# **History of Forensic Mass Spectrometry**

### Introduction

ass spectrometry (MS) has long held respect in the forensic community,<sup>1-3</sup> and contemporary legal critiques of forensic science agree that MS is "the near universal test for identifying unknown substances" and one of the gold standards of instrumental analysis.<sup>4</sup> Still, the MS community recognizes that even 'gold standards' have their limitations and must be fit for purpose.<sup>5-8</sup> In the history of forensic MS, one of the first mass spectrometers in a forensic laboratory was in Birmingham, UK in 1973. Zoro and Hadley reported details of the workload of this first mass spectrometer in a fascinating summary in 1976 (see Table 1). The greatest proportion of cases involved

Number of cases	Type of case	
59	Illegal possession of drugs	
47	Suspicious death	
18	Explosives	
17	Arson	
10	Miscellaneous	
8	Administration of noxious substance	
7	Driving under the influence of drugs	
7	Malicious damage	
4	Documents	
2	Biology	

the analysis of drugs, both in bulk form and in human bodily fluids. Fast forward 55 years to the modern era, and according to the Office of Justice Statistics, drug identifications remain the most frequently submitted evidence request in a typical forensic laboratory.<sup>9</sup>

**Table 1.** Distribution of case types of the first year of operation (1973) of a mass spectrometer in the Home Office Central Research Establishment in Birmingham, UK.<sup>8</sup>

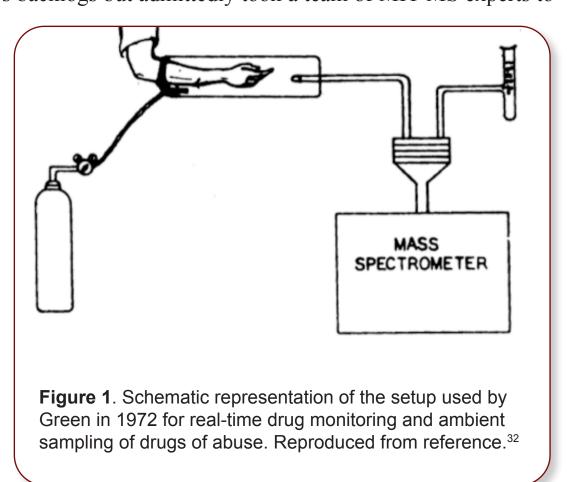
### **Drugs and Toxicology**

s described above, MS has found widest application in the analysis of drugs, drug metabolites and drug paraphernalia. In 1929, Bleakney developed the electron ionization (née impact) source for the analysis of gases and inorganic vapors.<sup>10</sup> He then extended the work to simple organics, like methane, in the late 1930s.<sup>11</sup> Although mass spectrometers were commercially available in the mid-1940s, they were big, expensive, oftentimes customized and difficult to operate.<sup>12</sup> Also, there was no guidance for interpreting the complicated spectra. Defying this latter problem, Beynon and McLafferty each contributed to the launch of organic MS in the mid-1950s.<sup>13-16</sup> From 1959 onwards, Biemann and Djerassi's groups were prolific in extending MS's capabilities to the analysis of natural products and botanical extracts, including various alkaloids, cannabis and cocaine.<sup>17-22</sup> At the Food and Drug Administration (FDA), in 1968, Martin and Alexander explained how they used high resolution MS (HRMS) and "cracking patterns" to help identify the hallucinogen dimethyltryptamine (DMT) in a casework sample.<sup>23</sup> They reported that "a problem that would have constituted a major research project a few years ago was reduced to an exercise problem in spectroscopic identification".

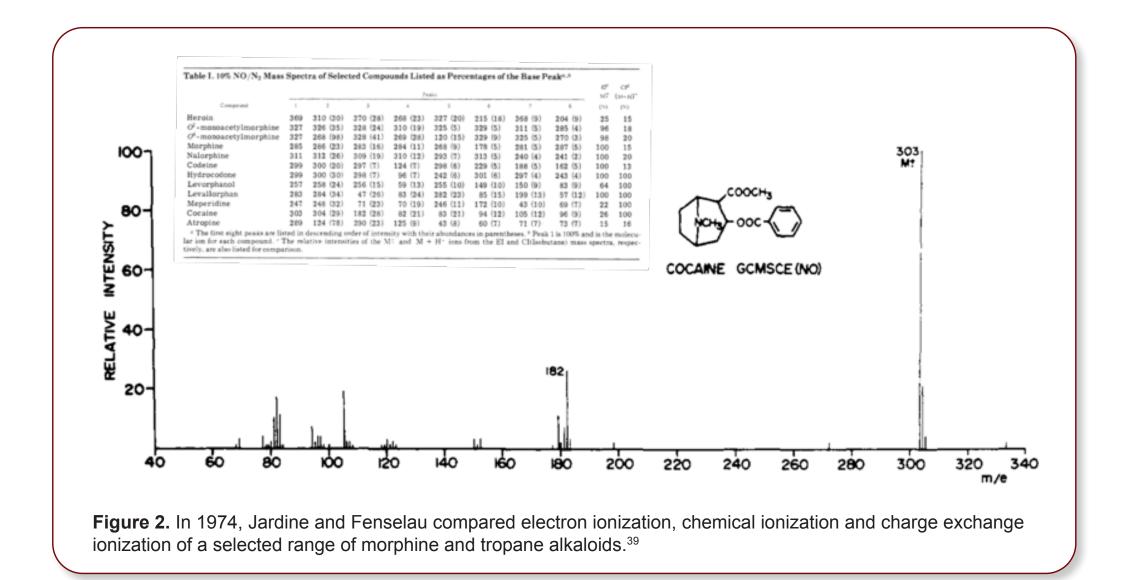
In 1968, Coutts and Locock reported on the characterization of eight common barbiturates and their mixtures in pills and capsules.<sup>24</sup> Between 1968-1970, Bellman and coworkers at the FDA reported on the analysis of several hallucinogenic drugs using MS.<sup>23, 25, 26</sup> These early applications included lysergic acid diethylamide (LSD), mescaline, psilocin and psilocybin, among others. Others quickly followed suit.<sup>27, 28</sup>

In 1970, Althaus et al. reported on the use of a gas chromatography-MS (GC-MS) system at Massachusetts Institute of Technology (MIT) to detect Darvon in stomach contents to solve a drug overdose case.<sup>29</sup> The case was apparently solved in about a day, which is a far cry from today's backlogs but admittedly took a team of MIT MS experts to

complete. By 1971, Fales' group at the National Institutes of Health (NIH) had solved more than 100 overdose cases using GC-MS and computerassisted database searching,<sup>30</sup> including the analyses of blood serum and stomach contents. In 1972, Skinner et al. reviewed the status of GC-MS for forensic toxicology.<sup>31</sup> In the same year, Green showed the potential of MS "fragmentography" to identify drugs from the headspace of drug samples, in pseudo real-time, with no sample preparation (besides dissolution in acid or base) (Figure 1).<sup>32</sup> He even showed the ability to detect alcohol in circulating blood in vivo (Figure 1)! Of course, the field of ambient sampling MS<sup>33</sup> has recently witnessed an enormous resurgence following the introduction of desorption electrospray ionization (DESI)<sup>34</sup> and direct analysis in real time (DART)<sup>35</sup> in the early 2000s.



In 1973, a Swedish team developed a GC-MS assay for  $\Delta^9$ -Tetrahydrocannabinol (THC) in human blood that was sensitive enough to detect if someone had smoked "one half-billionth of a gram".<sup>36</sup> The same year, Saferstein and Chao reported on the use of chemical ionization (CI)—which had been introduced by Munson



and Field in 1966<sup>37</sup>—to analyze drugs and drug mixtures.<sup>38</sup> By 1974, Jardine and Fenselau added charge exchange ionization to the analysis of drugs (Figure 2),<sup>39</sup> and many other groups were adding to the "forensic mass spectrometry" literature. Many early forensic applications were captured in Fenselau's comprehensive review of GC-MS in 1974.<sup>40</sup>

In 1977, MS data from the Environmental Protection Agency (EPA) was admitted as evidence in a case involving the detection of a pesticide known as tetrachlorodibenzo-p-dioxin (TCDD) in animal tissues from the Siuslaw National Forest.<sup>41</sup> The following year, a judge ruled to allow the MS test results as evidence in a capital murder case.<sup>42</sup> In 1978, GC-MS results were also admitted in a high priority case involving the American Meat Institute.<sup>43</sup> The concern was whether or not bacon had been adulterated by the addition of elevated levels of nitrosamines. MS was used in this case because it "is widely regarded as the best available technology".<sup>43</sup>



Designer Law for Designer Drugs: In 1986, the Controlled Substance Analogue Enforcement Act (CSAEA, 21 U.S. C. § 813) was signed into law to control compounds that were "substantially similar" to drugs

that were scheduled in the Controlled Substances Act (CSA) of 1970 (Pub. L. No. 91-513, § 202, 84 Stat. 1236). In 1992, United States v. Forbes (806 F. Supp. 232), a judge ruled that CSAEA's language was "unconstitutionally vague" and that alpha-ethyltryptamine (AET) was not substantially similar to the scheduled drugs dimethyltryptamine (DMT) or diethyltryptamine (DET). Instead of modifying the language, the DEA simply added AET to the list of scheduled drugs. In US v. Washam (2002, 312 F.3d 926), another judge found the language in CSAEA to be valid. Additional cases since 2003 have narrowed the language to include the "same core arrangement of atoms" test or the "structure and effect" test (e.g. *US v. Klecker*, 2003, 228 F. Supp. 2d 720).

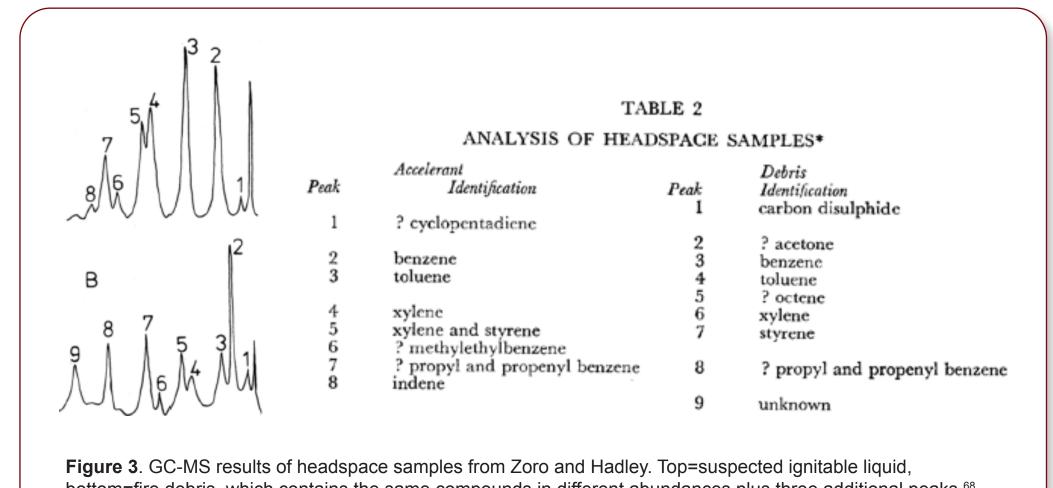
In the 1970s, a ruling was overturned thanks to the ability of negative CI-MS to detect dibromopropanol-a metabolite of the flame retardant Tris(2,3-dibromopropyl) phosphate (Tris-BP)—in childrens' urine.44, <sup>45</sup> In a review article on urinalysis in 1979, a probation officer named Bigger stated that although MS was "the most sensitive and specific technique available", it was "too expensive and too slow to be commonplace".<sup>46</sup> A survey of 100 crime labs in 1973 showed that mass spectrometers were the most desired piece of equipment, if unlimited funds were available,<sup>47</sup> and it only took a few years before GC-MS was commonplace in forensic laboratories.

Although Djerassi and others had analyzed various tropane alkaloids using MS in the 1960s and early 1970s,<sup>18, 48-50</sup> more than a dozen groups had contributed to the analysis of cocaine and its metabolites by the end of the 1970s.<sup>30, 38,</sup> <sup>39, 50-53</sup> However, Kondrat and Cooks were arguably the first to perform tandem mass analysis on cocaine in 1978.<sup>54</sup>

After the Controlled Substances Act of 1970, arguments continued over the need to distinguish harmless d-cocaine from the active drug, *l*-cocaine.<sup>55-58</sup> After some embarrassing problems with testimony about cocaine isomers,<sup>59</sup> one expert noted that *d*-cocaine "had also never been seen apart from *l*-cocaine".<sup>60</sup> Thanks to his testimony, we no longer have to identify the isomers of cocaine!

At the 1972 Olympics in Munich, GC-MS screening produced 7 adverse findings from 2079 tests of athletes' blood and urine.<sup>61,62</sup> The turnaround time averaged less than 24 hours per sample! Another major milestone was established in 1994 when Becchi et al. validated a method to distinguish exogenous from endogenous testosterone using GC-combustion-isotope ratio mass spectrometry (GC-IRMS).<sup>63</sup>





he composition of gunshot residue (GSR), also known as cartridge discharge residue<sup>69</sup> (CDR) or firearm discharge residue<sup>70</sup> (FDR), consists of the consumed and unconsumed particles from the primer and the propellant. The first tests used to determine whether or not someone had fired a gun by GSR was the paraffin test, which involved pouring hot paraffin wax—often painfully!—over a suspect's hand and conducting a color test on the cooled wax.<sup>71</sup> Because of the general unreliability of the color tests,<sup>72-75</sup> alternative elemental and mass spectrometric approaches were developed, including neutron activation analysis (NAA)<sup>76</sup>, graphite furnace atomic absorption spectroscopy (GFAAS),<sup>76</sup> GC-MS,<sup>77</sup> inductively coupled plasma-MS (ICP-MS),<sup>78</sup> liquid chromatography-tandem mass spectrometry (LC-MS/MS),<sup>79</sup> and DESI MS/MS.<sup>80, 81</sup> Whereas it was acceptable to use GC-MS in GSR cases in the 1980's,<sup>82</sup> the American Society for Testing and Materials (ASTM E1588-17) developed a standard in 1994 that recommended scanning electron microscopy/energy dispersive x-ray spectrosopy (SEM-EDS) to determine the presence of lead, antimony, and barium in the appropriate morphological particles; SEM-EDS remains the method of choice for GSR.<sup>83</sup>

As explained by Yinon in 1981—in his first of many books on the topic—the extreme sensitivity and selectivity offered by the mass spectrometer make it an ideal tool for the identification and forensic analysis of chemical explosives.<sup>84</sup> However, many explosives give no molecular ion by EI-MS, so much of the early work in the 1970s focused on chemical ionization.<sup>85-87</sup> Although mass spectrometers have been used as explosive detectors or "sniffers" since the 1970s,<sup>84</sup> they have only recently been identified by the National Research Council as desirable replacements for the considerably cheaper, but poorer resolution, ion mobility analyzers.<sup>88</sup>

A newer application to the field of forensics is the discrimination of explosives by using IRMS.<sup>89-95</sup> IRMS now meets Daubert criteria for admissibility,<sup>96</sup> and several reviews describe the huge variety of forensic applications of IRMS.<sup>97, 98</sup>

## ASMS History Committee Poster, 2020 Glen P. Jackson<sup>1\*</sup> and Mark A. Barkett<sup>2</sup>

<sup>1</sup>Department of Forensic and Investigative Science, West Virginia University <sup>2</sup>Dover Chemical Corporation

### Arson

n 1959, Joseph Nicol, a firearms technician at the Chicago police crime lab, suggested that crime labs at large Luniversities or oil companies could run GC-MS tests for high priority arson cases.<sup>64</sup> In 1976, Zoro and Hadley<sup>6</sup> published a review article that outlined the use of GC-MS for ignitable liquids (née accelerants) in place of GCflame ionization detection (GC-FID).<sup>66, 67</sup> Figure 3, from Zoro and Hadley's article, shows chromatograms of headspace samples of a suspected ignitable liquid and of the fire debris, the latter of which showed three additional compounds relative to the ignitable liquid.<sup>68</sup>

bottom=fire debris, which contains the same compounds in different abundances plus three additional peaks.<sup>68</sup>

### **Gunshot Residue (GSR) and Explosives**

### **Comparative Bullet-Lead Analysis (CBLA)**

The first successful attempt to match bullets with MS was in 1975 by Haney and Gallagher using spark source mass spectrometry (SSMS).<sup>99</sup> After the introduction of ICP-MS in 1980,<sup>100</sup> commercial instruments became a mainstay for trace metals analysis in just about every industry except the forensic community.

Because of problems with reporting the evidentiary value of CBLA, a court ruled CBLA by ICP-atomic emission spectroscopy (AES) to be inadmissible.<sup>101</sup> Although ICP-MS<sup>102</sup> and laser ablation (LA)-ICP-MS have the power to analyze sub-ppb level impurities, and even obtain isotopic analyses of trace elements, very few crime labs can afford the expense of these techniques.

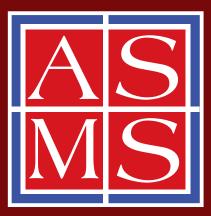
really applications of MS for hair analysis focused on the detection of trace-level inorganic impurities. Due to L'the low concentration of inorganic elements in human hair, only the most abundant elements could be studied. As early as the 1930s, scientists studied the concentration of iron in human hair using chemical extraction.<sup>103-114</sup> From the 1950s through the early 1960s, spectroscopic methods like flame atomic absorption (FAA) enabled the detection of the most abundant metals like iron and copper<sup>115-117</sup> and even mercury and lead exposure in cases of poisoning.<sup>118-120</sup> By the 1960s, NAA achieved new levels of detection for a few elements that were amenable to NAA.<sup>121</sup> In 1969, Yurachek et al. performed the first direct mass spectrometric study of trace elements in human hair using SSMS.<sup>120</sup>

Ion microprobe mass spectrometry (IMSS)—now secondary ion mass spectrometry (SIMS)—was first presented by Castaing and Slodzian 1962.<sup>122,123</sup> In its first forensic application, researchers at the McCrone Institute in 1977 used IMMS to link a strand of a suspect's hair with hairs found at a firebombed Planned Parenthood clinic. After several appeals, IMMS was found to be reliable, but its application to human hair ultimately failed to meet the admissibility criteria of the day "because the analytical technique used had not attained general acceptance in the scientific community, nor were the experiments conducted shown to be sufficiently reliable and accurate."<sup>124</sup>

In 1976, Zoro and Hadley described the application of pyrolysis mass spectrometry (Py-MS) to identify the presence of an antioxidant in the trace fragments of a polymer in a hacksaw to those of the stolen polymer-coated cable.<sup>68</sup> Pyrolysis-GC-MS (Pyr-GC-MS) was introduced to the forensic community by Saferstein et al. and Hughes et al. in their 1977 studies on man-made fibers and polymers.<sup>125, 126</sup> Since then, Pyr-GC-MS has also been applied to other trace polymeric materials, including binder, polymers and organic pigments in the automotive or architectural paints. In fact, such applications have been recommended by the support working group on materials analysis (SWGMAT) for more than 20 years.<sup>127</sup> Since the publication of these recommendations, methods such as LA-ICP-MS for trace metals in automotive paints<sup>128</sup> and IRMS for the analysis of white architectural paints have been applied with success, although not tested in court.<sup>97, 129</sup> Pyr-GC-MS is still commonly used in today's trace labs to study fibers and polymers.<sup>130</sup>

In 1978 Locke et al. demonstrated that SSMS could discriminate small glass samples,<sup>131</sup> and after Houck successfully coupled MS to ICP,<sup>132</sup> the forensic community slowly demonstrated the use of ICP-MS for the analysis of trace impurities in forensic glass samples.<sup>133-135</sup> By 2003, laser ablation (LA)-ICP-MS, which is now an ASTM standard,<sup>136</sup> was also demonstrated to be reliable for comparisons (trace) glass samples.<sup>137</sup>

APCI CBLA CI-MS CSA CSAEA DART DESI EA-IRMS EI-MS EDS EPA DMT FDA GC-MS GC-MS/MS GSR



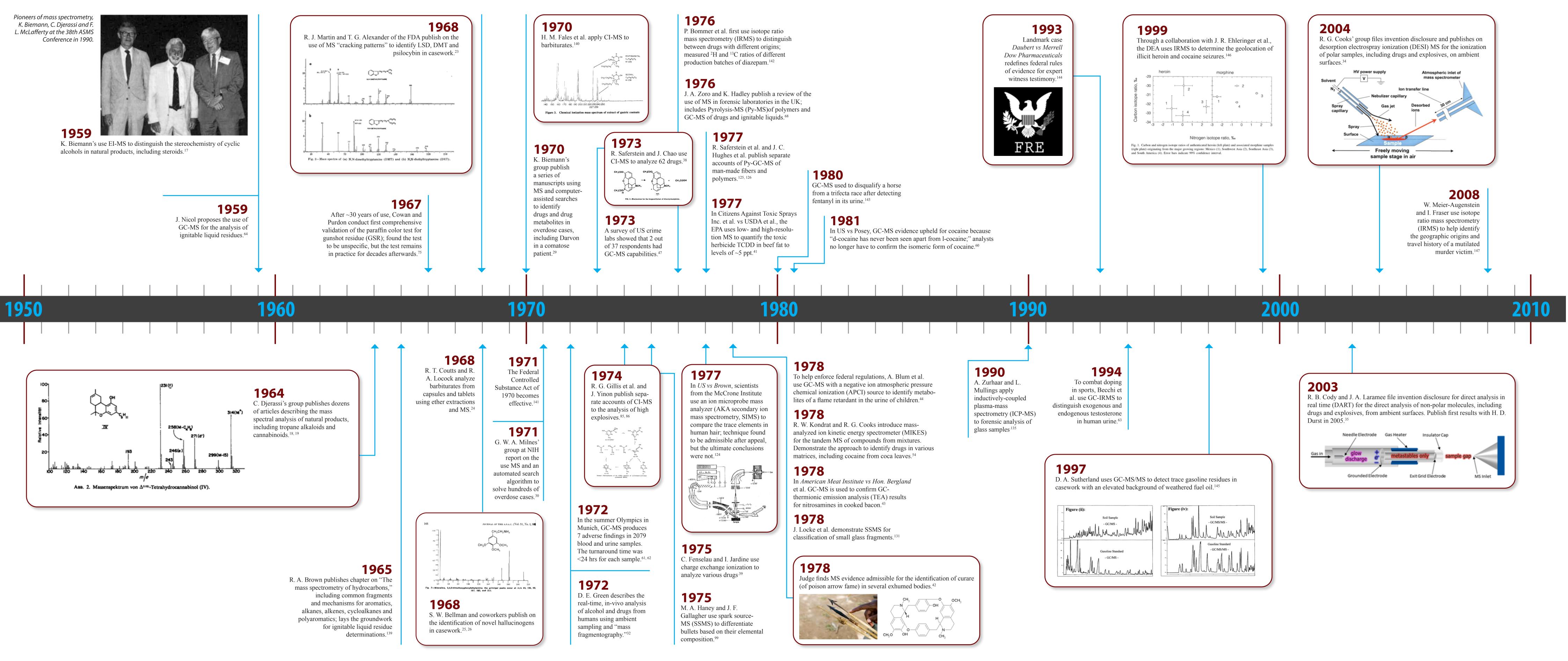
### **Trace, Fibers & Hair**

### Conclusion

Mass spectrometry has a long and essential history in the legal community and continues to provide some of the most reliable evidence in the forensic sciences. Although MS techniques have evolved dramatically over the years, there remains the perpetual problem of adequately supplying the finances and education required for forensic laboratories to possess and use the latest capabilities. These issues were identified in the 1950's<sup>64</sup> and 1970's,<sup>138</sup> and they are equally relevant today.<sup>4</sup>

Acronym Index			
Atmospheric Pressure Chemical Ionization	IMMA	Ion Microprobe Mass Analyzer	
Comparative Buller Lead Analysis	NIH	National Institutes of Health	
Chemical Ionization-Mass Spectrometry	ICP-MS	Inductively Coupled Plasma-Mass Spectrometry	
Controlled Substances Act	IRMS	Isotope Ratio Mass Spectrometry	
Controlled Substance Analogue Enforcement Act	LA-ICP-MS	Laser Ablation-ICP-MS	
Direct Analysis in Real Time	LSD	Lysergic Acid Diethylamide	
Desorption Electrospray Ionization	NAA	Neutron Activation Analysis	
Elemental Analyzer-Isotope Ratio Mass Spectrometry	PSAT	Pressure Sensitive Adhesive Tape	
Electron Ionization-Mass Spectrometry	Py-GC-MS	Pyrolysis-GC-MS	
Energy Dispersive X-Ray Spectrometry	Py-MS	Pyrolysis-Mass Spectrometry	
Environmental Protection Agency	SSMS	Spark Source Mass Spectrometry	
Dimethyltryptamine	SEM-EDS	Scanning Electron Microscopy/Energy Dispersive	
Food and Drug Administration		X-ray Spectroscopy	
Gas Chromatography-Mass Spectrometry	TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin	
Gas Chromatography-Tandem Mass Spectrometry Gunshot Residue	USDA	United States Department of Agriculture	

# History of Forensic Mass Spectrometry



## ASMS History Committee Poster, 2020 Glen P. Jackson<sup>1\*</sup> and Mark A. Barkett<sup>2</sup>

<sup>1</sup>Department of Forensic and Investigative Science, West Virginia University <sup>2</sup>Dover Chemical Corporation



ASMS History Committee Poster, 2020 Glen P, Jackson<sup>1+</sup> and Mark A. Barkett<sup>2</sup> Department of Forensic and Investigative Science, West Virginia University Part of Network Committee

### References for: History of Forensic Mass Spectrometry ASMS History Committee Poster, 2020

Glen P. Jackson<sup>1\*</sup> and Mark A. Barkett<sup>2</sup>

<sup>1\*</sup>Department of Forensic and Investigative Science, West Virginia University, Morgantown, WV, USA, 26506; t 304-293-9236; e glen.jackson@mail.wvu.edu
<sup>2</sup>Dover Chemical Corporation

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