Fatal drug overdoses are a leading cause of accidental death, surpassing both motor vehicle and gun-related fatalities. The increase in the number of fatal drug overdoses is due primarily to illicit opioids. The opioid crisis has impacted crime laboratories across the United States, particularly in the seized drugs and toxicology disciplines, through significant increases in case submissions containing synthetic opioids. Another complicating factor is the analytical complexity of these cases. Synthetic opioids, along with cannabimimetic agents and novel synthetic substances, require additional time and financial resources to process and identify. As these substances are continually evolving, additional reference materials must be obtained, and new analytical procedures must be developed and validated to identify these compounds. ASCLD recognizes that laboratories must purchase additional instrumentation to support these additional and often more complex analyses. This report is provided to outline some of these instruments and their potential value in the analytical process.

### Controlled Substances

1. **General Analysis**: For each analytical technique employed, it is critical that the limitations of each instrument’s selectivity (ability to discriminate new compounds) are considered. It is important to consider data from multiple instrumental sources used in the analysis when considering structurally similar (isomeric) compounds.

2. **Gas Chromatography–Mass Spectrometry (GC-MS)**: GC-MS is a routine, reliable technique which has adequate selectivity for the identification of most compounds encountered in crime laboratories, but there are known limitations in selectivity for the differentiation of stereo and positional isomers. Mass spectrometry should be coupled with other instrumental data in these instances to fully determine which isomer is present. Defined data acceptance criteria, as well as the analysis of multiple reference materials where isomeric compounds exist, will facilitate discrimination of these compounds. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $100,000-$120,000.
3. **Gas Chromatography–Infrared Spectrometers (GC-IR):** Although infrared spectroscopy is excellent for differentiating isomer compounds that differ by their substitution pattern (e.g., ortho/meta/para ring substitution), samples commonly contain more than one drug compound. The low concentration levels of many novel synthetic opioids also contribute to difficulties in sample preparation for traditional FTIR analysis. Therefore, without sample cleanup and isolation, traditional FTIR becomes a less effective technique. Coupling a gas chromatograph to an infrared spectrometer allows for mixture separation and differentiation of isomers with various substitution patterns. This technique provides both retention times and infrared spectra to aid in identification. Both gas phase and solid phase infrared spectroscopy instruments are available and may be used for differentiating between positional isomers. Spectral resolution should be considered when selecting instrumentation. General cost range to implement this technology (including equipment, installation, training, support and maintenance) is estimated to be $100,000-$150,000.

4. **Soft Ionization Mass Spectrometry Techniques:** Unlike the type of ionization used in GC-MS systems, ionization techniques like electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), desorption ESI (DESI), and direct analysis in real time (DART), are atmospheric pressure ionization techniques that can be used in combination with different mass analyzers. DESI and DART require little to no sampling preparation steps, making them amenable to the fast screening of samples. The capabilities will depend on the type of mass analyzer interfaced with the ionization technique. Single-stage mass spectrometers (like quadrupoles) mainly offer molecular weight information. Ion-trap, triple quadrupoles, and linear trap mass analyzers, among others, offer multiple mass analysis stages and both molecular weight and structural information. High-resolution MS analyzers like time-of-flight (TOF), orbitraps, etc. produce exact mass analyses and elemental compositions, which can then be used to search against libraries of elemental compositions based on empirical formulas of known compounds. This provides excellent information as to which reference materials are necessary for confirmation analysis. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $150,000-$400,000, depending on the type of mass analyzer selected.

5. **Liquid Chromatography with Tandem Mass Spectrometry (LC-MS/MS):** The capability of the techniques described above (section 4 - triple quadrupole, TOF, ion trap mass spectrometers, etc.) may be further enhanced by interfacing with a liquid chromatography system, which offers excellent differentiation of compounds with identical molecular weights by time separation, soft ionization, and fragmentation of multiple components of a mixture. Additionally, due to its sensitivity and selectivity, LC-MS/MS is an excellent quantitation tool for many of these compounds. Though higher in cost, one distinct advantage of this instrumentation is the simultaneous qualitative analysis and quantitation of multiple drugs within the same sample run. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $350,000-$450,000.

6. **Nuclear Magnetic Resonance Spectroscopy (NMR):** NMR Spectroscopy gives structural information, including the functional groups present and the positions of atoms in molecules. This allows for the identification of compounds and isomers. More sample is required than for mass spectrometry or infrared spectroscopy, and it must be in a relatively pure form in a deuterated solvent. Despite these limitations, the selectivity of NMR for the determination of isomers is high. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $350,000-$450,000.
Toxicology

1. **General Analysis:** Although robust for general analysis, the current practices relying solely on immunoassays, GC/MS screening and GC/MS confirmation/quantitation are generally not sufficient to capture novel synthetic opioid compounds at the low concentrations seen in toxicology samples. For each analytical technique employed, it is critical that the limitations of each instrument’s selectivity (ability to discriminate new compounds) are considered. It is also important to consider data from multiple instrumental sources used in the analysis when considering structurally similar (isomeric) compounds.

2. **Liquid Chromatography with Tandem Mass Spectrometry (LC-MS/MS):** The capability of the techniques like a triple quadrupole mass spectrometer or ion trap mass spectrometer may be further enhanced by interfacing with a liquid chromatography system, which offers excellent differentiation of compounds with identical molecular weights by time separation, soft ionization, and fragmentation of multiple components of the analyte precursor ion into meaningful product ions. Additionally, these instruments tend to have significantly better sensitivity and selectivity. Further, LC/MS/MS is a valuable tool for quantitating many of these compounds. Though higher cost, one distinct advantage of this instrumentation is the simultaneous qualitative analysis and quantitation of multiple drugs within the same sample run. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $350,000-$450,000.

3. **High-Resolution Mass Spectrometry (HRMS):** HRMS allows for screening for accurate masses and the separation of poly-drug samples (when coupled with a chromatograph) for mass spectral data. This technique helps detect a very specific molecular ion. When an isomeric opioid compound is indicated, additional analysis of the sample via LC/MS/MS for identification of the molecular ion may be accomplished. HRMS also provides the ability to re-process previously acquired data files for the presence of new compounds without having to re-sample and extract the submitted sample. Though higher in cost, one distinct advantage of this instrumentation is the simultaneous qualitative analysis and quantitation of multiple drugs within the same sample run. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $400,000-$550,000.

4. **Automated Sample Preparation:** Automated sample preparation for toxicology methods (using robotic platforms) minimizes personnel time required for labor intensive sample extractions, and aids the analysis of complex biological matrices. Solid phase extractions, which add multiple reagents over time, are particularly amenable to automation, but other types of extractions may also be possible. Robotics can also minimize potential human error that can occur with multi-step processes. General cost range to implement this technology to include equipment, installation, training, support and maintenance is estimated to be $200,000-$350,000 depending on the matrix complexity or level of automation.

To further assist laboratories implementing new technology, ASCLD is developing a contact list of experts who have experience with the various instrumentation listed in this document. When developed, the contact list will be posted in the Member Only area of the ASCLD website. If you would like to volunteer or nominate another to serve as a contact, please email Director Linda Jackson at Linda.Jackson@ascld.org.