Lesser and Lesser becoming Deadlier and Deadlier: Detecting Low Doses of Lethal Opioids

Introduction

In the global battle against the huge illicit drug trade, synthetic opioids are at best a moving target. The variety of synthetic drugs and their analogs continues to proliferate, creating a challenge to law enforcement and their analyzer equipment to continue to identify new substances in the field. Synthetic opioids such as fentanyl are relatively easy and inexpensive to create nowadays. And unfortunately, these drugs are becoming ever more potent, requiring less of the substance to deliver the same level of intoxication. As a result, overdosing, particularly by accident, is easier and more frequent than ever, and people are dying, not just because addicts may be taking too much of the drug intentionally, but in many cases because they don't know what they are taking, in reality.

Consider a comparison of heroin and fentanyl, both opioid drugs. Both are extremely potent, fast-acting, and can be lethal in as little as one dose. Heroin is derived from morphine, a natural substance that is removed from the seed of the opium poppy. Heroin is 25 times more potent than morphine and is distributed as a white or brown powder. Fentanyl, however, is a synthetic opioid that is 50-100 times more potent than morphine. Fentanyl is often manufactured in clandestine laboratories and is cheaper and easier to obtain than heroin; it is often used as a cutting agent or filler for heroin.

Carfentanil is a synthetic opioid much more powerful than fentanyl. Fentanyl is estimated to be 25–50 times stronger than heroin and 50–100 times stronger than morphine. About 2–3 milligrams of fentanyl can be lethal. That's roughly the size of 5–7 grains of salt. Carfentanyl, however, is estimated to be 100 times stronger than fentanyl, or 10,000 times stronger than morphine. As little as .00002 grams can kill a person.

Very tiny amounts of high-potency synthetic opioids like carfentanyl makes them easier to traffic, or as the concept is known today, micro-traffic, across a distribution network. Many agents transporting small, difficult to detect packets of a wide variety of potent, synthetic drugs is a more successful strategy than trying to smuggle bricks of a narrow range of drugs across a border as was done in the past. What is trending now, as far as the trend in the market goes, is that we are no longer seeing raw material, e.g., big bricks of fentanyl and cocaine and heroin coming over to be cut up by distributors in the United States, but rather, finished products in micro traffic quantities and distribution. The

business of narcotics has changed, and that pace continues to accelerate. Staying ahead of emerging trends and issues in the production, distribution and trafficking of narcotics is a prime focus of interdiction forces today including US Customs and Border Protection (CBP).

But consider that synthetic narcotics, made in a laboratory, are significantly more deadly and easier to manufacture as well as to develop than traditional naturally-derived drugs like morphine. They are also cheaper, so that fentanyl is added to heroin to increase its potency or may be disguised as highly potent heroin. Many users believe that they are purchasing heroin and actually don't know that they are purchasing fentanyl – which too often results in overdose deaths. The potency of synthetic drugs varies; it is inconsistent, based on whatever practices were in play at the illicit lab where the drug was manufactured, or the blending skills of the trafficker mixing up a batch. Quantities of substances in the mixture are constantly changing due to such things as price changes, or in accordance with what the manufacturer has access to. This unpredictable variability batch to batch is comparable to the drug user playing a deadly game of 'Russian Roulette.' Today's micro trafficking involves small quantities, with low doses of higher potency that offer a bigger high and are harder to detect.

Problems with detection

Sophisticated drug analysis instruments including the Thermo Scientific™ Gemini™ Analyzer have been primary tools in the hands of law enforcement for detecting and offering on-the-spot identification of substances in the field at interdictions. The Gemini analyzer is the world's only handheld instrument that incorporates both Fourier transform infrared (FTIR) and Raman spectroscopies in one unit. These two spectroscopies are complimentary techniques and enhance the ability of a user to identify unknown substances in the field. FTIR and Raman spectroscopy are excellent analytical techniques for identifying illicit drugs in pure form and in high concentrations in mixtures. These technologies are user-friendly and highly accurate, with editable libraries of hundreds of drug signatures stored in each unit for rapid and sure identification of drugs, analogs, and precursors.

However, in recent years the occurrence of low concentrations (1 - 10 wt%) of illicit drugs such as fentanyl, fentanyl analogs, and heroin in powdered mixtures and pills has risen. Detection of these drugs in lower concentrations with standard FTIR and Raman spectroscopies is difficult, because Raman and FTIR really are considered bulk detection capabilities, reliable for drugs in concentrations 10 wt%, but not as easy for concentrations below that. But now

that these drugs are being diluted so much and are such a small proportion of the total weight of the chemical that we're trying to identify, almost down to trace quantities, the technical capabilities of Raman and FTIR are at the edge of effectiveness. A bag of white pills containing carfentanyl in grain amounts might identify as acetaminophen, for example, yet contain enough carfentanyl in each pill to kill someone even though the amount is so small that the Gemini analyzer quite literally can't 'see' it.

LowDoseID: Gemini Keeping Ahead of Change

Lowering concentrations of powerful synthetic drugs in a given sample is pushing the envelope for the capabilities of the Gemini analyzer. To enable Gemini to accurately detect these lower drug concentrations in the field, Thermo Fisher developed LowDoseID™. This enhancement, operating like an upgrade, provides two new enhancements:

1. The ability to use the SERS (surface enhanced Raman spectroscopy) based H-Kit; and
2. The addition of a second Raman spectrum identification algorithm called Screener.

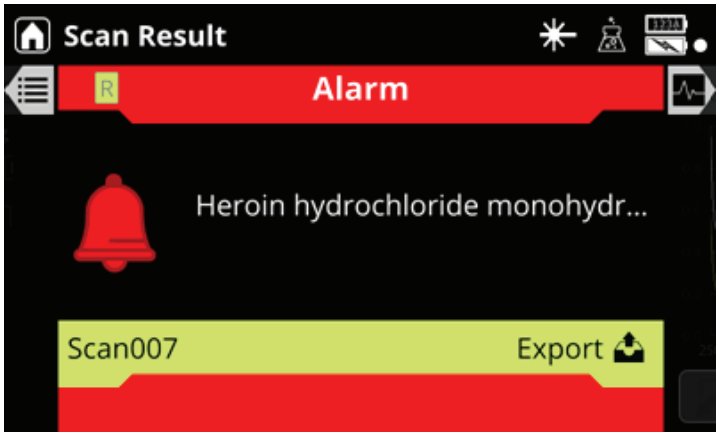
SERS, or Surface-enhanced Raman spectroscopy, also known as Surface-enhanced Raman scattering, is a technology that's been around for a while, but when combined with the existing capabilities of the analyzer, it suddenly makes it possible to regularly and reliably identify concentrations below 10 weight%, and in certain circumstances, chemicals down to 1% by weight in a given sample, which borderlines on trace capability. SERS requires handling and consumables, isn't as affective as mass spectrometry but doesn't have mass spectrometry's drawbacks, e.g., it's easy to use in the field. It's also arguably a better solution because it can do other jobs too, e.g., Bulk detection, and it is Anti-fluorescent.

SERS based H-Kit

SERS is an analytical technique whereby molecules of a substance are first absorbed onto the surfaces of nanostructures such as nanoparticles or roughened metal surfaces. The surfaces are typically gold and/or silver. These absorbed molecules can then show an enhanced Raman scattering signal when illuminated with the laser used in a typical Raman spectrometer. This enhanced signal can be several orders of magnitude larger than a "normal" Raman signal, thus allowing for the detection of low concentrations of illicit drugs in mixtures and pills.

Screener algorithm

In addition to the standard Raman spectrum identification (ID) algorithm found on the Gemini analyzer, Gemini with



LowDoseID now has a second Raman spectrum analysis algorithm called Screener. This algorithm is very similar to the one found in the Thermo Scientific ™TruNarc™ Analyzer; developed for identifying both pure drugs and drugs in mixtures. In contrast to the standard ID algorithm which answers the question "What unknown substances are present in my sample?" the Screener algorithm answers the question "Is a substance of interest present in my sample?". The Screener algorithm can analyze both normal Raman spectra and SERS H-Kit spectra. The Screener algorithm uses an Alert Configuration file containing the substances that a user wants to screen for. The pre-loaded default Alert Configuration file contains approximately 600 common illicit drugs, drug precursors, and cutting agents. The user can develop their own customized file by modifying this default file. Substances can be moved between the classifications, added to the file from the instrument's 12,700+ item Raman factory library or from a user generated library. The Gemini Analyzer with

LowDoseID has more than 700 illicit drugs, including fentanyl, heroin, cocaine, methamphetamine, fentanyl analogs, synthetic opioids, phenethylamines, synthetic cannabinoids, and cathinones, within its Raman factory library. It also contains numerous precursors, and many different cutting agents.

Conclusion

Just because a synthetic drug is of low concentration in a given sample of material does not make it less deadly or dangerous. What it does instead is make it difficult to detect using even sophisticated analyzer equipment that is not designed to ferret out nearly trace quantities of highly potent synthetic opioids. With low concentrations of very toxic drugs becoming increasingly common, the Gemini Analyzer with LowDoseID is a valuable addition to the analytical detection and identification toolbox of law enforcement and border protection and will doubtless save lives.

Find out more at **thermofisher.com/gemini**

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