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Interpretive Summary of Cross-Reactivity of Substances,
 Duration of Drug Detectability and Adulteration Testing/Specimen Validity Testing in
 Drugs of Abuse Screening Methods

CROSS REACTIVITY

Cross-reactivity of structurally similar substances is a problem associated with immunoassay methodologies, resulting in false positive or negative results. Screening technologies are predominantly immunoassay techniques which may prove high sensitivity but are of limited specificity. Manufacturers will test for common potential interfering substances and list these on the package insert, however it is not possible to test every compound. Also some compounds ingested in therapeutic dosage may not cross-react, however when abused in “mega” doses may significantly influence urine immunoassay results.

Listed below are potential reactants and cross-reactants with **most** immunoassay methodologies

Acetaminophen (see also Paracetamol)	Aceta, Acephen, Apacet, Dapacen, Feverall, Tylenol, Excedrin (combination), Panadol, Tempra	Non-reactive
Acetaminophen with Codeine (see also Paracetamol with codeine)	Tylenol 3, Tylenol with codeine	Positive for Opiates (OPI) Potential cross reactants: Dihydrocodeine
6-Acetylmorphine		Positive for Opiates (OPI)
Acetone		Non- reactive
Allobarbitol		Positive for Barbiturates (BAR)
Alphenol	No known trade names	Positive for Barbiturates (BAR)
Alprazolam	Xanax	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Amobarbitol	Amytal, Tuinal	Positive for Barbiturates (BAR)
	AMP: Adderall, Dexedrine,	Positive for Amphetamines/

Amphetamine/ Methamphetamine	Benzedrine M/AMP: Desoxyn, Didrex Eldepryl	Methamphetamines Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phentermine, Phenmetrazine, Ranitidine
Ampicillin	Penbritin, Polycillin, Principen	Non-reactive
Aprobarbital		Positive for Barbiturates (BAR)
Aspirin	Bayer Aspirin, Excedrin, ASA, Angettes, Asasantin, Caprin	Non-reactive
Barbital		Positive for Barbiturates (BAR)
Benzodiazepines	See individual Benzodiazepines listed	Potential cross reactants: Oxaprozin (Daypro), Sertraline
Bromazepam	Lexotan	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Brompheniramine	Dimetapp, Dimotapp, Dimotane	Non-reactive
Butabarbital	Butisol, Soneryl	Positive for Barbiturates (BAR)
Butalbital	Fioricet, Fiorinal	Positive for Barbiturates (BAR)
Butethal		Positive for Barbiturates (BAR)
Chlorazepate	Tranxene	Positive for Benzodiazepines (BZO)
Chlordiazepoxide	Librium	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Clobazam	Frisium	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Clonazepam	Clonopin, Klonopin, Rivotril	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Codeine Phosphate	Codafen Continus, Codeine Linctus, Pediatric BP, Galcodine, Kapake, Migraleve, Solpadol, Tylex	Positive for Opiates (OPI) Potential cross reactants: Dihydrocodeine
Co-Fluampicil	Magnapen	Non-reactive
Delorazepam	Briantum	Positive for Benzodiazepines (BZO)

Dexamphetamine Sulfate	Adderall, Adderall XR, Dexedrine	Positive for Amphetamine (AMP)
Diazepam	Diazemuls, Stesolid, Valclair, Valium	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Dihydrocodeine	DHC Continus, Paramol, Remedeine, Remedeine Forte	Positive for Opiates (OPI/MOR)
Doxylamine	Nyquil	Positive for Methadone (MTD)
Ecgonine		Positive for Cocaine (COC)
Ecgonine Methyl Ester		Positive for Cocaine (COC)
Efavirenz		Positive for Cannabinoids (THC) [Urinary metabolite only].
Estazolam	ProSom	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Ethylmorphine		Positive for Opiates (OPI) Potential cross reactants: Dihydrocodeine
Flunitrazepam	Rohypnol	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Hydrocodone	Lorcet, Loratab, Vicodin,	Positive for Opiates (OPI) and Oxycodone (OXY)
Hydromorphone	Dilaudid, Hydrostat	Positive for Opiates (OPI) and Oxycodone (OXY)
Ibuprofen	Brufen, Codafen, fenbid, Ibugel, Ibuspray, Motrin, Proflex	Non-reactive
Koalin and Morphine mixture	Diocalm, Entersan, Opazimes	Positive for Opiates (OPI)
Ketoprofen	Orudis, Oruvail, Powergel	Non-reactive
Lorazepam	Ativan	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Lormetazepam	Noctamide	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Medazepam	Anxitol, Lerisum, Medacepan, Nobritol, Nobrium	Positive for Benzodiazepines (BZO)
p- Methoxyamphetamine (PMA)		Positive for Methamphetamine (M-AMP) Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phenetermine, Ranitidine
Methadone, Hydrochloride	Dolophine, Methadose, Phisetone	Positive for Methadone (MTD)

d-Methamphetamine HCL	Desoxyn, Methedrine, Methamprex	Positive for Methamphetamine (M-AMP) Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phenetermine, Ranitidine
I-Methamphetamine HCL	Vick's Inhaler	Positive for Methamphetamine (M-AMP) Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phenetermine, Ranitidine
Methylenedioxyamphetamine (MDA)	Eve (slang), Love Drug (slang)	Positive for Amphetamine (AMP) Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phentermine, Phenmetrazine, Ranitidine
Methylenedioxymethamphetamine (MDMA)	Ecstasy (slang), XTC (slang), Adam (slang), E (slang)	Positive for Methamphetamine (M-AMP) and Ecstasy (MDMA) Potential cross reactants: Ephedrine, Pseudoephedrine, Phenylpropanolamine, Phentermine, Phenmetrazine, Ranitidine
Morphine	Astramorph, Cyclimorph, Duramorph, Morcap, Morphine Sulfate, MS Contin, Oramorph, Roxanol, Severedol	Positive for Opiates (OPI, MOR/MOP) Potential cross reactants: Dihydrocodeine
Naproxen	Aleve, Condrotec, Napratec, Naprosen, Naprosyn, Nycopren, Synflex	Non-reactive
Nicotine	Nicoderm, Nicorette, Nicotinell, Nicotrol, Niquitin	Non-reactive
Nitrazepam	Mogadon, Somnite	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Nordiazepam		Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Oxazepam	Serax, Ox-pam	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Oxymorphone		Positive for Oxycodone (OXY)
Penicillin	Combicillin, Mefoxin	Non-reactive

Pentobarbital	Nembutal	Positive for Barbiturates (BAR)
Phenobarbitone (see also Phenobarbital)	Luminal	Positive for Barbiturates (BAR)
Phenytoin	Dilantin, Epanutin, Epitard	Possible positive for Barbiturates (BAR). Urinary metabolite only.
Phenobarbital	Donnatal	Positive for Barbiturates (BAR)
Pholcodine	Galenphol, Strong BP, Pavacol-D, Thebacon	Positive for Opiates (OPI)
Procaine	Novocain	Non-reactive
Prazepam	Centrax, Demetrin	Positive for Benzodiazepines (BZO)
Pseudoephedrine	Afrinol, Sudafed, Tylenol Cold (combination)	Potential Positive for Amphetamine (AMP) and Methamphetamine (M-AMP)*
Quinidine		Non- reactive
Ranitidine	Pylorid, Zantac	Potential Positive for Methamphetamine (M-AMP). Urinary metabolite only.
Secobarbital	Seconal	Positive for Barbiturates (BAR)
Sertaline	Zoloft	Potential positive for Benzodiazepines(BZO).
Temazepam	Restoril	Positive for Benzodiazepines(BZO) Potential cross reactants: Oxaprozin (Daypro), Sertaline
Theophylline		Non- reactive
Triazolam	Halcion	Positive for Benzodiazepines (BZO) Potential cross reactants: Oxaprozin (Daypro), Sertraline
Tyramine		Non- reactive
(1R,2S)-(-)-N-Methyl-Ephedrine		Non- reactive

DURATION OF DRUG DETECTABILITY IN URINE AFTER USE

Drug	Duration
Amphetamines,	48 hours
Benzodiazepines	Highly variable
Cocaine	24-72 hours
Heroin/ Opiate, Oxycodone	24 hours
Marijuana THC - Cannabinoids	3-30 days
Methamphetamine	1-2 days

ADULTERATION TESTING/ SPECIMEN VALIDITY TESTING

Adulteration is the tampering of a urine specimen with the intention of altering the test results. The use of adulterants can cause false negative results in drug tests by either interfering with the screening test or destroying the drugs present in the urine. Diluting, flushing or adding adulterants to the sample after collection are ways that users of illicit drugs have attempted to defeat drug tests and invalidate the testing procedures. Diluting samples or adding household chemical such as detergents, bleach and soaps are some of the creative ploys that abusers have used to mask positive samples. Specimen tampering is very common in the United States and is expected to continue to grow in other areas of the world that use drug tests. There are many different types of adulterants; some are made to affect the test, others are made to affect the drug.

CREATININE (DILUTION):

Dilution is the most common type of adulteration. Dilution can be either “*in vivo*” (consuming excessive quantities of fluids in an attempt to dilute the urine) or “*in vitro*” (introducing liquid into a specimen that has already been collected). The intention of dilution is to make the concentration of drug in the urine lower than the detection limit (cutoff) of the test. Creatinine testing in conjunction with specific gravity testing is a good indication of dilution of the urine sample. The absence of Creatinine (<5 mg/dl) is indicative of a specimen not consistent with human urine.

SPECIFIC GRAVITY: (Less than 1.005):

Specific gravity tests for sample dilution. Values outside the normal range may be the result of specimen dilution or adulteration.

pH: (Less than 5.0 or greater than 8.0):

pH tests for the presence of acidic or alkaline adulterants in urine. Values outside the normal range may indicate that the specimen has been altered or spiked with acidic or alkaline compounds.

NITRITE: (Urinary tract infection):

Nitrite is a compound that is introduced into a urine specimen after collection. Nitrite works by oxidizing the major cannabinoid (THC-COOH) metabolite and making it undetectable. While this mechanism does work, the time needed for the reaction to occur is usually several hours. This means that after collection of the urine the rapid test maybe positive and when the sample is tested at the laboratory the nitrate will have modified the THC metabolite making it undetectable. Some commonly used commercial adulterants that contain nitrates are “Klear, Whizzes, Mary Jane 13”. Nitrites are sometimes found in people with urinary tract or bacterial infections.

GLUTARALDEHYDE:

Glutaraldehyde is an older adulterant that is introduced into the urine specimen after collection. It is not believed to affect the performance of lateral flow tests. Glutaraldehyde denatures the enzyme used in EMIT-like autoanalyzer reagents. Adulterants such as UrinAid and Clear Choice contain glutaraldehyde. Glutaraldehyde is not normally found in urine. However certain metabolic abnormalities such as ketoacidosis (fasting, uncontrolled diabetes, high-protein diets) may interfere with the test results.

OXIDANTS/PYRIDINIUM CHLOROCHROMATE (PCC):

Like nitrite, oxidants and PCC are introduced into a specimen after collection and are primarily meant to alter the structure of THC-COOH. Some commonly used oxidants are bleach, hydrogen peroxide and Urine Luck. Normal human urine should not contain oxidants or PCC. The presence of high levels of antioxidants in the specimen, such as ascorbic acid, may result in false negative results.