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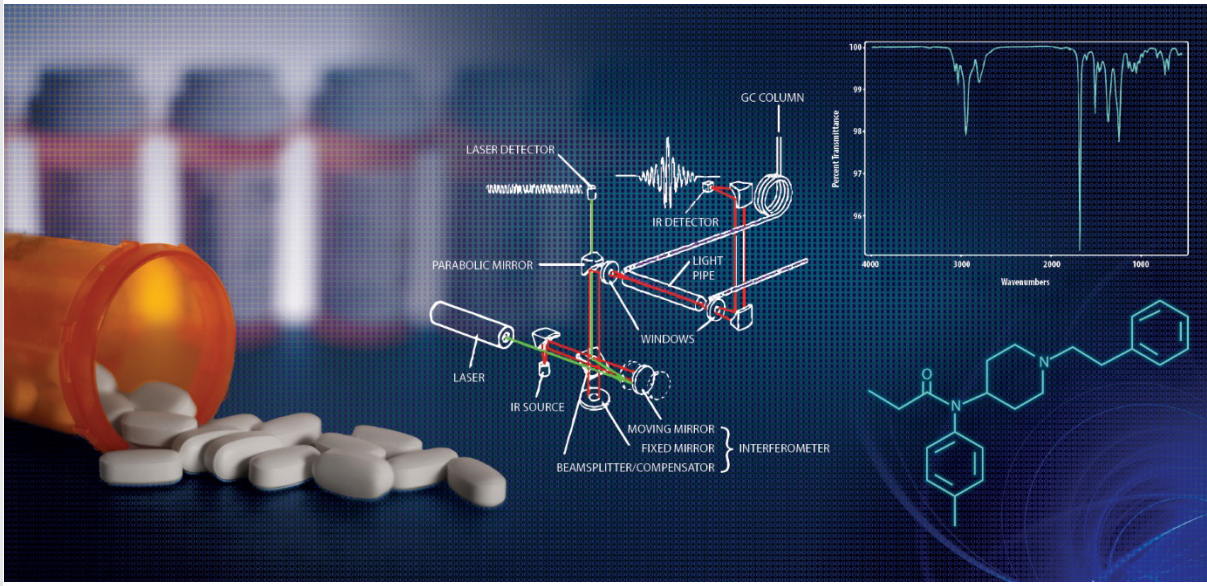
FTCOE Contact
Jeri Ropero-Miller, PhD, F-ABFT
Director, FTCOE
RTI International
jerimiller@rti.org

NIJ Contact
Danielle McLeod-Henning, M.F.S.
Physical Scientist
Office of Investigative and Forensic Sciences
danielle.mcleod-henning@usdoj.gov

Technical Contacts
Jeannette M. Perr, PhD
Drug Enforcement Administration
Jeannette.M.Perr@dea.gov

José R. Almirall, PhD
Professor Emeritus, Dept. of Chemistry and Biochemistry
Florida International University
almirall@fiu.edu

The Forensic Laboratory Needs Technology Working Group (FLN-TWG), formed by the National Institute of Justice (NIJ) in partnership with the Forensic Technology Center of Excellence (FTCOE) at RTI International, created this document in support of NIJ's mission to improve knowledge and understanding of federal, state, local, and tribal forensic science service providers' (FSSPs') technology needs.



TECHNICAL NOTE
Gas Chromatography Vapor-Phase Infrared Spectroscopy (GC-VIR)

Introduction

Seized drug samples are commonly analyzed using gas chromatography-mass spectrometry (GC-MS) and infrared spectroscopy (IR). These techniques are robust, well integrated into forensic laboratories, and familiar to analysts. Although commercial MS and IR libraries are readily available,[1; 2] GC-MS and IR may not be sufficient for the identification of new psychoactive substances (NPS),[3] even with libraries of known reference materials. Analytical limitations, such as similar fragmentation patterns from structural isomers[4] and polymorphism from various crystallization forms,[5] have been encountered. Complementary and alternative instrumentation to GC-MS and IR may be needed by forensic laboratories to meet the analytical challenges posed by NPS.

Gas chromatography infrared spectroscopy (GC-IR), first introduced in 1964,[6; 7] is a combination of a Category B technique coupled to a Category A technique as defined by the Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) recommendations[8] and ASTM E2329-17 Standard Practice for Identification of Seized Drugs.[9] GC-IR combines the separation capabilities of GC with the discrimination power of infrared spectroscopy for approximately the same cost as traditional GC-MS instrumentation.

GC-IR encompasses both vapor-phase infrared spectroscopy (GC-VIR), which is the focus of this report, and solid-phase infrared spectroscopy. Three interface types between the GC and IR detector exist:

matrix isolation (MI) and direct deposition (DD), which are solid-phase IR techniques and light pipe (LP), which is a VIR technique. The MI and DD interfaces have greater sensitivity compared to LP, while LP allows for real-time detection as the compound elutes from the GC. Polymorphism may occur during recrystallization of the condensates in solid-deposition interfaces but will not occur with the LP interface as the eluate remains in the vapor phase.

Solid-deposition interfaces, such as MI and DD, use a trapping medium to concentrate the GC eluate for detection offline. Each GC eluate in an MI interface is trapped within an argon matrix that is then condensed on a moving metallic substrate for measurement. Each GC eluate in a DD interface is condensed directly without a matrix onto a moving metallic substrate for measurement.

The LP interface passes the GC eluent into a light pipe providing real-time detection of eluates. The LP is heated (250 °C–280 °C) within a gold-coated borosilicate glass flow cell with KBr windows at both ends of the cell that allow light to pass through for detection. A makeup gas of nitrogen accounts for the greater internal diameter moving from the GC column to the flow cell.

GC-VIR provides separation and confirmation by generating functional group and structural information. Additionally, GC-VIR is capable of distinguishing structural isomers and diastereomers as well as eliminating polymorphs through VIR detection. Examples of a vapor-phase LP spectrum and a solid-deposition spectrum for para-methylfentanyl acquired at the same resolution are provided in **Figure 1.**

GC-VIR was not widely used until 30 years after the initial introduction[10] when improvements in sensitivity, dynamic detection range, quantitation, real-time detection, and library availability approached that of GC-MS.[11] Although GC-VIR differentiates positional isomers, this technique is less sensitive than GC-MS[4] with mass loadings of more than 25 ng on column for production of acceptable spectra in comparison to sub-ng mass loadings needed for a typical GC-MS analysis.[12; 13] Sample preparation for GC-VIR is similar to GC-MS, reducing process changes within the forensic laboratory.

Exhibit 1 summarizes the approximate cost, analysis time, and cost-saving considerations for GC-VIR instrumentation. GC-VIR instrumentation costs ~$120,000 compared to ~$100,000 for GC-MS instrumentation. However, GC-VIR typically results in unique spectra, even for positional isomers,[14; 15] that can help address current analytical challenges.

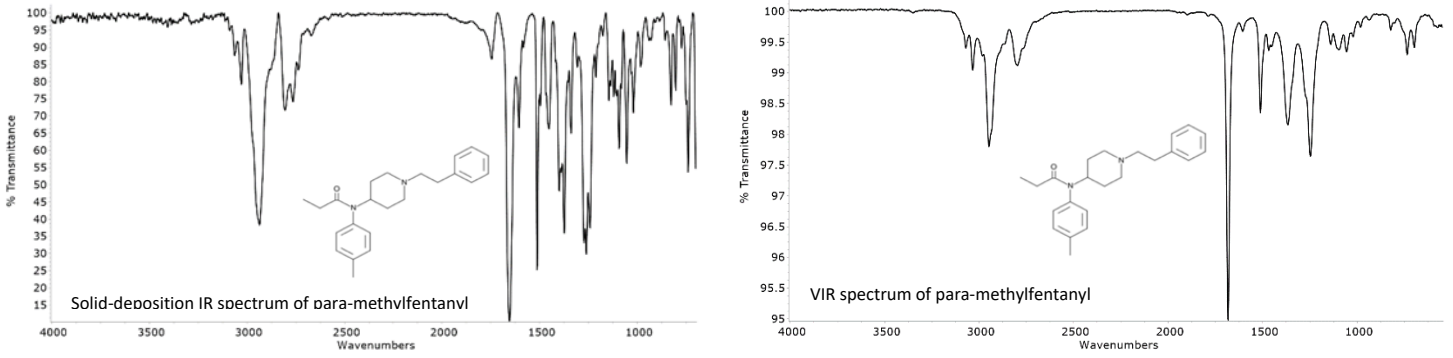


Figure 1. Comparison of a solid-deposition IR spectrum of para-methylfentanyl (deposited at ~25 °C) on the left and a VIR spectrum of para-methylfentanyl (collected at a LP temperature of 250 °C) on the right. Note: The solid-phase spectrum was provided courtesy of the Virginia Department of Forensic Science.

Exhibit 1. Summary of GC-VIR cost and analysis time considerations.

Initial Cost	Analysis Considerations	Cost-saving Considerations
~$120,000 for GC-VIR, including installation and training ~$275,000 for solid-state GC-IR	Same analysis time as a GC-MS method after cooling the detector. Liquid nitrogen is required to cool the detector	Adding VIR to a GC - ~$86,700 Adding VIR to a GC-MS - ~$97,550 These estimates include installation and training

GC-VIR has been reported for the identification of fentanyl related substances,[16; 17] isomeric ethoxyphenethylamines and methoxymethcathinones,[18] methylenedioxybenzyl-piperazines and methoxymethylbenzylpiperazines,[19] and methamphetamine and regioisomeric substances.[20] Cathinones, cannabinoids, and fentanyl related substances are common polymorphs and present positional isomers that may exist at low levels in complex matrices necessitating a separation technique and confirmatory detection technique—an ideal GC-VIR application.[21] VIR spectra are essentially independent of the instrument used for their measurement, simplifying the comparison of results between infrared libraries, with several emerging seized drug VIR libraries already available.[14; 22; 23]

Capabilities

GC-VIR enables the separation of complex mixtures while also maintaining laboratory GC sample preparation procedures as a SWGDRUG and ASTM 2329-17 Category B technique. The IR detector provides structural information as a SWGDRUG and ASTM 2329-17 Category A technique based on rotational and vibrational amplitudes between molecular bonds allowing for discrimination of positional isomers. The structural information acquired by IR spectroscopy is complementary (and often orthogonal) to the information acquired by mass spectrometry. While manufacturers offer solid-deposition and vapor-phase detector options, vapor-phase offers the advantages of ease of use and overcomes polymorphism. Although solid-deposition offers improved sensitivity, VIR resolution can be optimized for separation or sensitivity by decreasing or increasing the scan rate, respectively. Software enabling data interpretation and library creation is also available. Publicly available VIR libraries for seized drugs are emerging,[14; 22; 23] and VIR spectra are equivalent from instrument to instrument reducing the need for multiple infrared libraries.

Limitations

GC-VIR is not as sensitive as GC-MS by an order of magnitude.[14] However, increasing the sample concentration and decreasing the split ratio or switching to splitless injection mode will partially overcome this issue, although lower sensitivity may remain an issue when working with minor components within a mixture requiring additional sample preparation considerations. Implementing an additional instrumental technique into routine laboratory workflows (i.e., GC-VIR) requires additional acquisition, maintenance, training, and operational costs. Helium is commonly used although the cost of helium has dramatically increased because of decreasing availability. Hydrogen is not recommended as a carrier gas with GC-VIR due to the sensitive components of the LP interface. Nitrogen carrier gas results in longer analysis times and is not commonly used.

Installation needs

GC-VIR has modest acquisition and installation requirements —about $120,000 for GC-VIR compared to about $100,000 for GC-MS. GC-VIR instrumentation requires a source of liquid nitrogen to cool the detector and a source of nitrogen makeup gas, in addition to the chosen carrier gas.

Vendor considerations

At least two major and established vendors have an installed base of more than 20 instruments in the United States. The VIR detector can be procured and used with most GC vendors or retro fitted to existing GC instrumentation.

Space requirements

The GC-VIR instrumentation requires a physical footprint of 32” × 72” × 40”. Additional space and access for nitrogen makeup gas and carrier gas cylinders is also required. Access to multiple standard 120 V outlets is required. A power

stabilizer may be needed to produce optimal amperage/voltage for GC-VIR instrument conditions.

User training and skill level

The training and skill level for GC-VIR is comparable to GC-MS and Fourier transform infrared (FTIR) spectroscopy and may require software-specific training. Training will allow the examiner to easily process data for inclusion and review within the case file. Complimentary training sessions from the manufacturer may come with the purchase of a GC-VIR system or add-on IR detector. Additional training materials, references, validated methods, and standard operating procedures are publicly available (see early adopting laboratories below in Exhibit 2).

Implementation needs

GC-VIR has successfully been implemented in casework by several forensic laboratories (see early adopting laboratories below in Exhibit 2). Resources such as validation studies,[14] searchable public libraries,[14; 22; 23] and data interpretation tools are readily available. The points of contact from the early adopting laboratories section (Exhibit 2) may be able to share guidance on reporting and testimony and required consumables.

Validated methods

Several publications have reported methods and at least two validation studies have been completed.[14] An assessment of method parameters has been documented.[24] The LP and transfer line temperature are optimized between a temperature range that is low enough to prevent condensation of GC effluent yet not as high to negatively affect the linear response of the mercury-cadmium-telluride detector and signal-to-noise ratio. GC-VIR resolution is routinely optimized between 4-8 cm^{-1} to balance chromatographic quality against sufficient IR spectral data. Carrier gas flow and oven programming is optimized for chromatography, analysis time, and signal-to-noise ratio of the components.

Searchable libraries

Publicly available GC-VIR libraries for seized drugs are emerging,[15,23,24] and VIR spectra are equivalent from instrument to instrument reducing the need for multiple IR libraries. Library data can be easily shared between laboratories.

Data interpretation

GC-VIR chromatograms and spectral data are similar to GC, GC-MS, and traditional FTIR instrumentation leading to similar data interpretation. The manufacturer's software typically includes data analysis tools to assist the forensic analyst.

Reporting and testimony

GC-VIR is widely accepted analytical instrumentation, so no additional testimony requirements are expected. The points of contact from the early adopting laboratories section (Exhibit 2) may be able to provide specifics of reporting and testimony for GC-VIR analysis of seized drugs.

Consumables

In addition to GC consumables, other consumables, such as liquid nitrogen, carrier gas, and nitrogen makeup gas must also be considered. The cost associated with the gases and liquid nitrogen will depend on the supplier.

Early adopting laboratories

Exhibit 2. Point of contact information from early adopting laboratories that have implemented GC-IR into casework. This list may not be exhaustive but is intended to highlight points of contact for those interested in GC-IR implementation. Unless noted, contacts have implemented GC-VIR.

Laboratory	Point of Contact	Email	Phone Number
Drug Enforcement Administration Special Testing and Research Laboratory	Sherri Tupik	Sherri.L.Tupik@dea.gov	(571) 776-1866
Drug Enforcement Administration Southeast Regional Laboratory	Agnes Winokur	Agnes.D.Winokur@dea.gov	(786) 459-0114
Oklahoma State Bureau of Investigation	Mistie Burris Kevin Kramer	Mistie.Burris@osbi.ok.gov Kevin.Kramer@obsi.ok.gov	(405) 330-6724

Laboratory	Point of Contact	Email	Phone Number
Montana Department of Justice	Misty Icard Brook Knapp	MIcard@mt.gov Brook.Knapp@mt.gov	(406) 255-1104 or (406) 255-1105
*Virginia Department of Forensic Science	Stephen Hokanson	steve.hokanson@dfs.virginia.gov	(540) 283-5928
Pinellas County Forensic Laboratory	Reta Newman Michael Gilbert	rtnewman@co.pinellas.fl.us mgilbert@co.pinellas.fl.us	(727) 582 6810

*GC-DD only

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