking for Oxazepam.

Cocaine
Cocaine is rarely prescribed. Cocaine is extensively metabolized in the body to benzoylecgonine, ecognine methyl ester and ecognine. There are no known cross-reactive compounds with urine-based cocaine immunoassays but SureScreen's tests are very sensitive to low levels of benzoylecgonine in urine. Current US SAMHSA "screening" cutoff: 300 ng/ml, current GC/MS (industry standard) confirmation cutoff: 150 ng/ml of benzoylecgonine. Proposed changes in SAMHSA are to lower the screening cutoff to 150 ng/ml and GC/MS confirmation level to 100 ng/ml of benzoylecgonine.

Clonazepam (Klonopin)
Clonazepam is a benzodiazepine drug having anxiolytic, anticonvulsant, muscle relaxant and hypnotic properties. It is marketed predominantly under the trade name Rivotril. Clonazepam has an intermediate elimination half life of 18–50 hours, making it generally considered to be an intermediate-acting benzodiazepines. However, there are many drawbacks to clonazepam, including drowsiness and "paradoxical effects". "Paradoxical effect" is a reaction to a drug that has the opposite effect that was intended. An example is when a drug is supposed to decrease pain but instead increases pain. Additional short comings of clonazepam include a rapid tolerance, interference with fine motor skills, confusion, psychomotor agitation, loss of libido, short-term memory loss and hallucinations.
Clonazepam addiction happens relatively quickly, due in part to long half-life and highly addictive characteristics. Aspects of social pressures, stressful situations from work or self-medicating to avoid the pain of a trauma are often reasons of abuse. Often, clonazepam is used in conjunction with an assortment of other illicit drugs. This increases the likelihood of developing an addiction to other drug or alcohol types. Clonazepam is also known as Klonopin, K-pins, pins, K-cuts, Rivotril, Clonex, Paxam, and Kriadex.

Cotinine
Often the test of choice when looking for nicotine use or exposure. In urine, values between 11 ng/mL and 30 ng/mL may be associated with light smoking or passive exposure, and levels in active smokers typically reach 500 ng/mL or more. In saliva, values between 1ng/ml and 30 ng/ml may be associated with light smoking or passive exposure, and levels in active smokers typically reach 100 ng/ml or more. Cotinine assays provide an objective quantitative measure that is more reliable than smoking histories or counting the number of cigarettes smoked per day. Cotinine also permits the measurement of exposure to second-hand smoke (passive smoking).

Ketamine
Ketamine is a medication used mainly for starting and maintaining anaesthesia. Other uses include sedation in intensive care, as a pain killer, and as an antidepressant. It induces a trace like state while providing pain relief, sedation, and memory loss. Heart function, breathing and airway reflexes generally remain functional. Common side effects include a number of psychological reactions as the medication wears. This may include agitation, confusion and psychosis among others. Elevated blood pressure and muscle tremors are relatively common under the influence. Pharmacologically, ketamine is classified as an NMDA receptor antagonist, but it also acts at numerous other sites (including opioid receptors and monoamine transporters). Like other drugs in its class, such as phencyclidine (PCP), it is classified as a dissociative agent. Ketamine was reportedly used as a drug rape drug in the early 2000s, and found in donor's samples which were tested in SureScreen's laboratories.

Marijuana, Cannabis (THC)
THC (tetrahydrocannabinol) is a hallucinogenic, sedative drug considered the primary active compound of the 400+ chemicals in the *cannabis sativa* plant. While there is some legal use of THC, most THC drug test positives are the result of illicit use. Marijuana is the number 1 illegal drug in most countries. THC breaks down extensively in the body; most common metabolite is THC-COOH. This metabolite is also referred to as "carboxy-THC" or "THCA." The consumption of Sustiva (efavirenz), an HIV treatment drug, is known to produce metabolites that cross-react on many THC assays. Consumption of Hemp oil will not give a positive. The SureScreen test is considered "very sensitive" to low levels in urine. Current US SAMHSA "screening" cutoff: 50 ng/ml and GC/MS (industry standard) confirmation cutoff: 15 ng/ml of THC-COOH. No proposed changes to cutoffs in SAMHSA.

EDDP
EDDP is the most important metabolite of methadone. It is excreted in the bile and urine together with the other metabolite EMPD. EDDP is formed by N-demthylation and cyclisation of methadone in the liver. The part of the unchanged excreted methadone is variable and depends on the urine's pH value, dose, and the patient's metabolism. Therefore, detection of the metabolite EDDP instead of methadone itself is useful because interferences of the patient's metabolism are avoided. EDDP can be detected within 4 to 6 hours after use. It can be cleared by the body within 2 to 3 days after use.

Methadone
Methadone is an analgesic compound most commonly used to treat heroin/opiate addiction. In addition, the drug may be prescribed for pain relief. Patients prescribed methadone for opiate addiction are considered to be in "methadone maintenance." Patients in methadone maintenance are drug tested commonly to ensure they are (1) taking their methadone and (2) not taking heroin/opiates or other drugs. Methadone is found in urine as parent drug and as metabolites. The metabolites EDDP and EDMP are VERY different in structure from parent methadone, so they do not react with the drug test. SureScreen has a special EDDP test for those people who 'fast metabolise' methadone within 24 hours. Not a SAMHSA-regulated drug, common screening cutoff: 300 ng/ml, GC/MS confirmation 300 ng/ml.

Methamphetamine(s)
Methamphetamine is a stimulant drug that is very rarely prescribed, but there is a form (stereoisomer) of methamphetamine that is used in the Over-the-Counter Vick's Inhalers. Most positives are the result of illegal use; the drug is made illegally from pseudoephedrine. About 4-7% of a methamphetamine dose is broken down to amphetamine by the body. Common cross-reactants: are metabolites of Ephedrine, Ranitidine (Zantac), and MDMA. In addition, there are several therapeutic agents, such as Benzphetamine, that metabolize to methamphetamine (and amphetamine) in the body and could produce positive drug test results. It is also important to note that amphetamine is a metabolite of methamphetamine and will appear in the urine of a person who has taken methamphetamine. Current US SAMHSA cutoff: grouped together with Amphetamine(s) is 1,000 ng/ml. Current GC/MS (SAMHSA) confirmation cutoff is 500 ng/ml; MUST ALSO HAVE AT LEAST 200 ng/ml of amphetamine in the urine to report a viable "methamphetamine" positive. Proposed changes in SAMHSA are to change the screening cutoff to 500 ng/ml, change target drug from D-amphetamine (historical) to D-methamphetamine and change the GC/MS confirmation to 250 ng/ml; amphetamine must still be present in the urine "around cutoff" to report a methamphetamine positive GC/MS result.

MDMA
Ecstasy (also known by its chemical name, MDMA) is often seen as the original designer drug because of its high profile links to dance music culture in the late 80s and early 90s. Clubbers took ecstasy to feel energised, happy, to stay awake and to dance for hours. The effects take about half an hour to kick in and tend to last between 3 to 6 hours, followed by a gradual comedown.

Morphine/Opiates
Opiates are a large "class" of drugs used legally for pain-relief (morphine) and cough suppression (codeine). Heroin (diacetylmorphine) is an illegal opiate made from the opium poppy. In addition to the primary opiates, "synthetic opiates" are often used in pain relief. The original intent of creating synthetic opiates was to increase pain relief tendencies and reduce likelihood of dependence; synthetic opiates include hydrocodone (Vicodan), oxycodone (Oxycontin), hydromorphone (Dilaudid). Most synthetic opiates do not cross react very well with morphine-based opiate tests. SureScreen has a special test for Oxycodone. Poppy seeds contain codeine/morphine and, as such, can cause a "true positive" opiate test. Current US SAMHSA "screening" cutoff: 2,000 ng/ml (300 in UK) and current GC/MS (industry standard) confirmation cutoff: 2,000 ng/ml (300 in UK) for codeine and/or Morphine. Opiate cutoff of 300 was the historical SAMHSA cutoff within USA. Codeine and heroin metabolize to morphine in the body. Codeine is also eliminated unchanged.

Oxycodone
Oxycodone is a semisynthetic opioid synthesized from thebaine, an opioid alkaloid found in the opium poppy. It is an analgesic generally used for relief of moderate to severe pain. It was developed in Germany during 1917 in Germany as one of several new semi-synthetic opioids in an attempt to improve on the qualities of existing opioids.

Phencyclidine (PCP)
Phencyclidine (PCP) is a hallucinogen drug originally made for anesthetic use. It was discontinued due to "negative side effects." There is no current legal use of the drug, so the existence of it can be attributed to recreational use. The use of PCP illegally is not that common, and in the UK many customers have chosen to routinely screen for methadone instead. PCP is liquid; marijuana joints are sometimes dipped into PCP ("sherm"). Cross-reactants are Venlafaxine (Effexor), Lamotrigine (Lamictal). Current SAMHSA "screening" cutoff: 25 ng/ml and GC/MS (industry standard) confirmation cutoff: 25 ng/ml

Propoxyphene
Propoxyphene (PPX) is a mild narcotic analgesic found in various pharmaceutical preparations, usually as the hydrochloride or napsylate salt. PPX is a prescription narcotic analgesic structurally related to methadone, sold as Darvocet, Darvon, Dolene, Novrad. Peak plasma concentrations are achieved from 1 to 2 hours post dose. The metabolite has a longer half-life (30 to 36 hours) than parent propoxyphene (6 to 12 hours). In November 2010 the FDA concluded that PPX caused "serious toxicity to the heart". Subsequently, the FDA requested that manufacturers discontinue production of the drug. Additional research indicates that morphine addicts were able to prevent withdrawal syndrome more effectively with 800-1200mg of PPX, even though these dose sizes fall within the toxic level threshold.

Tramadol
Tramadol, like other opiates, stimulates brain opioid receptors but it also increases brain serotonin levels. It is a medicine used to treat moderate to severe pain. It is only available with a prescription. Other opiates include codeine, methadone and heroin. Although tramadol is not as strong as heroin, it shares many of the same effects and both are addictive. Cause fatigue, drowsiness, loss of appetite, nausea and retching, diarrhoea, and dizziness or fainting. Worsen side-effects and risks when used with certain antidepressants that tend to increase serotonin levels.

Tricyclic Antidepressants
Whilst low instances are reported, TCAs are occasionally abused. The SAMHSA cut off is set at 100ng/ml.