Toxicological Interpretation

is a post-testing, non-laboratory process whereby the significance of test findings is examined in relation to the context of the case. Variables such as, but not limited to specimen source, collection, timing, custody, maintenance, availability and condition can affect the interpretation of otherwise scientifically accurate and reliable test findings.

But then again, it could mean something else.

Toxicological Interpretation is the evaluation of toxicological test findings and represents a tool for establishing what drugs or combination a subject may have ingested and the degree of impairment the subject may have experienced following such ingestion. Interpretation of toxicological findings requires knowledge of both **pharmacokinetics** (what the consumer does to the drug - absorption, distribution, metabolism and elimination) and **pharmacodymanics** (what the drug does to the consumer – therapeutic effect, impairment, intoxication, death).

Drug distribution throughout the body is a complicated process. It is based upon many factors, including but not limited to the physical and chemical properties of the drug, the formulation of drug, the means by which the drug was ingested (oral, intravenous, inhalation, etc.) and the digestive (for oral ingestion) and circulatory functions of the subject. **Therapeutic doses** of drugs are those amounts which are prescribed for intended medicinal or therapeutic purposes and which are to be ingested pursuant to a prescribed manner and frequency. Therapeutic doses will result in a range of drug concentrations within the body intended to exert an expected assortment of medicinal or therapeutic effects on the subject. While unintended (side) effects may be manifest, such effects are expected to be minimized.

Non-therapeutic ingestion may occur when drugs are ingested in excess, which will result in **supratherapeutic** (above therapeutic) concentrations and have potentially toxic or in the extreme, lethal consequences. For example, prescribed doses of depressant drugs are intended to relieve anxiety but, as their doses increase, will cause inattention, incoordination, lethargy, stupor, coma, respiratory depression and death from asphyxia. Non-therapeutic ingestion may also include a manner or frequency not prescribed. This may include multiple drug combinations, repeated ingestion and subversion of the formulation. An example of the latter is where a drug formulated for oral, sustained release is crushed and insuflated (snorted) or dissolved and injected intravenously. Conversely, drugs ingested at insufficient or low doses will result in **subtherapeutic** (below therapeutic) concentrations and have minimal or no apparent effect.

Interpretation of toxicological findings begins with an understanding of which drugs and concentrations are therapeutic and which are not. Substances progress from innocuous to therapeutic to toxic depending upon the dose. This is due to the exacerbation of intended plus unintended (side) effects. Accordingly, a substance may be both medicinal and harmful, depending upon how much is ingested and by what means. "All things are poison and nothing is without poison, only the dose permits something not to be poisonous." Or "The dose makes the

poison." Paracelsus (Phillippus Aureolus Theophrastus Bombastus von Hohenheim), 1493 - 1541 <http://www.newworldencyclopedia.org/entry/Paracelsus>

The presence of one or more drugs at concentrations significantly higher than those expected from therapeutic doses may be considered, along with anatomical conditions or defects, in determining whether drug ingestion caused or contributed to death. Conversely, the lack of adequate drug in a subject may indicate non-compliance to therapy and allow for the conclusion that death was due to conditions that might otherwise have been survivable had the decedent been compliant with prescribed medication. An example of the latter is death from a seizure disorder controllable with anticonvulsant drugs.

Toxicological findings are used to assess or explain performance impairment relating to driving under-the-influence (DUI) of ethanol (alcohol) and/or drugs (DUID). Findings may also be used to establish drug/alcohol-related impairment in the actions, behavior or demeanor of a homicide victim or suspect, thereby, offering potentially mitigating circumstances when the case is adjudicated.

Drugs exert their pharmacological effects when they are present in a target organ or organ system that is susceptible to or affected by the substances which are present. The manifestation and/or toxicity of substances is the combination of all effects, intended and unintended.
For example, antidepressant drugs are intended to treat psychiatric disorders but may also cause cardiac arrhythmias when co-ingested with some other substances.

In order to establish impairment from toxicological findings, one must identify a relevant substance within a relevant specimen. A relevant substance is one that exerts pharmacological activity. A relevant specimen is one that reflects the drug status of a target organ.

Most ingested drugs are called "parent" drugs and are typically pharmacologically active. However, the body's normal metabolic processes act upon the ingested parent drugs and convert them into metabolites, which may keep or lose the pharmacological activity of the parent drug. Metabolites may co-exist with the parent drug or they may persist after the parent drug has been totally converted and/or eliminated. In the end, impairment may be established only if active substances are identified, be they parent drugs or metabolites.

That is not to say the identification of inactive metabolites is without value. Such toxicological findings may be sufficient to establish ingestion of or exposure to a related substance or to distinguish acute (single or short-term) from chronic (continuous or long-term) drug use.

The most significant target organs of forensic toxicological interest are the brain and nerves that comprise the central and peripheral nervous systems and the heart. Blood circulates within these organs and systems and as such, is the most recognized, relevant specimen for toxicological analysis. Urine is commonly collected for toxicological analysis. However, urine does not circulate within these systems so toxicological findings in urine cannot qualify as a

relevant basis for establishing impairment. **Substances in urine have been excreted and are no longer in "the system"**. Toxicological findings in tissues may be considered in postmortem cases only where sufficient scientific literature exists to relate such findings to death or impairment.

That is not to say the identification of substances in urine and tissues is without value. Such toxicological findings may be sufficient to establish ingestion of or exposure to a related substance or to explain certain observed performance or behavior, but not necessarily the reverse. Urine ethanol concentrations along with those in blood may be used to determine whether a subject's blood ethanol concentration is rising or falling. Tissues may be the only specimen available in cases of advanced decomposition.

When considering elevated blood drug concentrations as a contributing factor in death, one must consider that such concentrations may not remain static after death. Redistribution of some drugs may occur during the postmortem interval before specimens are collected for toxicological analysis. The result is potential non-uniform change in blood drug concentrations in different parts of the body. Furthermore, the blood matrix can change after death. Accordingly, drug concentrations in blood collected at different sites on the body may vary and what may appear as elevated may not necessarily reflect what existed at the point of death. Other uncertainties, such as whether the decedent was still absorbing a dose ingested shortly before death may also complicate determining whether said ingestion was indeed excessive and, therefore, contributory.

The effects of drugs (and ethanol, which is a drug) are continuous and progressive, which means manifestations generally increase with greater biological concentrations. Said concentrations are dependent upon the dose, the route of ingestion and the time since ingestion. However, the effects may present differently amongst individuals because impairment is the sum of all of the individual's mental and physical functional responses to drugs, both intended and unintended, which are not uniform. For example, with ethanol and depressant drugs, low concentrations will impair one's inhibitions, which may result in seemingly paradoxical excited behavior. With greater concentrations, this excitation gives way to inebriation. The point at which one subject is animated and another is lethargic, stuporous or dead depends upon variable biological characteristics and **tolerance**. Tolerance is (1) the resistance to some effects of drugs and (2) the physiological dependency on continued doses acquired through frequent and repeated exposure. Therefore, manifestations and outward appearances can be vastly different amongst individuals at any given dose.

While it is commonly said people respond differently to drugs (and ethanol), people ultimately respond the same; just to different degrees and at different doses.

There is a well-documented relationship between blood ethanol concentrations and accuracy of task performance. Specifically, as concentrations increase, the ability to properly operate a motor vehicle decreases and the likelihood of engaging in a traffic mishap increases. This relationship is reflected in the DUI *per se* laws. There is also a well-documented relationship

between blood drug concentrations and accuracy of task performance. However, because the degree of effects of drugs amongst individuals is so much more diverse than is with ethanol, definitive *per se* limitations are more difficult to scientifically establish and to legally apply. Some jurisdictions have zero-tolerance statutes for DUID whereas others employ the expertise of a toxicologist in Court to reconcile performance impairment with the presence of a drug or combination of drugs.

While laboratory findings are empirical, the specific effects of any individual finding or combination are holistic (require context).