An investigation into the application of a continuous screening, confirmation, and feedback cycle for the identification of synthetic cannabinoids in prisons

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Abstract

Synthetic cannabinoids are extremely commonplace within the prison system and cause problems for prisoners, law enforcement and health services. Prison post continues to be a popular smuggling route for synthetic cannabinoids and therefore drug screening techniques have had to be implemented to reduce the amount of synthetic cannabinoids entering into the prison. In England, and across the United Kingdom, Ion Mobility Spectrometry (IMS), in the form of Rapiscan Systems Limited Itemiser 3E® instruments, can be used to screen for drugs in post, however, previously unencountered substances will not be recognised to produce an alarm. Efforts need to be made to identify substances that do not produce an alarm as they are not currently in the instrument library but are of interest to the authorities. Further analysis may yield additional drugs that could be added to the library to increase chance of future detection. The screening, confirmation and feedback cycle was produced through the analysis of samples from West Midlands prisons that had indicated presence of synthetic cannabinoids *via* confirmatory techniques: Gas Chromatography-Mass Spectrometry (GC-MS), Liquid Chromatography-Mass Spectrometry (LC-MS), Fourier Transform Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance Spectroscopy (NMR).

This process resulted in 62 samples from the prison being analysed, 47 of which were paper samples. Of the 47 paper samples, nine were identified, by confirmatory analysis, to have at least one of the following synthetic cannabinoids soaked or sprayed on the paper: MMB-FUBINACA, 5F-MDMB-PICA, MMB-022 (MMB-4en-PICA), 4F-MDMB-BUTINACA and MDMB-4en-PINACA. Time-of-flight information regarding each identification was relayed to Rapiscan Systems Limited to inform library additions and updates. This was particularly pertinent for 5F-MDMB-PICA, 4F-MDMB-BUTINACA and MDMB-4en-PINACA, as 258 alarms for 5F-MDMB-PICA and 647 alarms for 4F-MDMB-BUTINACA and/or MDMB-4en-PINACA were seen after library additions and updates were produced. The library additions and updates would ensure that the instruments would alarm for future encounters of these drugs, and reduce the opportunity for synthetic cannabinoids to enter prisons.

The impact of screening regarding the number and types of drugs sent into prisons was also explored through the retrospective analysis of Itemiser 3E® data over a 40-month period. Over 72,000 items of data were evaluated, representing approximately 15,000 samples. These data were used to identify how long an emerging synthetic

cannabinoid was present within the prison environment prior to library additions and updates that would have enabled their detection. The results showed that the implementation of regular assessment and updates to the instrument libraries was greatly influential on the prevalence of 5F-MDMB-PICA, MDMB-4en-PINACA and 4F-MDMB-BUTINACA within the 2018-2021 period. This highlights the importance of intelligence sharing and analytical support, but also demonstrates the information that can be captured using this data processing method.

Finally, research was dedicated to gathering information on research groups in the UK and Europe working in the field, and the organisations that provide tools to aid drug identification, to determine best practice. The information gathered was used to produce recommendations that outline the key considerations that research groups would need to apply to undertake the analysis of intelligence-based samples for prisons in their local region. The research undertaken has directly benefitted the West Midlands prisons and Rapiscan Systems Limited, and has shown how the screening, confirmation and feedback cycles could be expanded to be implemented across England to reduce the amount of synthetic cannabinoids being smuggled into prisons and allow HM Prisons and Probation Service to gather intelligence on the substances being encountered.

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Chapter 1 Introduction and Literature Review

In the last decade, synthetic cannabinoids have shown an increase in popularity in prisons and as described below, this results in negative consequences for people in the United Kingdom and abroad. The primary focus of this literature review is to outline what synthetic cannabinoids are, the local and global perspectives surrounding intelligence, the methodologies for synthetic cannabinoid identification and how those methodologies are being used to address the synthetic cannabinoid problem in prisons.

1.1 Synthetic Cannabinoids

1.1.1 Misuse of Drugs Act 1971

The Misuse of Drugs Act 1971 defines controlled substances as any substances that are restricted by Schedule 2 of the Act. The introduction of the Misuse of Drugs Act 1971 superseded previous Acts of Parliament which were in place to control dangerous drugs within the United Kingdom (UK). With the introduction of the classification system, drugs such as lysergic acid (LSD), opium and amphetamine, which had been used for over 100 years, were assigned to either Class A, Class B or Class C groups dependent upon the harm incurred through their use. Since its establishment, amendments have been made to the Misuse of Drugs Act 1971 due to evidence of additional harms (such as with cannabis changing class from C to B in 2004), or when previously undocumented substances have been determined to be harmful and placed under Schedule 2.

1.1.2 NPS Definition

New Psychoactive Substances (NPS) are synthetic compounds produced with the intent to replicate the effects of traditional drugs (Home Office, 2018a). First recorded in the UK in 2008, NPS were not initially controlled substances due to the full extent of their effects being unknown, resulting in NPS originally receiving the name ‘legal highs’. However, increasing harm from NPS use was reported to police and intelligence agencies, so, in 2009, selected substances were added to the Misuse of Drugs Act 1971. With the first generation of NPS controlled, a second generation of NPS were produced and then controlled through the introduction of another amendment to the Misuse of Drugs Act 1971 in 2013. The development of a third generation of NPS prompted the creation of the Psychoactive Substances Act 2016 (Frinculescu *et al.*, 2017).

1.1.3 Psychoactive Substances Act 2016

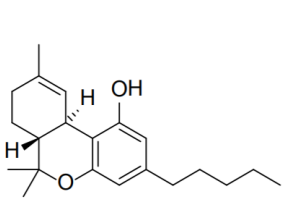
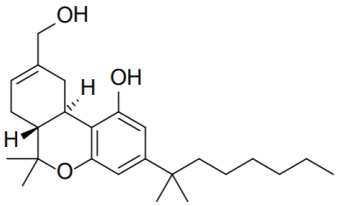
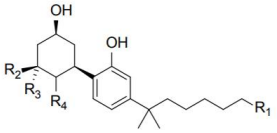
The Psychoactive Substances Act 2016 was introduced as a ‘blanket’ ban on all psychoactive substances in the UK, which are defined as any substance that can induce a psychoactive effect through consumption. The Act ruled that it is an offence to

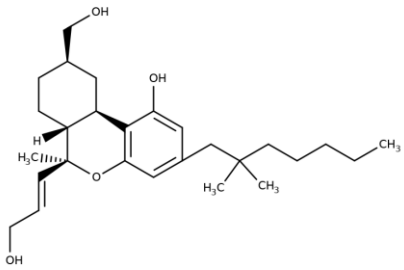
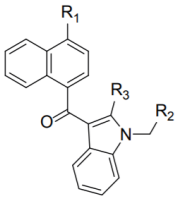
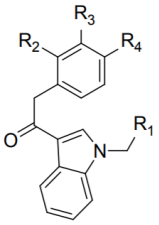
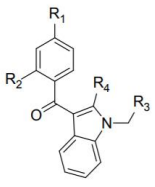
supply, possess with the intent to supply, produce, import, export or possess within a custodial institution any psychoactive substance. Although there are a few exemptions, such as caffeine and nicotine, most of the substances targeted were former 'legal highs' and their subsequent generations (Psychoactive Substances Act, 2016).

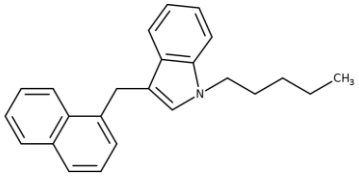
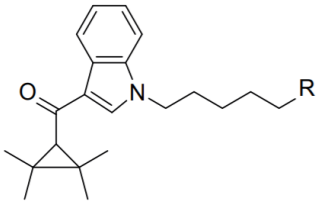
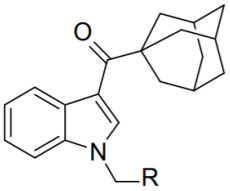
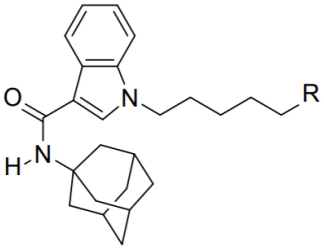
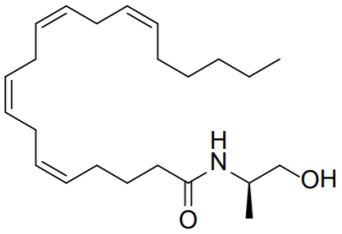
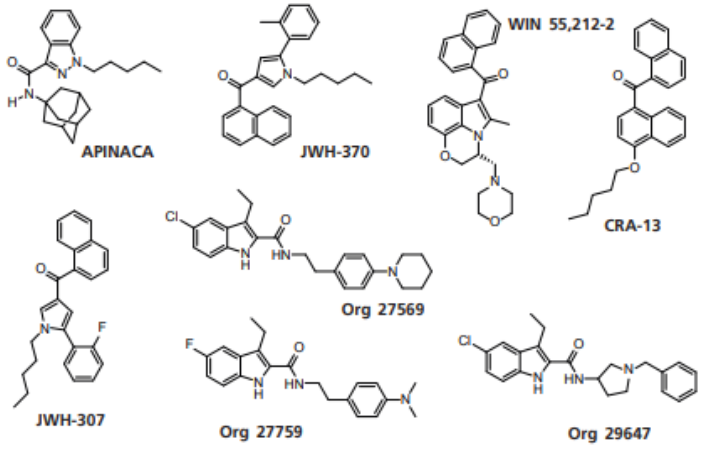
1.1.4 Classification of NPS

NPS can be classified according to their chemical and/or physiological properties, with the classifications including: piperazines, tryptamines, synthetic cathinones and synthetic cannabinoids (UNODC, 2018). Synthetic cannabinoids are substances that bind to and activate the CB_1 and CB_2 cannabinoid receptors in the body (UNODC, 2011), in a similar way as the classical cannabinoid delta (9)-tetrahydrocannabinol (Δ^9-THC), however the structures of the synthetic substances have evolved significantly over time. The United Nations Office on Drugs and Crime (UNODC) (2013) outlines how synthetic cannabinoids that were popular approximately a decade ago generally fit into one of the structure classifications seen below.

Table 1.1: Structure classifications of different types of cannabinoids as outlined in UNODC (2013), with example structures for each type.

Structure classification	Examples of structure
Classical cannabinoids	 d9-THC  HU-210
Non-classical cannabinoids	 **CP-47,497** (R_2=R_3=R_4=H, R_1=methyl) **CP-47,497-C6** (R_1=R_2=R_3=R_4=H) **CP-47,497-C8** (R_2=R_3=R_4=H, R_1=ethyl) **CP-47,497-C9** (R_2=R_3=R_4=H, R_1=propyl) **CP-55,940** (R_2=R_3=H, R_1=CH_3, R_4=3-hydroxypropyl) **Dimethyl CP-47,497-C8** (R_2=R_3=CH_3, R_4=H, R_1=ethyl)

Hybrid cannabinoids	 **AM-4030**
Aminoalkylindoles, which have sub-group types of:	
○ *Naphthoylindoles*	 **R_1=R_3=H** **AM-1220** (R_2=1-methylpiperidin-2-yl) **AM-2201** (R_2=4-fluorobutyl) **AM-2232** (R_2=butanenitrile) **JWH-018** (R_2=butyl) **JWH-019** (R_2=pentyl) **JWH-020** (R_2=hexyl) **JWH-022** (R_2=3-buten-1-yl) **JWH-072** (R_2=ethyl) **JWH-073** (R_2=propyl) **JWH-200** (R_2=4-morpholinylmethyl) **R_2=butyl, R_3=H** **JWH-081** (R_1=methoxy) **JWH-122** (R_1=methyl) **JWH-210** (R_1=ethyl) **JWH-387** (R_1=Br) **JWH-398** (R_1=Cl) **JWH-412** (R_1=F) **JWH-007** (R_1=H, R_2=butyl, R_3=methyl) **JWH-015** (R_1=H, R_2=ethyl, R_3=methyl) **JWH-073 4-methylnaphthyl** (R_1=methyl, R_2=propyl, R_3=H) **MAM-2201** (R_1=methyl, R_2=4-fluorobutyl, R_3=H)
○ *Phenylacetylindoles*	 **R_3=R_4=H** **Cannabipiperidiethanone** (R_1=1-methylpiperidin-2-yl, R_2=methoxy) **JWH-203** (R_1=butyl, R_2=Cl) **JWH-250** (R_1=butyl, R_2=methoxy) **JWH-251** (R_1=butyl, R_2=methyl) **RCS-8** (R_1=cyclohexylmethyl, R_2=methoxy) **R_1=butyl, R_2=H** **JWH-201** (R_3=H, R_4=methoxy) **JWH-302** (R_3=methoxy, R_4=H)
○ *Benzoylindoles*	 **AM-694** (R_1=R_4=H, R_2=I, R_3=4-fluorobutyl) **AM-694 chloro derivative** (R_1=R_4=H, R_2=I, R_3=4-chlorobutyl) **AM-2233** (R_1=R_4=H, R_2=I, R_3=1-methylpiperidin-2-yl) **RCS-4** (R_1=methoxy, R_2=R_4=H, R_3=butyl) **RCS-4-ortho isomer** (R_1=R_4=H, R_2=methoxy, R_3=butyl) **RCS-4 butyl homolog** (R_1=methoxy, R_2=R_4=H, R_3=propyl) **WIN 48,098** (R_1=methoxy, R_2=H, R_3=4-morpholinylmethyl, R_4=methyl)

○ *Naphthylmethylindoles*	 **JWH-175**
○ *Cyclopropoylindoles*	 **R=H** **UR-144** **R=F** **XLR-11**
○ *Adamantoylindoles*	 **R=butyl** **AB-001** **R=1-methylpiperidin-2-yl** **AM-1248**
○ *Indole carboxamides*	 **R=H** **APICA** **R=F** **STS-135**
Eicosanoids	 **AM-356**
Others, including naphthoylpyrrole (JWH-307) and indazole carboxamides (APINACA).	 **APINACA** **JWH-370** **WIN 55,212-2** **CRA-13** **Org 27569** **JWH-307** **Org 27759** **Org 29647**

1.1.5 Evolution of synthetic cannabinoid structures

In the last decade, synthetic cannabinoid generations have exhibited more varied structures, fuelled by the aim to evade detection and circumvent legislation (Ford and Berg, 2018; EMCDDA, 2022; King, 2022). Legislation changes in countries involved in production and exportation, plus some consumer countries, drives the need to produce new synthetic cannabinoids *via* structural diversity. This cycle leads to a cat-and-mouse game, especially in countries where list-based legislation will need to be updated to include the new moieties (Pulver, Riedel *et al.,* 2022). Although the UK has the Psychoactive Substances Act 2016 operating as a 'blanket ban', there is still variation exhibited, for example due to legislation changes in China (Norman *et al.,* 2021). This has resulted in the prevalence of some more recent groups of synthetic cannabinoids coming onto the market, such as cumyl γ-carbolines, cumyl carboxamides and OXIZIDs (oxoindolin-bearing compounds). Examples of simple synthetic changes are through additional or reduced numbers of carbons in alkyl tails (as seen in Figure 1.1 with indazole carboxamides 4F-MDMB-BUTINACA and 5F-MDMB-BUTINACA) or substitutions, such as an alkyl or halogen groups on the aromatic ring or alkyl chain (as seen in Figure 1.2 with indazole carboxamides 5F-AKB-48 and 5Br-AKB-48) (UNODC, 2019). Furthermore, there have also been exploratory changes that were previously unprecedented, such as synthetic cannabinoids with halogenated cores or the removal of a side chain, or both, as seen with ADB-5'Br-INACA, showing that the drug manufacturing process is constantly evolving (Pulver, Riedel *et al.,* 2022).

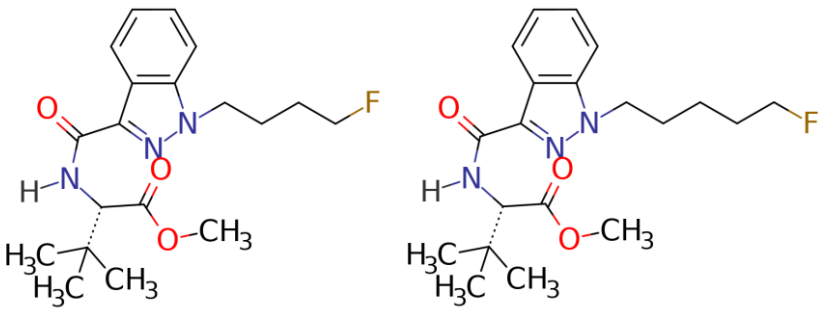


Figure 1.1: Indazole carboxamides 4F-MDMB-BUTINACA and analogue 5F-MDMB-BUTINACA with variation in alkyl chain

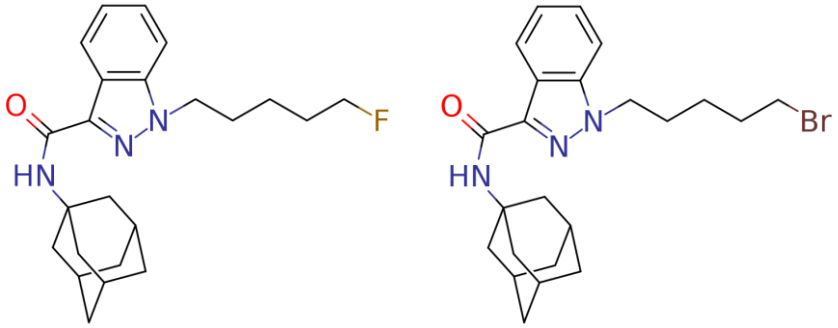


Figure 1.2: Indazole carboxamides 5F-AKB-48 and 5Br-AKB-48, with the difference being the halogen substitution at the end of the alkyl chain

In terms of naming of the synthetic cannabinoids, some of the early synthetic cannabinoids were named after those who first synthesised them, such as JWH-018 for John W. Huffman, or referenced popular culture in their countries of origin, such as AKB-48, named after a popular Japanese pop group (EMCDDA, 2016). However, the recent synthetic cannabinoids are named based on their structure, with the linked group, tail, core, linker naming system being implemented by the EMCDDA (EMCDDA, 2016) and expanded to include substitutions, as prefixes, where necessary (Pulver, Fischmann, Gallegos and Christie, 2022). Other naming systems do exist, as Cayman Chemical Company have previously used the head, core and tail naming system (Cayman Chemical Company, 2019a). An example of using the linked group, tail, core, linker system can be demonstrated by **APICA**: N-(1-**a**damantyl)-1-**p**entyl-1H-**i**ndole-3-**c**arbox**a**mide.

Synthetic cannabinoids are often colloquially referred to as ‘Spice’ or ‘Mamba’ by the media and the public (common brand names held by the first-generation substances) and are produced and sold in powder, herbal or liquid forms (FRANK, 2020). In prisons, they are often found impregnated into paper for concealment purposes (Ford and Berg, 2018; Rodrigues *et al.,* 2022). When the synthetic cannabinoids are administered, often *via* smoking a rolled cigarette or vaporising device (Frinculescu *et al.,* 2022; Giorgetti, Brunetti, Pelotti and Auwärter, 2022; Naqi, Pudney, Husbands and Blagbrough, 2019; Norman *et al.,* 2021; Peace *et al.*, 2017), the compounds pass through the blood-lung membranes to reach the central nervous system and key areas of the immune system (i.e., liver) to bind to the cannabinoid receptors CB_1 and CB_2. Although these compounds bind to the same receptors as Δ^9- THC, they cause different pharmacological effects. The strength of the binding interaction is measured through affinity (expressed as binding constant, K_i), which determines the pharmacological potency (O’Brien, 1986). Affinities can greatly vary for synthetic cannabinoids, with some synthetic cannabinoids having binding affinities between 2-

100 times greater than that exhibited by Δ^9 – THC when binding at the CB_1 receptor. With variations of potencies, the resulting health effects can be varied and unpredictable for those using synthetic cannabinoids (Castaneto *et al.*, 2014).

1.1.6 Health effects

The short-term health effects of synthetic cannabinoid use are varied depending on how the user reacts, and the homogeneity of the type of substance smoked. The most common adverse effects are nausea, paranoia, psychosis and sedation, plus more serious respiratory effects which can potentially lead to death (Moosmann, Angerer and Auwärter, 2015). Most accounts of short-term health effects are seen in case reports which detail some circumstances surrounding use, and the immediate presented health effects, such as synthetic cannabinoid-induced psychosis resulting in self-harm. Two such case reports were given by Meijer, Russo and Adhvaryu, (2014) and Malik *et al.,* (2020), and although there was no analytical confirmation of synthetic cannabinoid being used by the person affected in both, Evans-Brown and Sedefov (2018) suggests that when referring to case reports for intelligence gathering purposes, they are still very valuable as they can often be the first inference of symptoms that can inform medical responses. Van Hout (2017) highlighted that synthetic cannabinoids were the most common NPS associated with acute unpleasant side effects and mid- or long-term problems amongst a sample of 3023 recent NPS users from six European countries, with 69.7% reporting acute unpleasant side effects and 42.6% reporting mid- or long-term problems, including addiction and withdrawal. Long-term health effects of synthetic cannabinoids are still being determined, however Cohen *et al.,* (2020) noted out of a group of 30 chronic synthetic cannabinoid users, compared to 32 recreational cannabis users and 32 non-using participants, synthetic cannabinoid users showed more schizotypal, anxiety and depression traits compared to the other participant groups.

In terms of synthetic cannabinoid use in prisons, if the use results in adverse health effects, mental or physical, that requires urgent medical assistance, two members of staff must supervise the prisoner in an ambulance to a hospital. This results in an avoidable strain on health services, issues with staffing the prison and with a knock-on effect to those in the prison population that do not use synthetic cannabinoids.

1.1.7 Mixtures

The unpredictability and variety of health effects can often be due to multiple synthetic cannabinoids being mixed together within one sample. Frinculescu *et al.*, (2017) discussed how branded herbal packets from police seizures acquired in 2014 had multiple synthetic cannabinoids in one packet, with a common mixture being 5F-PB-22

and 5F-AKB-48. Some synthetic cannabinoids are mixed purposely and sold as such; however, some are mixed but not labelled accordingly, therefore increasing the likelihood of the user overdosing. More recently, Antonides, Brignall, *et al.*, (2019) identified mixtures within street herbal sample seizures from Manchester Metropolitan Police between 2017-2018, where AMB-FUBINACA was present alongside 5F-ADB (otherwise known as 5F-MDMB-PINACA) in a 1:5 ratio. For paper samples, Norman, Walker, McKirdy, *et al.*, (2020) have investigated how mixtures can also be soaked into prison letters. In some cases, low level concentrations alongside another cannabinoid may have been the result of contamination, and on one piece of paper, they found four synthetic cannabinoid types, which may have been due to haphazard mixing. Alongside this research, Norman, McKirdy, Walker, *et al.*, (2020) discovered potential purposeful mixtures, with some samples being determined as 50:50 mixtures after quantification. Furthermore, Norman, McKirdy, Walker, *et al.*, (2020) found 73% of paper samples impregnated with MDMB-4en-PINACA also featured 4F-MDMB-BUTINACA. Additionally, Giorgetti, Brunetti, Pelotti and Auwärter (2022) discovered a mixture of synthetic cannabinoids alongside a synthetic opiate on a letter seized from a German prison. The analysis resulted in the confirmed identification of MDMB-4en-PINACA, 5F-ADB and AP-237, plus two unconfirmed detections suspected to be due to low concentrations of 5F-MDMB-P7AICA and ADB-4en-PINACA all on one A4 handwritten letter, with no visible staining. Giorgetti, Brunetti, Pelotti and Auwärter (2022) outline that the presence of AP-237 could have been as an impurity rather than through intentional depositing, and warn that the decision to produce a soaked letter containing a synthetic opiate and synthetic cannabinoids raises great concern regarding polydrug use, whether that be intentional or unintentional, as well as unintended overdose or related health implications of the user due to the combination of central nervous system depressants potentially leading to an additive or synergistic effect.

1.1.8 Prevalence of synthetic cannabinoids

The number of different NPS substances on the market increased from 555 substances in 2020 to 618 in 2021, with 87 of those substances being newly identified, and 21% of the 2021 total being synthetic cannabinoids (UNODC, 2023). However, the World Drug Report 2022 outlines a decline of overall NPS use across the 77 participating countries since 2020 (UNODC, 2022). Prevalence data from Drug Misuse in England and Wales surveys showed a drop from 0.9% of the general population using NPS in 2014/2015 (first year NPS recorded) to 0.4% in March 2020, which remained the same into June 2022. Although this data includes young people (16-24 years old) who encompass a

large proportion of the users, it does not encapsulate the primary users: the prison population and homeless population, and therefore does not give a true representation of use (Office for National Statistics, 2020; Office for National Statistics, 2022; UNODC, 2022).

Drugs have been a known problem in prisons for decades with use of traditional and prescription drugs plaguing the prison service up until the increased popularity of synthetic cannabinoids and NPS in the UK in 2008. The use of drugs in prisons feed existing addictions, but can also lead to new addictions, with 7% of prisoners using traditional or prescription drugs for the first time during their sentence (Centre for Social Justice, 2015). NPS have been reported to have been used by prisoners in 22 European countries alongside traditional and prescription drugs (UNODC, 2020a). Furthermore, Van Hout (2017) stated that homeless people, prisoners, and other vulnerable groups in six studied European countries were significantly more likely to use synthetic cannabinoids daily (17.9%) compared to those who had tried synthetic cannabinoids recreationally in a nightlife setting or after purchasing online (2.8%). In the UK, it is estimated by prisoners that up to 90% of the prison population use synthetic cannabinoids, although in comparison, the estimated percentage from prison officials is stated to be approximately 60% (Centre for Social Justice, 2015; User Voice, 2016).

1.1.9 Detection of synthetic cannabinoid use in prisons

One of the greatest appeals of synthetic cannabinoids in prisons are that they are easy to access and believed to be difficult to identify. Under the Prison Act 1952, random Mandatory Drug Testing (rMDT) and Suspicion-Based Drug Testing can be undertaken to determine if people have taken drugs through the analysis of urine samples. However, synthetic cannabinoids and their metabolites are sometimes difficult to detect using drug screening assays of body fluid samples, as some compounds have poor stability after being metabolised and it is difficult to ensure that the MDT detects the most recent NPS substances on the market and that metabolite reference standards are available to confirm their presence in urine samples (HM Inspectorate of Prisons, 2015; Znaleziona *et al.*, 2015; User Voice, 2016; Ralphs *et al.*, 2017). To decrease the chance of synthetic cannabinoids being used in prisons, screening techniques can be employed to target the entry routes to intercept substances prior to them reaching the prisoners. The main entry routes are visitors, staff, ‘over the wall’, entering or returning prisoners, and through the post (O’Hagan and Hardwick, 2017; Norman, 2022). However, current screening techniques only produce an indication of the identification

of the drug and therefore must be used in conjunction with confirmatory analytical techniques.

1.2 Analysis and Identification of Synthetic Cannabinoids

The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) is an internationally recognised organisation which produce guidelines, recommendations, and reference material to aid the confirmatory identification of controlled substances. The 18 approved techniques for controlled substance identification are listed in Table 1.2. Category A provides structural identification on a molecular level, Category B provides identification through specific physical or chemical characterisation and Category C provides identification through non-specific physical or chemical characterisation (SWGDRUG, 2019).

Table 1.2: SWGDRUG Categories of analytical techniques determined through selectivity (techniques within categories not listed in specific order) (SWGDRUG, 2019).

Category A	Category B	Category C
Infrared Spectroscopy (IR)	Capillary Electrophoresis (CE)	Colour Tests
Mass Spectrometry (MS)	Gas Chromatography (GC)	Fluorescence Spectroscopy
Nuclear Magnetic Resonance Spectroscopy (NMR)	Ion Mobility Spectrometry (IMS)	Immunoassay
Raman Spectroscopy	Liquid Chromatography (LC)	Melting Point
X-Ray Diffractometry (XRD)	Microcrystalline Tests	Ultraviolet (UV) Spectroscopy
	Pharmaceutical Identifiers	
	Thin Layer Chromatography (TLC)	
	Cannabis only: Macroscopic and Microscopic Examination	

1.2.1 Ion Mobility Spectrometry

Ion Mobility Spectrometry (IMS) is a Category B technique for the analysis of drugs, with the identification occurring from the chemical characteristics resulting from the chemical structure, rather than a direct determination of the structure itself (SWGDRUG, 2019). In terms of detection, the measured time in milliseconds (ms) for

ions to reach the detector is characteristic to the shape and size of the analyte ion (Marchand, Livet, Rosu and Gabelica, 2017). Portable IMS technology is favoured by those who need fast results as it does not require extensive user skill to operate or any sample preparation, as the thermal desorber extracts the sample directly from the swabs (GE Security, 2008). This appeal, plus the fact that it can simultaneously detect explosives and drugs, makes devices such as the Rapiscan Systems Limited Itemiser 3E® very popular within the security industry with use in ports, aviation, event security, customs and border protection, defence, prisons and law enforcement (Rapiscan Systems Limited, 2019).

Ion Trap Mobility Spectrometry (ITMS™), patented by Rapiscan Systems Limited and featured in the Rapiscan Systems Limited Itemiser 3E®, uses a ^{63}Nickel source for ionisation. The ionisation of target ions *via* radiated beta particles, aided by ammonia dopants to reduce the interference of non-target molecules, is undertaken in an electric field to guide the ions to the drift tube for separation prior to detection. This configuration increases sensitivity as more ions can pass through the drift tube to the detector, compared to traditional IMS, which uses an ion eliminating shutter grid (GE Security, 2008). A schematic of an ITMS™ system can be seen in Figure 1.3 (GE Security, 2008).

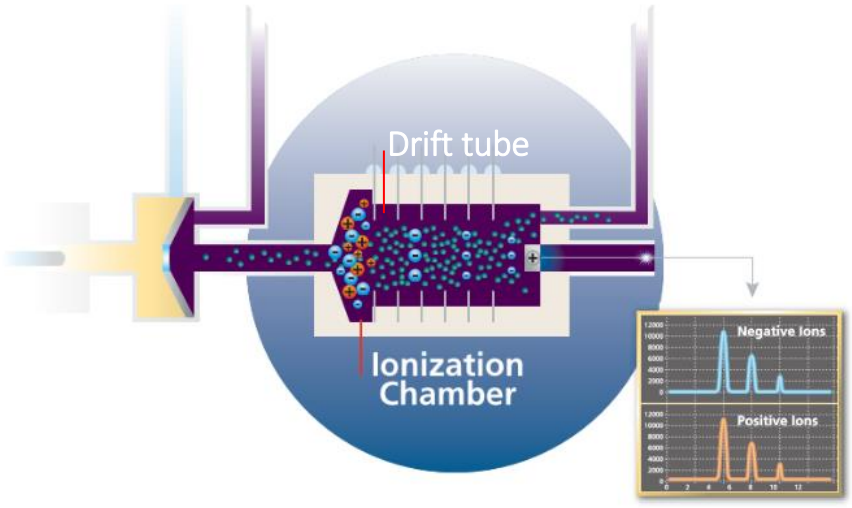


Figure 1.3: Schematic of Ion Trap Mobility Spectrometry (GE Systems, 2008)

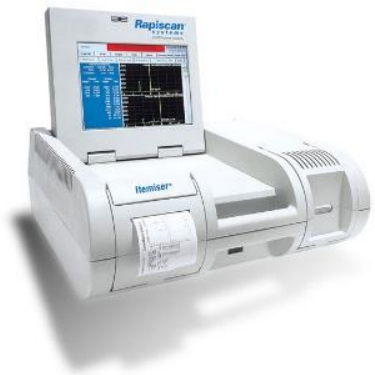


Figure 1.4: Rapiscan Systems Limited Itemiser 3E® (Rapiscan Systems Limited, 2019)

Other IMS technologies are also available, such as the IONSCAN600 from Smiths Detection, London UK, with Metternich *et al.*, (2019) outlining the use of this instrument for the detection of synthetic cannabinoids in a German prison as a successful screening technique for herbal samples, paper, cosmetics and food.

Rapiscan Systems Limited had more than 90 Itemiser 3E® instruments in 67 of the 122 prisons across England and Wales in 2022 (Chandler, 2022b). They can be used to swab surfaces within the prison for general screening, to swab staff or visitors' hands and belongings, to swab surfaces and objects within prisoner's cells or to screen post entering the prisons. Samples are swabbed using a Teflon-coated fibreglass trap which is inserted into the thermal desorber at the front of instrument, resulting in a peak on the plasmogram screen after 8 seconds (as seen in Figure 1.4). This does require someone to handle the sample, which does not need to occur with a portable Raman spectrometer as it can be used through glass or plastic evidence bags (Metternich *et al.*, 2020), however IMS is still suitable as long as health and safety considerations are in place. If the Itemiser 3E® library identifies a substance from the time-of-flight characteristics, it will indicate the identification through an alarm. If the library does not have a substance listed, it cannot identify what the sample is, resulting in a peak to show that a substance is present but no alarm, as shown in Figure 1.5. This is a problem with emerging synthetic cannabinoids that have not been added to the library, as the synthetic cannabinoid may be screened but not identified *via* an alarm, therefore able to enter the prison. Continuous updates to the library need to be made through confirmatory analysis of synthetic cannabinoids, and this is a common issue amongst portable techniques, such as bench-top NMR (Antonides, Brignall, *et al.*, 2019) and Raman spectrometry (Metternich *et al.*, 2020).

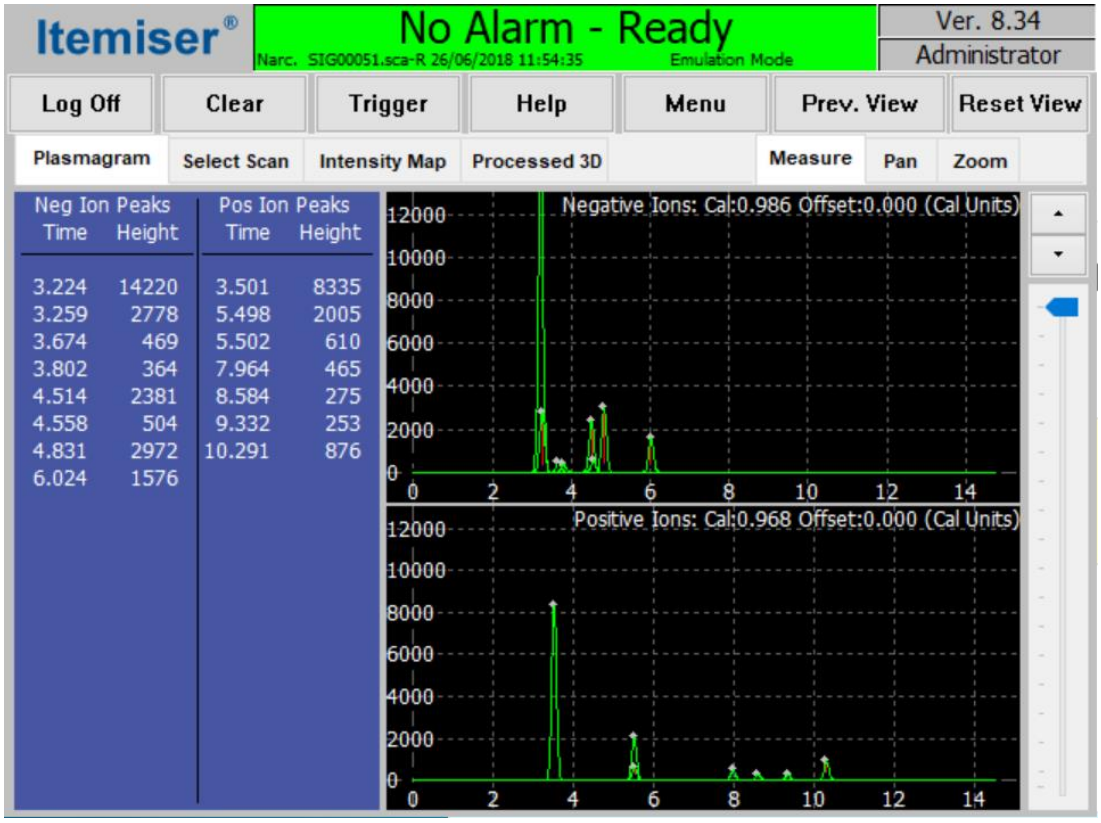


Figure 1.5: Example of the Itemiser 3E® screen after swabbing a sample that has a peak between 8-10 ms but which does not cause a detection alarm

1.2.2 Chromatographic techniques

Gas Chromatography (GC) is a common separative technique used qualitatively and quantitatively for volatile compounds, with separation based on physical properties and the interaction with the stationary phase (Carlin and Dean, 2013). When coupled with a detector such as a Mass Spectrometry, it becomes a hyphenated technique (GC-MS), combining both a Category A and Category B technique from the SWGDRUG (2019) recommendations. GC-MS is a well-established method for the identification of drugs, harnessing the ability to identify samples on a molecular structure level due to the mass-to-charge ratio determination and fragmentation patterns from the MS, plus chemical characterisation through GC (SWGDRUG, 2019). GC-MS can be used to compare to certified reference standards through fragmentation patterns or identify structures of previously undocumented compounds alongside techniques such as NMR (Hudson and Ramsey, 2011; Uchiyama *et al.*, 2014; Angerer *et al.*, 2016; Risseeuw *et al.*, 2017), plus be used for identification of seized samples of herbal, paper, powder or liquid synthetic cannabinoids with appropriate sample extraction and preparation methods (Seely *et al.*, 2013; Mogler *et al.*, 2017; Peace *et al.*, 2017; Burns *et al.*, 2018; Ernst *et al.*, 2019; Norman, Walker, McKirdy, *et al.*, 2020). GC-MS has also been utilised for rapid simultaneous qualitative and quantitative identification of non-thermally

labile substances, informing analysts of the compounds and the dosages users are acquiring (Choi *et al.*, 2013; Moosmann, Angerer and Auwärter, 2015; Frinculescu *et al.*, 2017). Norman, Walker, McKirdy, *et al.*, (2020) utilised GC-MS for quantification of synthetic cannabinoids concentrations in paper to produce a heatmap of a sample. The heatmaps depicted varied concentrations across the paper and highlighted inhomogeneity caused by drying methods, with drip drying showing greater concentrations of the drug at the bottom of the paper. Problems can occur when using chromatography coupled with mass spectrometry, for example when identifying samples with regioisomers without relevant standards for retention time comparison. Structurally differentiating techniques such as FTIR (Smith *et al.*, 2014) or NMR (Fowler *et al.*, 2015) are therefore a default recommendation alongside GC-MS to allow for a more promising chance of identification through the differentiation of isomers. Chikumoto *et al.*, (2019) also explains how the use of electrospray ionization–triple quadrupole mass spectrometry with varied collision energies can differentiate regioisomers in synthetic cannabinoids and can be applied to gas chromatography or liquid chromatography. Kranenburg *et al.*, (2020) utilises a similar technique with GC-MS for effectively differentiating between cathinones with ring isomeric differences through changing collision energies and implementing chemometric techniques.

Liquid Chromatography- Mass Spectrometry (LC-MS) is another example of a hyphenated Category B and A technique (Table 1.2) (SWGDRUG, 2019), although LC separation occurs through relative affinities to the stationary phase or liquid mobile phase, primarily due to polarity of the analyte (Rouessac and Rouessac, 2007). It is therefore favoured for non-volatile and thermally labile samples and a highly popular technique for drug analysis in various sample types. C18 columns are regularly used, including by all those cited below, and often utilise water (with a buffer such as ammonium formate) and acetonitrile (or methanol in the case of Cooman *et al.*, (2020)) as mobile phases (Angerer, Möller and Auwärter, 2018; Ford and Berg, 2017; Giorgetti, Brunetti, Pelotti and Auwärter, 2022; Norman, Walker, McKirdy, *et al.,* 2020). Formic acid is also often added into one or both mobile phase eluents to aid positive ionisation when using a QTOF-MS (Ford and Berg, 2017; Giorgetti, Brunetti, Pelotti and Auwärter, 2022; eds. Kowalska, Sajewicz & Sherma, 2018; Norman, Walker, McKirdy, *et al.,* 2020).

Furthermore, the addition of time-of-flight mass spectrometry allows for accurate mass determination of compounds, increasing selectivity and confidence in identification of unknown compounds through library matching and structural elucidation (Wu & Colby, 2016). Cooman *et al.*, (2020) investigates the use of triple quadrupole liquid

chromatography with mass spectrometry/mass spectrometry for quantitative NPS determination in oral samples, using deuterated NPS samples as internal standards to validate a solid phase extraction method for synthetic cannabinoids and cathinones. However, Norman, Walker, McKirdy, *et al.,* (2020) outlines how, although ideal, deuterated NPS internal standards greatly increase the cost of the analysis, which can cause issues when dealing with a large number of samples and potential target analytes.

Ford and Berg (2017) describe the use of Ultra-Performance Liquid Chromatography (UPLC) coupled with Time-of-Flight Mass Spectroscopy (TOF-MS) for the identification of synthetic cannabinoids in paper using accurate mass determination. Furthermore, Angerer, Möller and Auwärter, (2018) also used liquid chromatography to investigate the drying methods and paper types using HPLC-DAD (High Performance Liquid Chromatography coupled with a Diode Array Detector), where concentration mapping highlighted higher concentrations of synthetic cannabinoid on the edge of the paper that entered the synthetic cannabinoid solution first when dried flat. Alternatively, Giorgetti, Brunetti, Pelotti and Auwärter (2022) used both LC-MS/MS and HPLC-DAD to successfully semi-quantify mixtures of synthetic cannabinoids MDMB-4en-PINACA and 5F-ADB alongside a synthetic opiate AP-237 present on an A4 letter and associated envelope to estimate total mass of each drug.

Some researchers have found that using both GC-MS and LC-MS enables identification of minor compounds within the prison paper samples for batch profiling (Norman, Walker, McKirdy, *et al.,* 2020). Norman, Walker, McKirdy, *et al.,* (2020) explains how they used undiluted synthetic cannabinoid samples to overload the GC-MS, as alongside the large concentrations of the primary compound, there would be higher concentrations of minor components within the sample than if the sample had been pre-diluted. Furthermore, Norman, Walker, McKirdy, *et al.,* (2020) outlines how tentative identification of fragmentation patterns was conducted through comparison to online libraries after undiluted samples were used for the GC-MS or diluted for the UHPLC-PDA-QToF-MS. The compounds detected using this method were identified as synthesis by-products or degradation compounds, however with consistencies of impurities being found in different samples, there could be potential indication of intelligence for linking batches alongside chiral analysis for enantiomer identification (Norman, Walker, McKirdy, *et al.*, 2020). Norman, Walker, McKirdy, *et al.*, (2020) proved that GC-MS can successfully analyse synthetic cannabinoids alongside LC-MS, with their methods successfully identifying synthetic cannabinoids in 354 paper samples.

1.2.3 Nuclear Magnetic Resonance

Nuclear Magnetic Resonance (NMR) is a qualitative and quantitative spectroscopic technique used for structural determination of organic and inorganic samples in solution or solid state. NMR data are gathered through the interactions between the nuclei of atoms and two magnetic fields (static and oscillating). This results in resonance signals of the nuclei from absorbing definite frequencies from the magnetic fields, therefore producing a spectrum of the change in magnetic field (ppm) against intensity. Structural elucidation is possible due to the interactions of atoms influencing other neighbouring atoms, which alters the chemical shift of the atoms and indicates the structure. Functional groups can also have characteristic changes in resonance, allowing for identification of the type of compound present (Rouessac & Rouessac, 2007). Due to structural determination being key to identifying unknown substances, NMR is a widely applied technique for identification of novel substances in forensic science (Santos *et al.*, 2018) and is a Category A technique for the analysis of drugs (Table 1.2) (SWGDRUG, 2019).

In terms of synthetic cannabinoids, Moosmann *et al.*, (2012), Angerer *et al.*, (2016) and Risseeuw *et al.*, (2017) demonstrate the use of high-resolution NMR for structural elucidation of novel substances, with Angerer *et al.*, (2016), Lee *et al.*, (2018), Gilbert *et al.,* (2021), and, more recently, Wang *et al.,* (2022) documenting NMR use for structural elucidation of specific synthetic cannabinoids compounds for the first time in marketed or seized samples. NMR has also been utilised for quantification of synthetic cannabinoids, with Dunne and Rosengren-Holmberg, (2017) outlining the use of NMR for determination of the dosage of active ingredients within herbal smoking mixtures, and Fowler *et al.*, (2015) using NMR to screen and quantify within an hour. Limitations of NMR are that it can have relatively low sensitivity, and consumables, such as deuterated solvents, are expensive, but costs can be reduced by utilising reusable items where possible. Furthermore, NMR is not a separative technique, therefore resulting in difficulties with mixed samples. However, this can be overcome by using a separative technique coupled with NMR, such as LC-NMR, a technique which could enable a wide range of sample types to be analysed, though it is a rarely utilised technique (eds. Kowalska, Sajewicz & Sherma, 2018).

In terms of field analysis, benchtop or low-field NMR became more prevalent over the last few years, with popularity influenced by the portable and cheaper nature of the technique, as there is no necessity for large superconducting magnets and cryogenic conditions when operating at 60 MHz compared to high resolution NMR operating at an average 400MHz (Grootveld *et al.*, 2019). Benchtop NMR has been used for the

identification of synthetic cannabinoids in herbal samples, with both Assemat *et al.*, (2017) and Antonides, Brignall, *et al.*, (2019) using an Oxford Instruments Pulsar™ benchtop NMR spectrometer. Assemat *et al.*, (2017) utilised benchtop NMR alongside high-field NMR for the analysis of synthetic cannabinoids in 13 herbal samples but noted that structural elucidation could not be undertaken using benchtop NMR as it can only indicate which characteristic bonds are present. This is helpful when the presence of synthetic cannabinoids is suspected, however for unknown compounds, a confirmatory technique would need to be applied alongside the benchtop NMR, similar to the process needed for IMS. Issues were also seen in the method, where sample preparation to reduce the inhomogeneity was not applied to the benchtop NMR samples, which may have reduced the extraction of enough active pharmaceutical compound from the herbal bulking substance. To reduce the likelihood of this occurring, Antonides, Brignall, *et al.*, (2019) used a much larger sample amount of herbal synthetic cannabinoid. Furthermore, to increase accessibility of non-specialists using the Oxford Instruments Pulsar™ benchtop NMR, Antonides, Brignall, *et al.*, (2019) developed an automated library matching system to allow ease of interpretation of the spectra. The automated system can aid with the common issue of deciphering mixtures as NMR is not a separative technique, however partial matches in mixtures featuring synthetic cannabinoids often did not concur with the GC-MS identifications. Additionally, three of the 24 synthetic cannabinoid samples analysed by Antonides, Brignall, *et al.*, (2019) did not concur between the GC-MS and benchtop NMR, potentially due to low concentration issues, and therefore could not be identified using the benchtop NMR without additional confirmatory testing.

1.2.4 Sample preparation and sampling

The publication of research surrounding the analysis of synthetic cannabinoid soaked paper has steadily become more abundant over the last few years. A method for the extraction of synthetic cannabinoids from paper was first noted with Ford and Berg, (2018), with their article outlining how synthetic cannabinoids could be soaked into paper as a concealment method to aid smuggling into prisons. Their extraction process utilised methanol as the solvent followed by sonication and centrifugation. Metternich *et al.*, (2019) later investigated extraction from paper by soaking the paper samples in methanol, followed by a pre-concentration step of evaporating to dryness and reconstituting before GC-MS analysis. For qualitative analysis, a method of sonicating two approximate 1cm^2 samples from two opposite corners in 0.25mL of methanol for five minutes to produce the intended overloaded chromatograms was used by Antonides *et al.,* (2020) and Norman, Walker, McKirdy, *et al.*, (2020). For quantitative

analysis, Norman, Walker, McKirdy, *et al.*, (2020) noted how they were the first to quantify synthetic cannabinoid concentrations in prison post using 3 mm hole punches (modelled to align with intelligence surrounding hole punches to 1cm^2 being approximate doses to fit within a vaporising device), by soaking in 0.25mL of 75:25 dichloromethane: methanol solution three times, with the extracted solution combined and diluted for GC-MS. The repeated solvent use was described to act as a wash to ensure no synthetic cannabinoid would be left in the paper. Dichloromethane was utilised due to reliable extraction capability from the paper, however due to the potential volatility issues with pre-pierced septa, methanol was also included in the solvent extraction to act as a keeper, reducing the chances of variation across samples and allowing for a wider polarity range for extraction (Norman, Walker, McKirdy, *et al.*, 2020).

To tackle potential inhomogeneity of synthetic cannabinoid distribution across the surface of infused papers, selective sampling was suggested by Norman, Walker, McKirdy, *et al.*, (2020) for future analysis. The suggested method used 1cm^2 cuttings from multiple areas, such as the method they used in common with Antonides *et al.,* (2020) with sampling two opposite corners. It was noted that this could be extended to the centre and all four corners of the paper dependent upon size and shape of the sample and combined for qualitative or quantitative analysis of the paper, as variation in concentrations across the paper can arise from soaking and drying methods (Angerer, Möller and Auwärter, 2018; Norman, Walker, McKirdy, *et al.*, 2020).

Herbal synthetic cannabinoid extraction, on the other hand, is a more studied area, as the herbal medium was the primary type of synthetic cannabinoid product at the start of the NPS popularity boom from 2008 and are still prevalent amongst homeless communities in England (Smith, Sutcliffe and Banks, 2015; Gilbert, *et al.*, 2021). The extraction methods for herbal samples may be altered for use with paper samples, with UNODC, (2013) stating that medium or non-polar solvents can be used, listing methanol, ethanol, acetonitrile, ethyl acetate, acetone or isooctane. The use of methanol is popular for sample preparation of herbal samples (Hudson and Ramsey, 2011; Moosmann, Angerer and Auwärter, 2015; Frinculescu *et al.*, 2017; Ford and Berg, 2018), however it could cause an issue with some of the early synthetic cannabinoids, with Tsujikawa *et al.*, (2014) stating that the use of alcohols as solvents can degrade the analyte, as found when extracting synthetic cannabinoid PB-22 with methanol and ethanol, resulting in thermal degradation of the ester bond during GC-MS analysis. Furthermore, Norman, Walker, McKirdy, *et al.*, (2020) comments that during their analysis, indole-3-carboxamide and indazole-3-carboxamides samples were

degrading in the GC liner, which may have been due to dissolution or thermal degradation. In the short term, the GC liner was replaced to overcome the issue, with no degradation products prevalent after the change, but this warrants further investigation as it may be an issue for researchers using GC-MS as a standard analytical technique, and further highlights the importance of also utilising LC-MS.

1.2.5 Standards

Reference standards are required in qualitative analysis to confirm the identity of unknown drugs in seized samples, especially when spectral library data is not available, or when quantitative analysis to determine the concentration of the drug in the sample extract is required. They are commercially available from various suppliers, such as Cayman Chemical Company or Chiron AS. However, as discussed by Cooman *et al.*, (2020) when identifying synthetic cannabinoids in oral fluids, reference standards can be expensive and, depending on how novel the substances are, certified reference standards may not be commercially available. For a free and largely open-source option, large scale organisation monographs and libraries can be utilised for tentatively identifying samples, as mentioned in Norman, Walker, McKirdy, *et al.,* (2020), however, this option cannot be used for quantitative analysis. Therefore, some researchers opt for the route of using materials extracted from seized samples as standards, following detailed characterisation to determine identity and establish purity. Metternich *et al.*, (2020) used seized powders provided by the European Union ADEBAR Plus project (see Table 1.3) as reference standards once their purity was determined by quantitative NMR. Norman, Walker, McKirdy, *et al.,* (2020) also used this technique for synthetic cannabinoids extracted from impregnated paper as a reference standard until the chirality was able to be confirmed through bought certified reference standards from Chiron AS when available. Table 1.3 features information on a select amount of large, international organisations and local or national groups that are popular for providing information for NPS identification, and these are discussed in depth alongside other organisations and research groups in Chapter Chapter 4.

Table 1.3: International and national groups that contribute data for identification of NPS, including the organisation name, information on funding affiliations, the service provided and the country of origin. International and national groups are separated by the bold line

Organisation name	Funding affiliation	Services provided	Country of origin
Cayman Chemical Company	Private business corporation	Supplier of reference standards (including NPS), assay kits and contract services for synthesis and drug discovery. Downloadable spectra from spectral library and synthetic cannabinoid specific resources	United States of America
Center for Forensic Science Research and Education - NPS Discovery team	Education Foundation	Provide monographs, trend reports and public health alerts shared online and through social media	United States of America
National Institute of Standards and Technology (NIST)	United States Department of Commerce	Mass spectral library	United States of America
Response Project	European Union	Provide monographs for NPS and an FTIR library	Slovenia
Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG)	United States Drug Enforcement Administration and the Office of National Drug Control Policy	Provide monographs for NPS and an FTIR library	United States of America

Organisation name	Funding Affiliation	Services provided	Country of origin
ADEBAR project	International Security Fund – European Union	Provides seized samples as standards when not available to purchase through certified companies and provides analytical and pharmacological data for NPS	Germany
HighResNPS	University of Copenhagen	Closed user group for sharing crowd sourced high resolution mass spectral data and methods for download	Denmark
Manchester Drug Analysis & Knowledge Exchange (MANDRAKE)	Manchester Metropolitan University and Greater Manchester Police	Provides intelligence testing facilities primarily for Greater Manchester Police. Contributes to harm reduction public health alerts	England
Welsh Emergency Department Investigation of Novel Substances (WEDINOS)	Cardiff Toxicology Laboratories with Public Health Wales	Provides a sample testing service for traditional drugs and NPS. Analysis results shared online, with trends and public health alerts disseminated through daily social media updates	Wales

There is also the option to synthesise synthetic cannabinoids for reference standards. The patents for many synthetic cannabinoids can be accessed online through patent searching; many synthetic cannabinoids were first synthesised and investigated for therapeutic use by academics and pharmaceutical companies during the twentieth century (Thakur *et al.,* 2009), however when the psychoactive effects were identified, they were not investigated further. More recently, publications like Banister *et al.*, (2016) outline the synthetic routes needed to produce many synthetic cannabinoids through investigating variants from a core structure, such as the 16 valinate and *tert*-leucinate variants on nine indole/indazole carboxamide synthetic cannabinoids to highlight potential emerging threats that could easily be produced and sold. This information allows researchers to easily produce their own standards, such as Norman, Walker, McKirdy, *et al.,* (2020) who used the methods published by Banister *et al.*, (2016) to produce (S)-5F-MDMB-PICA and (S)-4F-MDMB-BINACA for their research, plus increases awareness of upcoming potential threats.

Prediction of future synthetic cannabinoids, or prophetic synthetic cannabinoids, can be undertaken to apply a proactive approach to detection and is possible by following popular analogues and affinity responses with subsequent potency and familial groups within synthetic cannabinoid types, resulting in prediction of the next logical synthetic cannabinoids that are similar to an existing popular compound, exhibit the desired short term health effects, and are not currently controlled to evade drug legislation. Predicted synthetic cannabinoids then may be produced using patents from 1970 – 2000 by experienced illicit synthetic chemists (Banister & Connor, 2018). The evolution of synthetic cannabinoids has occurred in this fashion since 2008, however where there is the outlook of prediction, there is the potential to prepare for the next likely synthetic cannabinoids prior to use. This technique has been adopted at the Clinical Toxicology Laboratory, University of California and was able to aid health care providers to quickly identify the compound using LC–QToF-MS and affinity response informed potency after the mass overdose of 33 people in the Brooklyn area in 2016 from K2 (AMB-FUBINACA) (Adams *et al.*, 2017). With prior prophetic compounds being stored in a library a year earlier, an identification was able to be produced quickly and information was able to be transferred back to law enforcement and health care providers, increasing the potential for lives to be saved (Business of Drugs: Synthetics, 2020). Not all events result in fast intervention: in May 2020, 11 people died in Hungary from the result of a new emerging synthetic cannabinoid 4F-MDMB-BICA. The compound was first discovered in Europe through the EMCDDA in March 2020 (Evans-Brown, 2020). The news surrounding the deaths was published on Twitter to warn of more potential

fatalities by Michael Evans-Brown, a representative from the EMCDDA who specialises in early warning and risk assessment (Evans-Brown, 2020). In reply, Samuel Banister tweeted that he had produced 4F-MDMB-BICA as a prophetic cannabinoid reference standard in February 2020 and shared the standard with partners and collaborators in the United States of America, Europe, Australia and New Zealand. However, this prophetic stage does not eradicate drug use and prevent deaths, as it is difficult to control which compounds are being obtained and used across a continent. On the other hand, in more of a closed setting with more active detection of drugs being used, such as in prisons, there is more potential for this technique to halt the samples reaching prisoners and therefore prevent short term health effects or fatalities.

1.2.6 Global and local perspectives

From a global perspective, World Drug Report 2020 (UNODC, 2020a) states that the availability of synthetic cannabinoids seems to be reducing, however it may be due to national and international control measures deeming them no longer an NPS, with the United Nations definition being “an NPS is a psychoactive substance that is not under international control but has similar properties to those of substances under international control. The moment such a substance is controlled at the international level, it ceases to be an NPS”. There is also comment in the World Drug Report 2020 (UNODC, 2020a) that a decrease in availability may be due to control of manufacture and trade of NPS in China. China is known to be the primary origin of NPS, with India being the secondary source, as highlighted by the World Drug Report 2020, where between 2014-2018, 27% of NPS were manufactured or exported from China due to their large-scale pharmaceutical facilities (UNODC, 2020a). To combat this issue, 32 NPS were declared as nationally controlled in China in August 2018 (UNODC, 2018), adding to the 116 NPS controlled in 2015 (UNODC, 2015). Of the 32 controlled in 2018, eight were synthetic cannabinoids, including AMB-FUBINACA, ADB-FUBINACA, 5F-ADB and NM-2201. Although these substances were controlled, synthetic cannabinoids were still the most common type of NPS found in China between June 2018 – June 2019, with both 5F-ADB and NM-2201 (3rd and 8th respectively) still being prevalent synthetic cannabinoids in China at the time as recorded by the NPS Monitoring Programme of China (NNCC, 2019), with the most prevalent at the time, 5F-MDMB-PICA, not being controlled nationally by the August 2018 legislation change (NNCC, 2019; UNODC, 2020a).

Furthermore, the popularity of 5F-MDMB-PICA was mirrored in Scotland, as Norman, Walker, McKirdy, *et al.,* (2020) noted that a lack of legislation changes in China for 5F-MDMB-PICA, with their legislation being based on specific structures and analogues

being controlled, resulted in the popularity of 5F-MDMB-PICA and analogues in Scotland. The impact of China is further highlighted by Norman, Walker, McKirdy, *et al.,* (2020), with the relationship between synthetic cannabinoids being controlled in China in August 2018 resulting in less seizures of the same synthetic cannabinoids in Scottish prisons in late 2018 into 2019. To ensure this nature of tracking can occur, information needs to be shared by researchers, drug monitoring programmes and early warning systems to ensure awareness around the world.

To address this evolving issue, the Chinese government implemented a class-wide, generic control on synthetic cannabinoids in July 2021 (UNODC, 2021), yet synthetic cannabinoids are still being produced. As the generic control is still structure based, some synthetic cannabinoids will not be covered by the legislation, and those that are may still be produced, with Wang (2022) discussing the discovery of novel synthetic cannabinoids in Chinese case work. This production still leads to exportation, with an example being the novel synthetic cannabinoid ADB-5'Br-BUTINACA. This compound, which was detected in a herbal sample analysed by the NPS Discovery team, Center for Forensic Science Research and Education in United States of America (Krotulski, *et al.,* 2022) features a brominated indazole core which evades the structure-based class-wide ban, and is therefore not covered by the 2021 Chinese legislation update.

Early Warning Systems (EWS), such as the European Union Early Warning System for NPS run by the European Monitoring Centre for Drugs and Drug Addictions (EMCDDA), are managed by organisations that monitor information on NPS through collecting and sharing data acquired by forensic providers, customs and border agencies, academic researchers and hospitals to warn the countries involved of the potential dangers surrounding an emerging substance and to provide data to help member countries detect them, determine their prevalence of use and to introduce legislative and harm reduction measures. Information can be collected from an event, such as from poisonings, or from test purchases of emerging NPS being sold on the black market. Communications from the EU EWS are disseminated to 30 European countries, plus Europol, to ensure law enforcement and health care professionals are aware of the chemical composition of the substance, the physical characteristics and the acute effects exhibited after use. Furthermore, in terms of intelligence, the EU EWS will also share information on potential organised crime groups that may be influential in production and import/export of the NPS into countries within Europe, plus any information on existing uses, such as in veterinary or industrial settings (EMCDDA, 2020). There are international EWS, such as the UNODC Global SMART (Synthetics Monitoring: Analyses, Reporting and Trends) programme which was launched in 2008

and focuses on amphetamine type substances used in East and South-East Asia, plus recent expansion to South America (UNODC, 2019). There are also local EWS, such as the Welsh Emergency Department Investigation of Novel Substances (WEDINOS) (WEDINOS, 2023a), as mentioned in Table 1.3, for disseminating harm reduction information within the United Kingdom, plus the High Alert project, which is specific to New Zealand (High Alert, 2020). Without these EWS, organisations and research groups, key information surrounding harm reduction and preventative care would not be known, however more effort could be made to ensure that the information gathered is shared appropriately to ensure a more cohesive and organised defence against the threat of NPS.

From a prison perspective, at the time of writing, synthetic cannabinoids from English prisons are only officially subjected to confirmatory analysis by private forensic providers such as Eurofins Forensic Services or Abbott Limited if it is part of a criminal offence and proceeding, therefore testing for samples for intelligence purposes is limited. Currently in Scotland, synthetic cannabinoids soaked in paper and intercepted by prison staff can be sent to the Leverhulme Research Centre for Forensic Science at the University of Dundee (Norman, Walker, McKirdy, *et al.,* 2020; Norman *et al.,* 2021), and in Wales, samples can be sent to the WEDINOS project for intelligence based analysis, however there is no equivalent central hub for testing and intelligence in England. This research aims to outline how a central hub could provide testing and intelligence for the West Midlands region through collaboration with the West Midlands Regional Security Group & Intelligence Hub, otherwise known as the West Midlands Prison Group, and Rapiscan Systems Limited, however expansion and further collaborations would be needed to service all English prisons.

1.2.7 Aims

The aims of this research project are (i) to apply screening and confirmatory techniques to produce an effective method to identify synthetic cannabinoids that have entered prisons, and (ii) to investigate methods surrounding feedback and dissemination of results to benefit the criminal justice system and provide more effective harm reduction to people using drugs in prisons.

1.2.8 Objectives

Objective 1 – Work in conjunction with prison staff using the Rapiscan Systems Limited Itemiser 3E® to undertake sampling of seized prison post to identify previously unencountered synthetic cannabinoids, with the results and information disseminated to the prison and Rapiscan Systems Limited. Collected samples will be identified through structural elucidation using relevant confirmatory techniques (GC-MS, LC-MS,

FTIR & NMR) to undertake the screening, confirmation and feedback cycle, which will be ongoing throughout the research.

Objective 2 - Collect data from Itemiser 3E® instrument records to determine trends of synthetic cannabinoid detection across the West Midlands region and provide representative information on the impact of Itemiser 3E®, and this project, on synthetic cannabinoid prevalence in West Midlands prisons.

Objective 3 - Review the impact of major contributors within the area and their approaches to disseminating information on synthetic cannabinoids to determine the potential avenues for the longevity of intelligence-based analysis of synthetic cannabinoids from prisons in England.

New knowledge will be contributed to the area through addressing the issues raised within the literature review and by meeting the aims and objectives listed above.

Chapter 2 Analysis of Suspect Samples

2.1 Introduction

Prison post and legal correspondence soaked or sprayed with synthetic cannabinoid-laced solvents can be used as a method to smuggle synthetic cannabinoids into prisons by organised crime groups. As part of the effort to reduce the smuggling, prison staff were trained by staff from Rapiscan Systems Limited to swab each piece of post and analyse with the Itemiser 3E®. Legal correspondence between prisoners and their legal advisor is protected by Rule 39 of the Prison Rules 1999 legislation to ensure privacy for the recipient and states that legal correspondence (otherwise known as Rule 39 letters), should not be stopped, opened or read by anyone other than the recipient unless the Governor suspects that the letter is illegitimate and may contain harmful contents. Due to the fact that staff cannot regularly open Rule 39 letters, Rule 39 legislation can be exploited and used for concealment of drugs (Blakey, 2008). In some prisons, such as HMP Featherstone (and those in Scotland, as outlined by Norman, McKirdy, Walker, *et al.*, (2020)), Rule 39 letters have still been screened to reduce the chance of fake legal correspondence evading screening. At HMP Featherstone, the process of sampling through a small slit in the envelope allowed for the privacy of the document to be maintained. This method was developed by Rapiscan Systems Limited for their training and later integrated into official guidelines: The Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework (Ministry of Justice, 2021) was created to certify that the Prison Rules 1999 were still met while ensuring that the samples were included in the screening process. This process is important as if the Rule 39 letters were not tested, significant amounts of synthetic cannabinoid-soaked paper could be smuggled into prisons. One example from BBC News (2021) highlights how envelopes stamped as “Solicitors Letter Rule 39 Applies Legal Correspondence” and “Private & Confidential” were sent to HMP Birmingham, HMP & YOI Brinsford, HMP Featherstone, HMP Hewell, HMP Lancaster Farms, HMP Oakwood, HMP Ranby, HMP & YOI Swinfen Hall and HMP Whitemoor were seized and contained 30 sheets of synthetic cannabinoid-soaked paper in total.

The following chapter outlines the analysis *via* ITMS™, GC-MS, LC-MS, FTIR and NMR that was undertaken to uphold a screening, confirmation and feedback cycle and provide West Midlands prison staff intelligence regarding the synthetic cannabinoids attempting to be smuggled into prisons to meet Objective 1. Most samples were submitted to the University for confirmatory analysis from HMP Featherstone due to a

collaboration running from January 2018, however the research expanded to include other West Midlands prisons due to a collaborative agreement with the West Midlands Prison Group in August 2020.

2.2 Materials and Methods

2.2.1 Itemiser 3E® Methods

Upon arrival, regular prison post was opened, read and checked by prison staff and then placed on a sterile surface for screening with the Itemiser 3E®. This analysis should have been conducted daily, however when this was not possible, due to staff shortages or workload strains, focus would turn to prioritising the legal post and any letters that had obvious staining or smells. The prison staff were required to wear disposable powder-free nitrile gloves and to check for contamination by swabbing the gloves between each sample. The swabs, as shown in Figure 2.1, are made of Teflon-coated fibreglass woven into a crosshatch for sample collection from surfaces (Rapiscan Systems Limited, 2022). If the gloves become contaminated (i.e., presence of drugs are indicated on the Itemiser 3E®), then the gloves need to be changed. The sterile surface was often a clean sheet of paper which has previously been swabbed and analysed by the Itemiser 3E® to check for presence of drugs and would be checked between each sample. Similar to the gloves, the sterile paper was changed upon presence of a drug. For Rule 39 post, a small slit was cut into the envelope to ensure that the contents could not be read but still allowed access for the trap to swab between the sheets of paper.

In terms of daily use, the Itemiser 3E® was operated using the conditions outlined in Table 2.1 and calibrated once a day with cocaine-laced calibration traps. Once an instrument passed the calibration check, it would be cleared down ready for samples. The suspect paper would then be taken out of the envelope and swabbed front and back with the Teflon-coated trap, preferably pressing firmly and swabbing three times either side, then inserted into the Itemiser 3E® for eight seconds. A plasmogram displays the output from the spectrometer including drift times, or time-of-flights, and a separate table lists the drift times and abundances (referred to as “strength”). If the drift time falls within the defined range for a substance in the library and surpasses the threshold strength value, then a “Drugs Detected” alarm would be triggered to indicate a match to a potential drug.

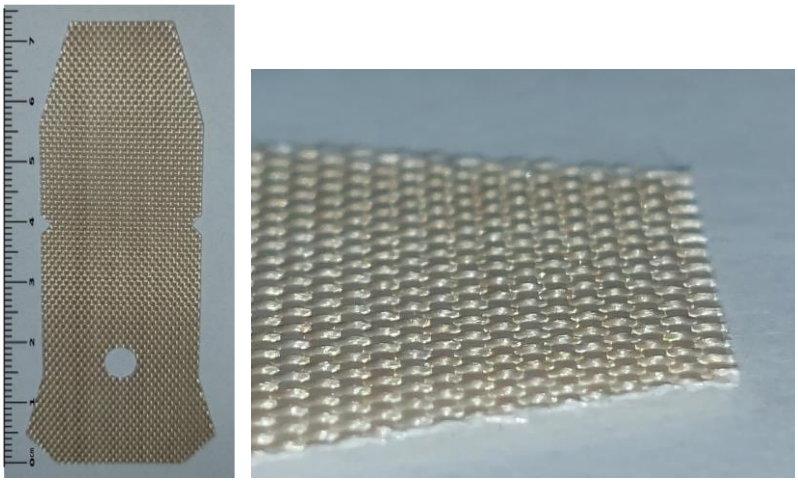


Figure 2.1: Photographs of Itemiser 3E® trap for swabbing

Table 2.1: Rapiscan Systems Limited Itemiser 3E® operating conditions

Operating conditions	
Detector	Ion Trap Mobility Spectrometer
Operational mode	Narcotics – positive ion
Chemical dopant for ionisation	Ammonia
Run time	8 seconds
Ionisation source	^{63}Nickel source
Desorber temperature	235°C

In addition to responding to alarms, Rapiscan Systems Limited trained their users to classify substances within the 9-10 ms region as potential synthetic cannabinoids. This was first suggested by Rapiscan Systems Limited due to most known synthetic cannabinoids recorded in the library at the time of analysis falling within that range and therefore the working theory was that this window would capture any structurally varied but similar synthetic cannabinoids. This was especially important as if the Itemiser 3E® encountered a new 9-10 ms positive ion in that region which was not featured in the library, the Itemiser 3E® would not alarm to indicate a match to a library substance. In this instance, if a prison post sample had a time-of-flight between 9-10 ms but no alarm, prison staff were trained to place the post into an evidence bag, complete the corresponding evidence details on the bag and include the Itemiser 3E® print out so the information could later be corroborated with confirmatory techniques at Staffordshire University. The majority of samples were given a unique reference number when submitted and logged at Staffordshire University with the initials MJA for the author, followed by sequential numbers in order of submission (the only exceptions were from HMP Ranby: RANBY1 and RANBY2). The synthetic cannabinoid window was later amended to 8-10 ms to account for ADB-4en-PINACA and ADB-BUTINACA, which were identified to fall into the 8-9 ms window through the work of the researchers

at the Leverhulme Research Centre for Forensic Science. Communication surrounding the synthetic cannabinoid window was adjusted to allow for this update in 2022.

To maintain the continuity of the samples, the description, bag number and dates were recorded by staff at the West Midlands Prison Group in a logbook and dog handlers transported the samples to the University. Once at the University, the samples were logged in the research logbook as per Staffordshire University's Home Office drug licence, the West Midlands Prison Group logbook was signed to prove the samples had been received and all samples were kept in a locked cupboard. Information recorded in the research logbook consisted of unique reference number, date and time received at the University, any evidence numbers and descriptions from the bag, bag number, the time and date of when the samples were packaged and who by, plus any corresponding Itemiser 3E® data (time-of-flights and any alarmed substances). The original agreement at the start of the research was to keep samples as long as needed or destroy them, however with the introduction of the Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework (Ministry of Justice, 2021), a new agreement was established to ensure that any samples that were classed as personal letters or were no longer required would to be returned to the West Midlands Prison Group to be destroyed and the research logbook updated accordingly to note any samples no longer retained at the University.

2.2.2 Analytical Methods

2.2.2.1 Materials

Table 2.2: Materials list

Solvents	Origin
Acetone – Deuterated	Cambridge Isotope Laboratories Incorporated, 50 Frontage Road, Andover, Massachusetts, USA
Acetone – HPLC grade	Fisher Scientific, UK Limited, Bishop Meadow Road, Loughborough, Leicestershire LE11 5RG, UK
Chloroform - Deuterated (chloroform-d) (99.8%) with 0.05% v/v tetramethylsilane (TMS)	Cambridge Isotope Laboratories Incorporated, 50 Frontage Road, Andover, Massachusetts, USA
Chloroform – Reagent grade	Fisher Scientific, UK Limited, Bishop Meadow Road, Loughborough, Leicestershire LE11 5RG, UK
Methanol – Analytical grade	Fisher Scientific, UK Limited, Bishop Meadow Road, Loughborough, Leicestershire LE11 5RG, UK
Methanol – Optima, LC-MS grade	Optima LC/MS Grade, Fisher Scientific, Meadow Road, Loughborough, UK

Nitrogen	BOC Limited oxygen free, Priestley Road, The Surrey Research Park, Guildford, Surrey, UK
Filters	Origin
0.2 µm x 25 mm nylon syringe filters	Fisher Scientific, UK Limited, Bishop Meadow Road, Loughborough, Leicestershire LE11 5RG, UK
Whatman 0.45 µm x 13 mm Disposable polyvinylidene fluoride (PVDF) Filter	Whatman GE Healthcare Limited, Amersham Place, Little Chalfont, Buckinghamshire, HP7 9NA, UK
LC-MS Mobile phase	Origin
Water – LC-MS grade*	Honeywell – Burdick & Jackson, 1953 S. Harvey Street, Muskegon, MI, 49442, USA
Elga Veolia Biofilter*	Elga Veolia, Lane End Business Park Lane End, High Wycombe, HP14 3BY, UK
Formic Acid	Optima Fisher Chemical, LC-MS A117-50 Janssen Pharmaceuticalaan 3a 2440 Gel-Belgium
Ammonium formate	Sigma Aldrich, LiChropur ≥ 99.0%, 3050 Spruce Street, St. Louis, MO 63103, USA
Nylon 66 Membranes 0.2 µm x 47 mm	Supelco, 595 Harrison Road, Bellefonte, PA, USA
Vacuum filter apparatus for eluent	Sigma Aldrich, 3050 Spruce Street, St. Louis, MO 63103, USA
Acetonitrile – Optima LC-MS Grade	Optima LC/MS Grade, Fisher Scientific, Meadow Road, Loughborough, UK
Glassware and accessories	Origin
Chromacol 300 µL Amber Insert Vials 03-FISV(A)	Chromacol, Thermo Scientific, Am Parir 20, D52379 Langerwehe, Germany
Perkin Elmer 9 mm Blue Screw Cap with PTFE/silicone liner with slit	Perkin Elmer, 710 Bridgeport Avenue, Shelton, CT 06484, USA
Chromacol 2 mL Screwtop Clear Narrow Neck 8-425	Chromacol, Thermo Scientific, Am Parir 20, D52379 Langerwehe, Germany
Chromacol 8 mm Seal Silicone/red polytetrafluoroethylene (PTFE) GC Septa 8-ST14X	Chromacol, Thermo Scientific, Am Parir 20, D52379 Langerwehe, Germany
Chromacol 8 mm Slit Seal Silicone/ PTFE LC Septa 8-ST15	Chromacol, Thermo Scientific, Am Parir 20, D52379 Langerwehe, Germany
Chromacol 8 mm Screw Cap Black 8-SC	Chromacol, Thermo Scientific, Am Parir 20, D52379 Langerwehe, Germany
Wilmad Precision NMR tubes 527-PP-7	Wilmad, 1172 NW Boulevard Vineland, NJ 08360, USA
500 mL Grade A volumetric flask and other Grade A glassware	Fisher Scientific, UK Limited, Bishop Meadow Road, Loughborough, Leicestershire LE11 5RG, UK
Standards	Origin
Methadone HCl	Sigma Aldrich, 3050 Spruce Street, St. Louis, MO 63103, USA

**Agilent Technologies provided the bottle of LC-MS grade water (Honeywell – Burdick & Jackson, USA) for the mobile phase upon the purchase of the LC-MS in August 2019. The Elga Veolia biofilter (Elga Veolia, High Wycombe, UK) was used for the mobile phase from July 2021 onwards.*

2.2.2.2 Sample Preparation

Sample preparation has been a major aspect of the research design, as at first, method development was needed to determine how to extract synthetic cannabinoids from paper. Features of the initial sample extraction method, such as suggested solvents and use of sonication, were inspired by Marinho and Leite (2010), describing how 1 cm^2 paper should be used for analysing LSD in blotting paper, plus information from Tsujikawa *et al.*, (2014) and UNODC (2013), where both referred to herbal or powder synthetic cannabinoid extraction methods.

This resulted in the first sample preparation method using 1 cm^2 paper soaked in 1 mL of HPLC grade acetone (Fisher Scientific, UK). The paper was then sonicated for 20 minutes and the solution transferred to an autosampler vial (Chromacol, Thermo Scientific, Germany) through a 0.45 µm polyvinylidene fluoride (PVDF) syringe filter (Whatman, GE Healthcare, UK) (Method 1) ready for GC-MS analysis. Acetone was a recommended solvent in the UNODC (2013) guidelines for herbal synthetic cannabinoid extraction, plus acetone, predominantly from nail varnish remover, was suggested as the primary solvent to prepare the samples through intelligence from HMP Featherstone at the start of the research, which has since been documented by EMCDDA (2018), Antonides, Cannaert, *et al.* (2019) and Metternich *et al.* (2019) as a solvent used for soaking synthetic cannabinoids into paper, therefore it was solvent of choice at the start of the analysis period.

This method was later refined to reduce the chance of ink interference, due to 1 cm^2 of paper likely including ink present on a lined page, therefore resulting in the development of GC-MS Method 2: 3.5 hole punches of paper were used (with diameter of 0.6 cm per hole punch = area 0.28 cm^2 per hole punch using $\pi r^2 \rightarrow 1\ cm^2/0.28\ cm^2 =$ 3.54 hole punches), then 1 mL acetone added, sonicated for 20 minutes and the solution transferred to an autosampler vial. With no detection of synthetic cannabinoid presence in the first four samples using Method 1 (MJA1, MJA2, RANBY1 and RANBY2), a pre-concentration step was introduced; solutions were evaporated to dryness using a nitrogen stream (Oxygen free by BOC, UK), followed by reconstitution with 250 µL of HPLC grade acetone and transferred into 300 µL insert vials for analysis (Chromacol, Thermo Scientific, Germany). This pre-concentration step later appeared to be unnecessary.

A small study was also implemented to compare Method 2 to the sample preparation method outlined in Ford and Berg (2018), with 3.5 hole punches of weighed paper placed into a 1.5mL plastic Eppendorf tube with 0.5 mL analytical grade methanol, sonicated for 10 minutes, then placed in a centrifuge at 5000 rpm for 5 minutes. Then,

to match the pre-concentration step used in Method 2, the sample was evaporated under a stream of nitrogen and reconstituted in 250 µL analytical grade methanol (Method 3). This was repeated for three replicates from each of the three paper evidence samples and focused on the extraction of 5F-MDMB-PICA to compare retention times.

Following the introduction of LC-MS, the sample preparation was re-investigated so that the same sample could be prepared for GC-MS and then diluted for LC-MS. The samples collected between 2018-2019 were prepared using the established method of 3.5 hole punches of paper being weighed and sonicated in 1 mL HPLC grade acetone, evaporated with nitrogen and reconstituted with 250 µL HPLC grade acetone. For LC-MS, 10 µL of the GC-MS sample was transferred into an autosampler vial, evaporated under a stream of nitrogen and reconstituted with 1 mL LC-MS grade methanol (Optima, Fisher Scientific, UK), then diluted 1000 times using LC-MS methanol and analysed (LC-MS Method 2).

Further method development work was undertaken to streamline the sample preparation for GC-MS and LC-MS, as the concentration step followed by dilution step was cumbersome and not time effective, plus the response on the GC-MS was sufficient to not require a concentration step. The revised method followed 3.5 hole punches or 1 cm^2 of sample paper being weighed and sonicated for 20 minutes in 1 mL of a suitable solvent. Both methanol and acetone were trialled as solvents and were both shown as suitable for analysis. Once the sonication was complete, the solution was filtered using a 0.2 µm nylon syringe filter (Fisher Scientific, UK) and transferred to a clean autosampler vial labelled for GC-MS analysis. The LC-MS sample was then taken from the GC-MS sample, with a 50 µL aliquot of this solution removed, transferred to a clean autosampler vial labelled for LC-MS analysis and 950 µL of HPLC acetone or LC-MS grade methanol added for LC-MS analysis, resulting in a 1:20 dilution (Method 4).

All powder or paste samples were prepared as a 1 mg/mL solution in methanol for GC-MS as suggested by UNODC (2013). The powder was accurately weighed (to four decimal places) (HR-250A, A&D Company Limited, Japan) to approximately 10 mg in a 10 mL Grade A volumetric flask (Fisher Scientific, UK) and made to volume in LC-MS grade methanol. 1 mL of the solution was then filtered through a 0.2 µm nylon syringe filter into an autosampler vial, with a 1000x dilution of the GC-MS solution utilised for LC-MS (Method 5). For one sample which consisted of 110 seeds, 5 seeds were randomly selected to attempt to gain a representative sample and soaked in 2 mL of

reagent grade methanol, then the solution was transferred into an autosampler vial for analysis (Method 6). The table depicting samples and the corresponding sample preparation method used can be found in Appendix 1 – Sample preparation method tables Table 1.

In terms of the NMR samples, the preparation method for the first sample analysed was based on the early GC-MS method, with 3.5 hole punches of the sample added to 1 mL reagent grade chloroform (Fisher Scientific, UK) and sonicated for 20 minutes, followed by the solution being evaporated to dryness and reconstituted in 1 mL deuterated chloroform (Cambridge Isotope Laboratories Incorporated, USA). The sample was then transferred to an NMR tube (Wilmad, USA) for analysis (NMR Method 1). As with the GC-MS and LC-MS method, this was later streamlined, resulting in all NMR samples being prepared using the final method of 3.5 hole punches of sample added directly into 1 mL deuterated chloroform (Cambridge Isotope Laboratories Incorporated, USA) and sonicated for 20 minutes, then the solution transferred into an NMR tube (NMR Method 2). The sample preparation methods per sample are collated in Appendix 1 – Sample preparation method tables Table 2.

Most FTIR samples were able to be applied directly to the attenuated total reflectance (ATR) accessory, however some samples, previously used for GC-MS, had evaporated and were reconstituted in 1 mL HPLC grade acetone prior to analysis, with approximately 3 drops of solution from a Pasteur pipette dispensed onto the ATR window and allowed to evaporate, creating a film across the window. One sample had originally been solvated in methanol and still remained in solution; therefore 3 drops were taken directly from the GC-MS sample without the need to reconstitute (samples and corresponding sample preparation methods used are summarised in Appendix 1 – Sample preparation method tables Table 3).

2.2.2.3 Gas Chromatography – Mass Spectrometry

The GC-MS method was a general screening temperature program following adaptation of methods from UNODC (2013) and Tsujikawa *et al.*, (2014), with the operating conditions shown in Table 2.3 and Table 2.4. All samples, apart from MJA8, were analysed using the Perkin Elmer Clarus 500 GC-MS. MJA8 was analysed on the Perkin Elmer Clarus 690 GC and SQ8T MS due to the replacement of the Perkin Elmer Clarus 500 GC-MS occurring at the end of the sample analysis stage of the research, resulting in the Perkin Elmer Clarus 690 GC and SQ8T MS being the new instrument for liquid injection. Both GC-MS instruments were single quadrupole, and therefore produced m/z values accurate to the integer.

Table 2.3: Perkin Elmer Clarus 500 GC-MS operating conditions

Operating conditions	
GC oven conditions	Initial temperature 80 °C for 1 minute, ramp 12 °C per minute to 300 °C and held for 10 minutes
Injection parameters	1.0 µL injection volume with 20:1 Split 250 °C Injection temperature
Carrier gas	Helium Grade A (BOC, UK) at 1.5 mL/minutes
Column	Supelco SLB-5 MS 30.0 m x 320 µm x 0.25 µm (Merck, Germany)
Mass Spectrometer Detector	Solvent delay: 3 minutes Transfer temperature: 300 °C MS source temperature: 250 °C Electron Ionisation: 70 eV Scan parameters: 40-500 Da
Total run time	29.33 minutes
Software	TurboMass Version 5.4 with National Institute of Standards and Technology Mass Spectral Search Program Version 2.0 2002

Table 2.4: Perkin Elmer Clarus 690 GC and Clarus SQ8T MS operating conditions

Operating conditions	
GC oven conditions	Initial temperature 50 °C for 2 minutes, ramp 15 °C per minute to 300 °C and held for 6 minutes
Injection parameters	1.0 µL injection volume with 20:1 Split 250 °C Injection temperature
Carrier gas	Helium Grade A (BOC, UK) at 1.5 mL/minutes
Column	Perkin Elmer Elite 5-MS 30.0 m x 250 µm x 0.25 µm (Perkin Elmer, USA)
Mass Spectrometer Detector	Solvent delay: 4 minutes Transfer temperature: 300 °C MS source temperature: 250 °C Electron Ionisation: 70 eV Scan parameters: 50-500 Da
Total run time	24.67 minutes
Software	TurboMass Version 5.4 with National Institute of Standards and Technology Mass Spectral Search Program Version 2.3 2017

Once mass spectra were produced, online reference comparison became routine in the research and primarily utilised the Cayman Chemical Company GC-MS Drug Identification Tool (Cayman Chemical Company, 2022a), the Response Project Database (Response, 2022) and the SWGDRUG Drug Monograph table (SWGDRUG, 2022) due to the searching capabilities when the base peak or relative molecular masses were acquired from the mass spectrum. Named compounds would then be searched primarily on the Cayman Chemical Company website (Cayman Chemical Company, 2022b) to access a reference spectrum, however the SWGDRUG drug monographs (SWGDRUG, 2022) and the NPS Discovery monographs produced by the

Center for Forensic Research and Excellence (CFSRE, 2022) were also used to compare to the sample spectra. For each sample spectra, the relative molecular mass, the base peak and the top ten most abundant peaks were compared to the reference spectrum to gain the tentative identification.

Although certified reference standards were not utilised, all synthetic cannabinoid samples were analysed using more than one technique classified as Category A or B by the SWGDRUG (2019) guidelines, and similar conclusions reached, therefore there was high confidence in the identifications made.

2.2.2.4 Liquid Chromatography – Quadrupole Time of Flight – Mass Spectrometry

The method outlined by Ford and Berg (2016) for the analysis of synthetic cannabinoids in urine was adapted for the Agilent 6500 Series (LC-QToF-MS), with the operating conditions outlined in Table 2.5.

Table 2.5: Agilent 6500 Series Quadrupole-Time of Flight Liquid Chromatography-Mass Spectrometry System operating conditions

Operating conditions	
HPLC System	Agilent 1260 Infinity II HPLC
QToF System	Agilent 6500 Series Quadrupole-Time of Flight Liquid Chromatography-Mass Spectrometry System
Detector	Agilent 6550 iFunnel with Dual AJS (Agilent Jet Stream) electrospray ionisation positive ion mode
Column	Agilent Zorbax Extend-C18 50 mm x 2.1 mm x 1.8 µm (set at 50 °C) (Agilent, USA)
Total run time	12 minutes
Mobile phase	Acetonitrile (Solvent A) and 1 mmol/L ammonium formate (pH3) + 0.1% formic acid (Solvent B)
Gradient of mobile phase	10% Solvent A, 90% Solvent B for 9 minutes, then 90% Solvent A, 10% Solvent B for final 3 minutes
Flow rate	0.4 mL/minutes
Nozzle voltage	3.0 kV
Capillary voltage	3.0 kV
Drying gas flow	14 L/minutes at 200 °C
Scan rate	1.5 spectra/sec in centroid mode
Scan range	40-1000 m/z
Acquisition Software	Data Acquisition 10.0
Data Analysis Software	Qualitative Analysis 10.0

The 1 mmol/L ammonium formate (pH3) solvent for the mobile phase was prepared using ammonium formate (Sigma Aldrich, MO, USA) made to volume in Grade A glassware in ultra-pure water (filtered with the Elga Veolia Biofilter (Elga Veolia, UK)) and 0.1% v/v formic acid added (Optima Fisher Chemical, Belgium). The solvent was then filtered under vacuum through 0.2 µm x 47 mm Nylon 66 Membranes (Supelco, PA, USA). The Honeywell LC-MS water was replaced with the Elga Veolia Biofilter once the bottle had been used.

Interpretation and analysis of the results gained from the LC-MS centred around the Personal Compound Database and Libraries (PCDL), using the Agilent Forensic Toxicology PCDL provided with the instrument and the development of an in-house bespoke PCDL (produced with the data shown in the Excel spreadsheet in Appendix 2 – In-house synthetic cannabinoid Excel spreadsheet for PCDL). The Agilent Forensic Toxicology PCDL contains traditional drug samples, pharmaceutical samples and some new psychoactive substances including synthetic cannabinoids. The PCDL can be periodically updated through Agilent and currently has 9,200 compounds, with accurate-mass MS/MS spectra for approximately 3,900 compounds (Agilent, 2020), however due to the nature of the project including newly emerging substances which could take a long time to be available between the periodic updates, focus turned to producing a PCDL for the project.

Work was undertaken to find the chemical formula, SMILES codes, CAS and/or ChemSpider numbers, accurate masses and GC-MS spectra (with base and molecular ion peaks recorded) for synthetic cannabinoids which were prevalent at the time of analysis and previously popular. These data were used to populate the in-house synthetic cannabinoid Excel spreadsheet, and the data were inputted into the PCDL format for the LC-MS. Synthetic cannabinoids listed as current threats in quarterly bulletins or included within literature were the focus of the investigations, with the information on the compound being collected from ChemSpider (ChemSpider, 2022), Cayman Chemical Company (a chemical manufacturer that shares product monographs) (Cayman Chemical Company, 2022b), the Center for Forensic Science Research and Education's NPS Discovery scheme (CFSRE, 2022) and the Response project (an EU funded project for the sharing of NPS information) (Response, 2022), with all data cross-checked. Prior to July 2022, data for 152 synthetic cannabinoids were collected. All data were collated in an Excel spreadsheet and inputted into the PCDL to allow for Find by Formula compound matching using the Agilent MassHunter Qualitative software. The Find by Formula method allowed for targeted and untargeted searching of the library, with targeted searches using relative molecular mass ranges for an efficient and succinct search when the type of chemical compound is suspected, whereas untargeted searching takes much longer to search through the PCDLs and may retrieve many unrelated compounds, yet allowed for a wider reach when the compound was unknown. Furthermore, with the ability to add .mol files, structures could be directly compared to the spectra when using the Find by Formula function in the Agilent Qualitative software. For each sample analysed, both the in-house PCDL

and the Agilent Forensic Toxicology PCDLs were used for the Find by Formula function.

2.2.2.5 Nuclear Magnetic Resonance Spectroscopy

The operating conditions for the NMR are outlined in Table 2.6 and the full table for the operating conditions and respective experiments are outlined in Appendix 3 – Full NMR operating conditions Table 4. All samples were analysed using the autogain function to optimise the shim settings.

Table 2.6: Jeol ECX 400 Nuclear Magnetic Resonance Spectroscopy operating conditions

Operating conditions	
NMR System	Jeol ECX 400 Nuclear Magnetic Resonance Spectrometer
Solvent	Deuterated chloroform (chloroform-d) (99.8%) with 0.05% v/v tetramethylsilane (TMS)
Probe	5 mm direct liquid probe
Software	Jeol Delta 5.0.4
Experiments	^{1}H, ^{13}C, ^{19}F, $^{13}C\{^{1}H\}$/ppm (carbon_dept_dec) 45°, 90° and 135°, HMBC ^{1}H – ^{13}C, HMQC ^{1}H – ^{13}C, HSQC ^{1}H – ^{13}C and COSY ^{1}H-^{1}H

2.2.2.6 Fourier Transform Infrared Spectroscopy

Infrared spectra were obtained using Thermo Fisher Nicolet iS10 with Attenuated Total Reflectance (ATR) accessory and Perkin Elmer Spectrum 2 with ATR accessory. Extracted solutions produced for GC-MS analysis were used for the FTIR analysis. Operating conditions can be seen below in Table 2.7 and Table 2.8.

Table 2.7: Thermo Fisher Nicolet iS10 FTIR Spectrometer operating conditions

Operating conditions	
FTIR	Thermo Fisher Nicolet iS10 FTIR Spectrometer
ATR Accessory	Smart Orbit Type IIa diamond crystal
Resolution	4 cm^{-1}
Scans	32
Scan range	4000-400 cm^{-1}
Data format	Transmittance (%T)
Instrument pressure	45 psi
Detector	DTGS (deuterated triglycine sulphate)
Window	KBr
Software	EZ-Omnic 9.7.46

Table 2.8: Perkin Elmer Spectrum 2 FTIR Spectrometer operating conditions

Operating conditions	
FTIR	Perkin Elmer Spectrum 2

ATR Accessory	Universal ATR with diamond crystal
Resolution	4 cm^{-1}
Scans	4
Scan range	4000-450 cm^{-1}
Data format	Transmittance (%T)
Detector	Lithium tantalite (LiTaO3)
Window	Potassium bromide (KBr)
Software	Spectrum IR Version 10.7.2

The full chemical names for each abbreviated synthetic cannabinoid encountered are featured in Appendix 4 - List of abbreviated synthetic cannabinoids.

Ethical approval was granted using a disclaimer only form. Procedural risk assessment and ethical approval documents are available upon request.

2.3 Results and Discussion

2.3.1 Samples

In total, 62 samples were received by the University from screening by prison staff at eleven prisons. Of the 62 samples, 47 of the samples were letters or similar (for example, a diary), with 42 of these provided by the West Midlands Prison Group. The remaining five samples were taken from prisons in the East and South of England and were provided *via* collaboration with Rapiscan Systems Limited or the West Midlands Prisons Group. The sample types were initially split into paper and non-paper samples, however with powder samples such as MJA19 and MJA52 having associated intelligence to suggest they were synthetic cannabinoid powders, samples were then categorised into paper, powder or other, which encompassed the remaining miscellaneous samples submitted. Non-paper samples were not prioritised unless there was intelligence or suggestion of synthetic cannabinoids presence. Samples were excluded when confirmatory techniques were unlikely to further any investigation or lend to the purview of the PhD research, such as MJA51, which was mouse poison from a trap in the prison, and MJA9, which although contained some concealed tissue paper, was spoiled due a leakage of suspected condensed milk.

Of the total 62 samples, 32 had Itemiser 3E® results submitted with the sample, and of the 47 paper samples, 28 had accompanying Itemiser 3E® results.

The categories of samples encountered were:

- Samples with an Itemiser 3E® printed results page present which included a peak between 8-10 ms but the peak had not alarmed to any substances in the library

- Samples with no Itemiser 3E® printed results page present and a record from the prison that it had not alarmed to any substances in the library
- Samples which had an Itemiser 3E® printed results page indicating an alarm for a known synthetic cannabinoid
- Samples which had no Itemiser 3E® printed results page and no inference of drugs from testing but suspicious visual observations such as staining, or intelligence to suggest suspicion was warranted
- Samples that had an Itemiser 3E® printed results page indicating an alarm for a drug other than a known synthetic cannabinoid

The full list of received samples, including evidence numbers, brief descriptions and key Itemiser 3E® results can be seen in Table 2.9, with the drift times of interest seen in bold.

Table 2.9: Descriptions of evidence submitted to the University for research and corresponding Itemiser 3E® results

Evidence number	Visual observation	Key Itemiser 3E® results from submission
MJA1	A4 letter on prisoner-to-prisoner letter paper	**9.402, 9.407** and **9.461 ms**
MJA2	Letter on ring-bound shorthand notebook lined paper	**9.358, 9.373** and **9.390 ms**
RANBY1	Piece of plain paper with slight discoloured blue areas	No print-out present
RANBY2	3 pages from a diary	No print-out present
MJA3	Homemade birthday postcard	6.490 ms, **9.155 ms** and 12.397 ms
MJA4	2 pieces of plain but worn paper	No print-out present
MJA5	Orange paper card with bats and Halloween motif printed on	5.199 ms, 6.523 ms, 8.528 ms and **9.381 ms**
MJA6	Orange paper card with orange pumpkin and Halloween motif printed on	2 Itemiser 3E® result print outs included: a - 5.224 ms, 6.476 ms, 7.901 ms (= triggered cocaine) and **9.353ms** b - 5.255 ms (= triggered 5F-PB-22), 6.516 ms and 7.917ms (= triggered cocaine)
MJA7	Small piece of paper	No print-out provided, however retrospective testing = **9.104 ms**
MJA8	Small piece of paper	3.432 ms, 3.897 ms, 4.207 ms, 6.046 ms, 6.541 ms and **9.099 ms**
MJA9	Princes Peaches tin outer with small can inner, likely to be condensed milk. Pieces of tissue below with strong off-milk smell. Congealed white paste in smaller tin which grew mouldy over time	No print-out present
MJA10	110 seeds and small fragments - Look like orange seeds.	2 Itemiser 3E® result print outs included:

		a – 3.345 ms (dopant peak), 5.194 ms, 5.992 ms, 6.488 ms, 7.031 ms, **9.406 ms** (= triggered 5F-MDMB-PICA), **9.503 ms** and **9.969 ms** b – 3.315 ms (dopant peak), 5.717 ms, 6.525 ms, 7.088 ms, **9.381 ms** (= triggered 5F-MDMB-PICA), **9.953 ms** and 10.885 ms
MJA11	Homemade postcard	3.355 ms (dopant peak), 4.767 ms, 5.175 ms, 6.529ms, 7.941 ms, **9.633 ms** (= triggered 5F-AKB-48), 10.684 ms and 10.880 ms
MJA12	Funky Pigeon card with scratch marks, looks like a glue stick with scrapings from Itemiser 3E® trap	No print-out present
MJA13	Dad birthday card	No print-out present
MJA14	Piece of impregnated paper	4.846 ms, 5.978 ms, 6.025 ms, 6.570 ms, 7.824 ms, **9.165 ms**, **9.675ms** (= triggered 5F-AKB-48) and **9.959ms**
MJA15	Card with scratch markings	3.4454 ms (dopant peak), 5.974 ms, 6.549 ms, 7.938 ms (= triggered cocaine), 8.805 ms, 8.812 ms and 10.666ms
MJA16	Card with scratch markings	3.469 ms, 10.253 ms, 10.292 ms and 10.307 ms
MJA17	Piece of paper with orange smudges	3.457 ms, 5.987 ms, 6.087 ms, 6.550 ms, **9.190 ms** (= triggered 5F-ADB/ MMB-FUBINACA) and 12.913 ms
MJA18	Letter with strong sweet smell	6.519 ms, 7.924 ms (= triggered cocaine) and **9.461 ms** (= triggered 5F-MDMB-PICA)
MJA19	Yellow powder/paste	No print-out present
MJA20	Piece of paper with strong sweet smell	No print-out present
MJA21	Letter with strong sweet smell and wet marks on envelope, paper almost opaque	3.458 ms (dopant peak), 6.554 ms, 7.046 ms, **9.527 ms**, **9.995 ms**, 10.066 ms, 10.558 ms and 10.639 ms
MJA22	Letter that is stained slightly yellow, ink run and strong sweet smell	No print-out present
MJA23	Letter on photo paper, heavy yellow staining and strong sweet smell	No print-out present
MJA24	Black card, drawing and 4 pieces of paper for letter with strong sweet smell	No print-out present
MJA25	2 pieces of paper with strong sweet smell	No print-out present
MJA26	Letter with obvious staining, brown/transparent in places and ink colour gone in some places	No print-out present
MJA27	10 sheets of letterhead paper from a national law firm (same as MJA28)	10 Itemiser 3E® print-out results present (1 per page) - 8 sheets triggered 5F-AKB-48, 2 sheets triggered PCP, 2 sheets triggered

		morphine, 1 sheet triggered pseudoephedrine
MJA28	Blank sheet of letterhead paper from a national law firm (same as MJA27)	No print-out present
MJA29	1 handwritten page letter and 12 printed pages of images of tracksuits and trainers. 1 return envelope	No print-out present
MJA30	3 printed pages from Flannels website, 1 handwritten A5 letter	No print-out present
MJA31	2 printed pages (one from Flannels website, one from JD Sports trainers webpage), 1 handwritten letter and 2 child's drawings	No print-out present
MJA32	2 A4 pieces of paper, no signs of staining or tampering in a Rule 39 envelope	3.281 ms (dopant peak), 3.954 ms, 5.002 ms, 5.198ms, 5.996 ms, 7.186 ms and 8.881 ms (= triggering heroin and heroin mix)
MJA33	4 pieces of A4 Solicitors letterhead paper. Paper looks slightly grained and grey like a photocopy but not	3.295 ms (dopant peak), 3.958 ms, 4.170 ms, 5.016 ms, 5.200 ms, 5.312 ms, 6.019 ms, 6.072 ms, 6.331 ms (= triggering MDMA)
MJA34	A4 Rule 39 Solicitor letterhead paper	3.357 ms (dopant peak), 4.077 ms, 4.838 ms, 6.218 ms (= triggering MDA/4-MMC)
MJA35	A4 Solicitor letterhead letter	3.304 ms (dopant peak), 3.965 ms, 5.453 ms, 7.328 ms (= triggered PCP)
MJA36	A4 Solicitors letterhead paper	3.388 ms (dopant peak), 3.423 ms, 4.080 ms, 5.419 ms, 5.636 ms (= triggered amphetamine), 6.902 ms
MJA37	4 A4 letters from Solicitors. Same letter twice, one in English (x 2 pages) and one in Vietnamese (x 2 pages)	3.291 ms, 3.963 ms, 5.221 ms, 6.326 ms, 6.519 ms, 7.255 ms (= triggered PCP)
MJA38	1 suspected cannabis bud A compacted ball of tobacco 6 paper wraps containing a green herbal substance 10 pieces of paper with strong sweet smell inside the toilet roll tube An evidence bag dated 12/01/2019 with a piece of tissue in Pieces of plastic bag and a finger from a blue rubber glove	2 Itemiser 3E® print outs included: a a - 3.442ms (dopant peak), 6.992ms, 7.855ms, **9.323ms** (= triggered 5F-ADB/MMB-FUBINACA) b - 3.449ms (dopant peak), 7.008ms, **9.147ms** (= triggered ADB-FUBINACA) and 10.316ms
MJA39	Colourless solution with light blue floating lumps. Blue/green lump at top of squeeze top bottle, so likely topped up with colourless liquid. Alcohol like smell from both	No print-out present
MJA40	5 pieces of lined paper with obvious waxy staining and Itemiser 3E® print outs stapled 14 pieces without print outs and obviously stained until almost	5 Itemiser 3E® result print outs included: a - 3.676 ms (dopant peak) and **9.191 ms** (= triggered 4F-MDMB-BUTINACA) b - 3.712ms (dopant peak),

	translucent for some Strong sweet talcum powder type smell	5.485ms and **9.165 ms** (= triggered 4F-MDMB-BUTINACA) c - 3.832ms (dopant peaks) and **9.180 ms** (= triggered 4F-MDMB-BUTINACA) d - 3.153ms (dopant peaks) and **9.153 ms** (= triggered 4F-MDMB-BUTINACA) e - 3.534ms (dopant peaks) and **9.155 ms** (= triggered 4F-MDMB-BUTINACA)
MJA41	45 photographs (no visual distortion to images) and one child's painting	No print-out present
MJA42	17 pieces of plain paper, 2 sheets of blank MG11 statement forms 2 pieces of carbon paper 1 piece of paper with address only stuck to the inside of envelope to prevent moving 1 black and white screenshot from phone with usernames 1 printed profile 1 piece of paper regarding trial information 1 clingfilm flat package containing tobacco and cigarette papers	3 Itemiser 3E® print outs included: a - 3.452 ms (dopant peak) and 5.947 ms (= triggered ephedrine/ pseudoephedrine), b - 3.450 ms (dopant peak), 5.980 ms (= triggered ephedrine/ pseudoephedrine), 6.560 ms and 7.969 ms (= triggered cocaine) c - 3.448 ms (dopant peak), 5.901 ms (= triggered ephedrine/ pseudoephedrine), 6.538 ms and 7.969 ms (= triggered cocaine)
MJA43	1 page from InsideTime.org regarding extended determinate sentences 7 pages of 8 pages (page 2 of 8 missing) of legislation.gov Criminal Justice Act 2003 Chapter 5 (dangerous offenders) 21 pages of 31 pages (22-31 missing) of Criminal Justice Act 2003 Chapter 6 2 pages of 2 pages Criminal Justice Act 2003 Chapter 5A (40 total)	3 Itemiser 3E® print outs included: a - 3.438 ms (dopant peak), 5.987 ms, 6.458 ms, 6.698 ms, 7.059 ms, 7.497 ms (= triggered tramadol), 7.811 ms (= triggered nimetazepam), 7.925 ms (= triggered cocaine) and **9.093 ms** (= triggered 4F-MDMB-BUTINACA) b - 3.443 ms (dopant peak), 7.894 ms, 7.904 ms, 7.907 ms (= triggered cocaine) and **9.124 ms** (= triggered ADB-FUBINACA and 4F-MDMB-BUTINACA) c - 3.443 ms (dopant peak), 7.894 ms, 7.904 ms, 7.907 ms (= triggered cocaine), **9.124 ms** (= triggered ADB-FUBINACA and 4F-MDMB-BUTINACA)
MJA44	Moonpig thank you card	3.169 ms (dopant peak), 3.874 ms, 4.663 ms, 5.723 ms, 6.013 ms, 6.540 ms (= triggered MDEA) and 7.521 ms
MJA45	Envelope with name of recipient and Rule 39 written on envelope but no solicitors stamp and underpaid postage. Inside contained two sheets of paper from the Police and Criminal Evidence Act 1984, then covered front and back	2 Itemiser 3E® print outs included: a - 4.395 ms, 5.240ms, 6.482 ms, 7.06 ms and 7.378 ms (= triggered PCP) b - 6.484ms, 7.078ms and 7.366ms (= triggered PCP)

	with wedges of A5 paper, with 5 or 6 pages in each. Some small orange stains sampled	
MJA46	1 page letter from solicitor with COVID prison guidelines Pages 1 to 5 of the COVID-19 National Framework for Prison Regimes and Services (no obvious staining present) 10 pages of similar documentation, however obviously stained, with slight wet look to pages and orange/brown stains present. Pages 6 to 16 of COVID-19 National Framework for Prison Regimes and Services (no obvious staining present)	No print-out present
MJA47	1 lined rectangular piece of paper (slightly yellow) 3 lined blueish tinges and shiny in places scraps of white paper 4 pieces of prison issued yellowed lined paper. Two whole pieces, one halved and one L shape 1 long rectangular piece of paper, plain white with pink staining Intelligence to suggest could be a mix of baby oil, battery acid and toilet cleaner	No print-out present
MJA48	Prison issued deodorant - Faintly blue liquid inside and fragranced like deodorant.	No print-out present
MJA49	2 Sure roll-on deodorants. Yellow oil freely dripped from roll on.	No print-out present
MJA50	Used glittery opaque Primark lip plumper. No ingredients list present.	2 Itemiser 3E® print outs: a – 5.285 ms (= triggered 5F-PB-22) b- 5.285 ms (triggered 5F-PB-22) and **9.794 ms**
MJA51	Blue grains of mouse poison in sample pot. No ingredients or manufacturer details present.	No print-out present
MJA52	Pale yellow clumpy powder	No print-out present
MJA53	Purple/blue liquid in sample bottle from a cell kettle. Light lavender smell.	No print-out present
MJA54	2 thank you cards glued together to allow for a void between the two fronts of the cards. 1 small envelope containing one white cigarette paper wrap. White cigarette paper wrap containing brown powder	2 Itemiser 3E® print outs: a – 3.453 ms (dopant peak), 5.521 ms, 5.845 ms, 6.429 ms, 6.534 ms, 8.755 ms, 8.829 ms and **9.305 ms** (= triggered MMB-FUBINACA/ 5F-ADB)

		b - 3.451 ms (dopant peak), 6.512 ms, 7.124 ms, 7.917 ms, 8.938 ms, **9.234 ms**, **9.251 ms** (= triggered MMB-FUBINACA/ 5F-ADB), **9.285 ms** and 10.467 ms
MJA55	Grey/brown powder. Slight gravy smell. Intelligence suggests it potentially could be monkey dust	3.725 ms (dopant peak), 7.474 ms, 7.866 ms and **9.643 ms** (= triggered 5F-AKB-48)
MJA56	23 printed pages. All legislative with one page in particular from "…www.defence-barristers.co.uk/appealing-against-a-crown-court-sentence". "Printed 13/04/21 9:20pm page 11 of 10" in red. Another large print title "Speeding section 269: Determination of minimum term in relation to mandatory life sentence". 3 slightly yellowed pages in centre. Plain pages at back and 14 from front/9 from the back, when red www... is at front	No print-out present
MJA57	Drumstick bath crystals pot containing a 2nd class stamp, some crystals in the pot. Solution tested pH 5, colourless with white powder settling through	5.678 ms (= triggered amphetamine, amphetamine DTK* and MDA)
MJA58	2021 diary in plastic postal packaging. Sweet smell on paper	3.446 ms (dopant peak) and 10.246 ms
MJA59	Jeyes Odour Neutraliser bottle with lid made out of gloves and tape	3.658 ms (dopant), 6.524 ms and 8.803 ms (= triggered heroin). Positive out of date heroin MMC ampule test also included
MJA60	Supreme Imports branded Vitamin D3 pot including a slight orange tinted (very faint) gel consistency. Fruity sweet smell, similar to shampoo or soap	No print-out present

**Drug Testing Kit (DTK). These definitions were produced for when water-based sample dilution methods were used for bulk powder samples prior to Itemiser 3E® screening.*

2.3.2 Pilot solvent extraction study

To verify that both acetone and methanol could be used for solvent extraction, and to compare solvent extraction Method 2 to Ford and Berg's (2018) suggested sample preparation (Method 3), a small study was conducted to compare the GC retention times with compounds that did produce chromatography peaks, resulting in the retention times being shown to be very similar if not the same. The results for 5F-MDMB-PICA featured in samples MJA3, MJA5 and MJA6 saw solvent extraction Method 2 with acetone having a retention time of approximately 19.68 minutes with standard deviation 0.048 (n = 9) and solvent extraction Method 3 with methanol having a retention time of approximately 19.69 minutes with standard deviation 0.053 (n = 9), informing that methanol could also be utilised within the research alongside acetone for solvent extraction. Although the peak areas for each measured retention time were

recorded, these data cannot be used quantitatively at this time to determine relative concentrations as repeated extractions on the paper were not undertaken to ensure all 5F-MDMB-PICA present was extracted, and different areas of the paper were used, which can differ in concentration due to different soaking and drying methods (Angerer, Möller and Auwärter, 2018). Nevertheless, this experiment demonstrated that there was very little difference in GC retention times between acetone and methanol. Acetone was favoured more when applying the drying stages due to quicker evaporation times, however methanol was preferred later in the analysis period when using the same samples on both the GC-MS and LC-MS.

A summary table for the results of the study can be found in Appendix 5 – Pilot solvent extraction study results.

2.3.3 Positive indications of synthetic cannabinoids on paper

MJA5 and MJA6

MJA5, a homemade Halloween card, was submitted to the University for analysis due to the peak between 9-10 ms on the Itemiser 3E® (as seen in Table 2.9), indicating a presence of a synthetic cannabinoid, however there was no library match to infer which synthetic cannabinoid could be present. There was also accompanying intelligence surrounding the sample as the printed ink of the card smudged slightly when swabbed with the sample trap, plus another Halloween card addressed to a different prisoner was posted to the prison within the same week (MJA6). The Itemiser 3E® results for the second card, MJA6, indicated a presence of cocaine and 5F-PB-22, a synthetic cannabinoid popular around 2014 (Frinculescu *et al.*, 2017). The 9.353 ms peak of interest for MJA6 was very similar to MJA5 (9.381 ms), with the alarm range for each compound in the Itemiser 3E® library usually ±0.040 ms. Therefore, MJA5 and MJA6 were seen to be potentially from the same supplier and containing the same unknown compound.

When analysed *via* GC-MS, good chromatography peaks were achieved for each sample. The main chromatography peaks for both samples were at very similar retention times (approximately 19.7 minutes), as shown in Figure 2.2, corroborating a link between the two compounds. The mass spectra produced for both also showed great similarity, as seen in Figure 2.3, further inferring the same compound was present for both. The NIST 2.0 library had the highest match result as melatonin (2TMS derivative) for both MJA5 and MJA6, however, with 509 and 520 match scores for each, this identification was dismissed (NIST Mass Spectrometry Data Center, 2008). This was derived from the basis of >900 being considered an excellent match, 800-900 a good match and 700-800 a fair match (NIST Mass Spectrometry Data Center, 2008).

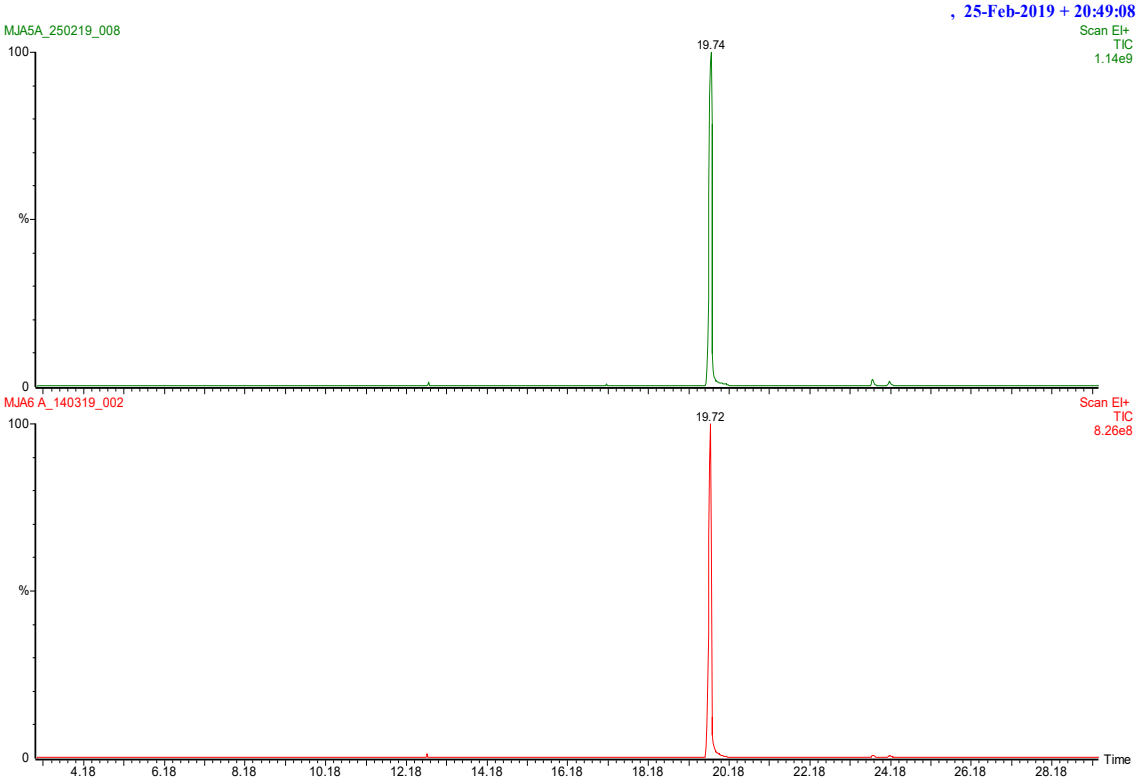


Figure 2.2: GC chromatogram for MJA5 (green) and MJA6 (red)

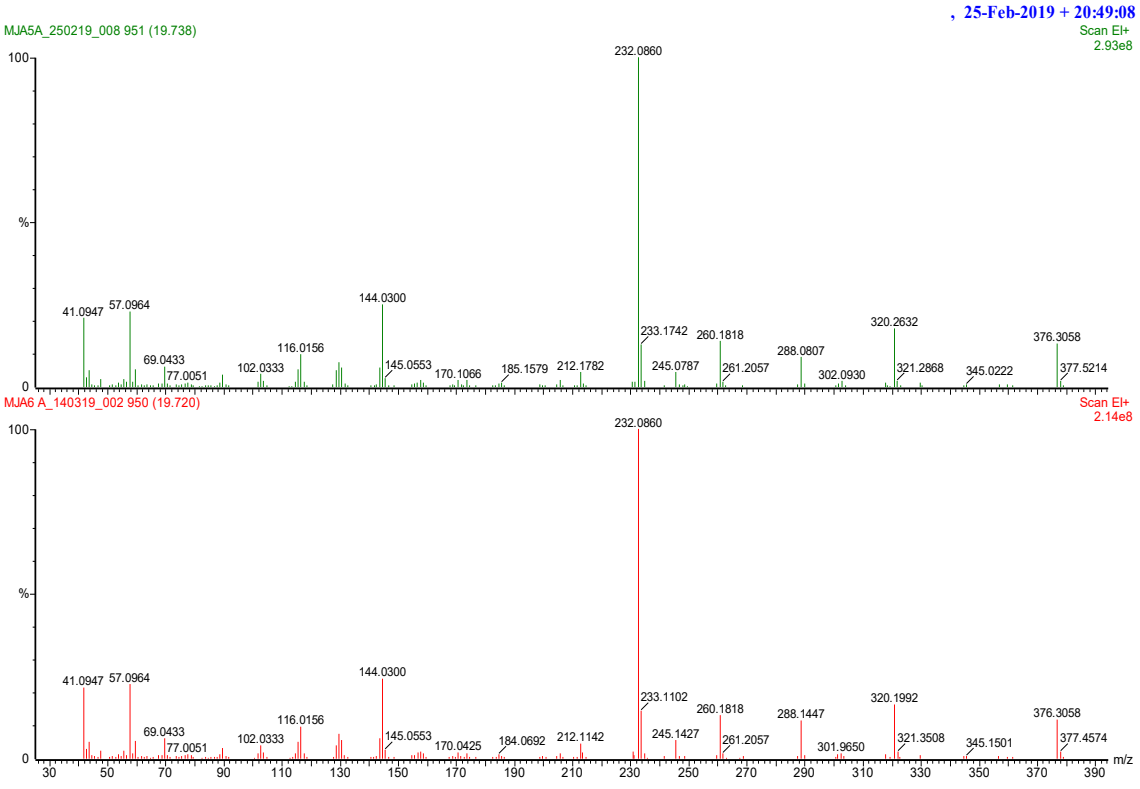


Figure 2.3: MS spectra for MJA5 (green) and MJA6 (red)

As the NIST 2.0 library was insufficient, online searches for synthetic cannabinoids with similar base peaks and relative molecular masses were conducted (as the in-house

synthetic cannabinoid Excel database was developed later in the research timeframe). The identification of MJA5 and MJA6 was primarily achieved by comparison of the sample spectra base peaks, relative molecular masses and the top ten most abundant peaks to the reference spectrum for 5F-MDMB-PICA, which was found using the Cayman Chemical Company GC-MS Drug Identification Tool (Cayman Chemical Company, 2022a) and an annotated version including fragmentation information is shown in **Error! Reference source not found.**. Structures for the core fragments are depicted when they could not be shown easily by the annotated chemical structure with labelled cleavage points and are also provided for the base peaks throughout. An asterisk marks the particular m/z values which are shown on the annotated chemical structure with labelled cleavage points. Some m/z values may have been the result of multiple fragment types, and therefore there may be a suggested core fragment as well as an asterisk correlating to a labelled cleavage point on the annotated chemical structure. Although SWGDRUG (2019) guidelines states that certified reference standards are needed for conclusive identification *via* GC-MS, certified reference standards were not available for this research and therefore only tentative identifications, or inferences, have been made. Furthermore, the identification of 5F-MDMB-PICA on both MJA5 and MJA6 confirmed that sample preparation Method 2 could successfully extract 5F-MDMB-PICA from paper, and therefore it was hoped this extraction method could be applied to other synthetic cannabinoids.

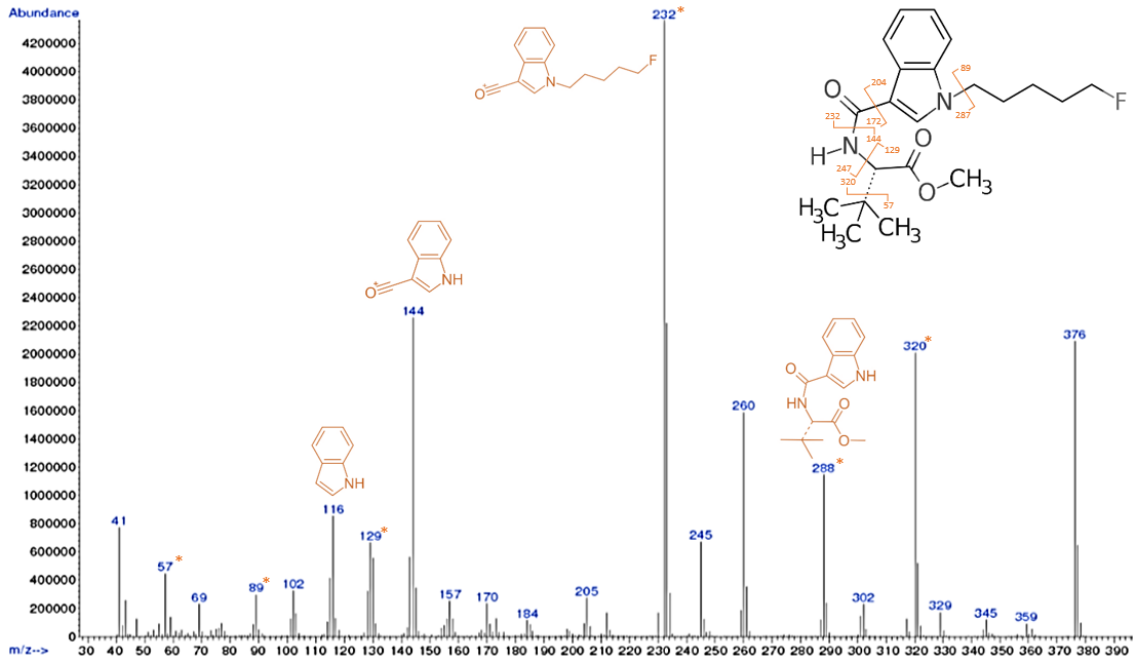


Figure 2.4: MS spectrum for 5F-MDMB-PICA from Cayman Chemical Company (2016) annotated by the author

5F-MDMB-PICA was not included in the Itemiser 3E® library but was known to be popular around the time of analysis (2019) in the local West Midlands region through discussions with staff at Eurofins Forensic Services who were analysing seized samples from local police constabularies (Newman, 2019). The analytical results and the drift time information from MJA5 and MJA6 were communicated to Rapiscan Systems Limited, which resulted in 5F-MDMB-PICA being added onto the Rapiscan Systems Limited Itemiser 3E® libraries, therefore enabling detection *via* the Itemiser 3E® throughout prisons in the UK. In addition, the presence of 5F-MDMB-PICA on both Halloween cards (MJA5 and MJA6) enabled intelligence to be fed back to the prison to demonstrate multiple prisoners may be linked to the same distribution network.

In terms of the smaller peaks in MJA5 and MJA6 with retention times of approximately 12, 17 (MJA5 only), 23 and 24 minutes (Figure 2.2), these were also investigated to determine if cocaine and 5F-PB-22 were present as indicated by the Itemiser 3E® results (Table 2.9). The peaks at approximately 12 minutes for MJA5 and MJA6 were both suggested to be L-Leucine, N-(3-methyl-1-oxobutyl)-, methyl ester by the NIST 2.0 library, however both had very poor match scores, with 560 and 565 calculated respectively (NIST Mass Spectrometry Data Center, 2008), and therefore this indication was dismissed. The base peak was also observed for both spectra at 86 m/z, but as the base peak for cocaine and 5F-PB-22 are 82 and 232 m/z respectively, the peaks with retention times at 12 minutes were dismissed from further investigation. The peak at 17.150 minutes for MJA5 was suggested to be diisooctyl phthalate by the NIST 2.0 library with a match score of 787, indicating potential plasticiser contamination (PubChem, 2022a). The mass spectra for the peaks at retention times 23.7 and 24.2 minutes for MJA5 and those at 23.8 and 24.2 minutes for MJA6 (Figure 2.5, Figure 2.6, Figure 2.7 and Figure 2.8 respectively) included a base peak at 232 which is not indicative of cocaine, and had a base peak of 82. Furthermore, none of the eight most abundant mass spectrum peaks listed in Moffat, Osselton and Elliott (eds.) (2022) were featured in the spectrum, plus cocaine is already listed in the NIST 2.0 library, therefore cocaine was either not present within the sample upon extraction, not extracted (as cocaine is only very slightly soluble in acetone) (SWGDRUG, 2005b) or surface level contamination from the sender (Norman, Walker, McKirdy, *et al.,* 2020).

Once 5F-MDMB-PICA had been identified for the peaks at approximately 19 minutes for MJA5 and MJA6, the MS spectrum for MJA6 was added to an in-house GC-MS library to aid future detection. For MJA5, the mass spectra for peaks at retention times 23.7 and 24.2 minutes both indicated the presence of 5F-MDMB-PICA as their first identification, with match scores of 672 and 673 respectively. Although these scores

were poor (NIST Mass Spectrometry Data Center, 2008), there was significant similarity to the mass spectrum seen in **Error! Reference source not found.**. To investigate if the mass spectra for the 23.7 and 24.2 minutes peaks were from the presence of 5F-PB-22, which has the same relative molecular mass, manual checking of the mass spectrum peaks present was undertaken. Although there were major similarities between the spectra, primary peaks at m/z 317, 288 and 345 were present in the sample spectra (Figure 2.5 and Figure 2.6) which are not expected for 5F-PB-22 (

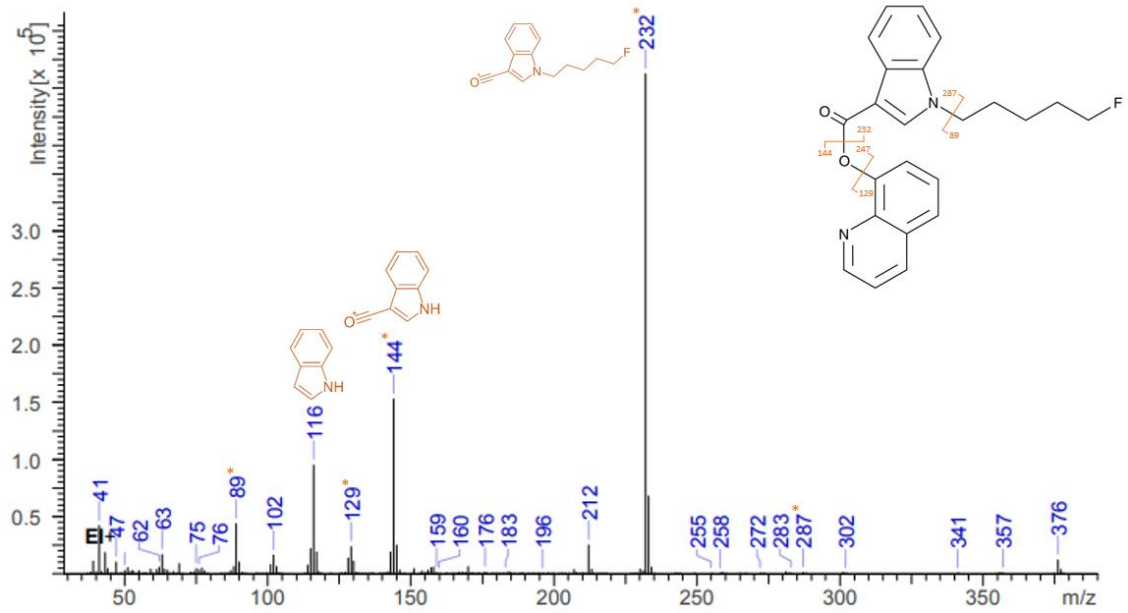


Figure 2.9). Additionally, there should not have been any issues with the solvent extraction and thermal degradation of 5F-PB-22 as acetone was used rather than an alcohol as discussed by Tsujikawa *et al.,* (2014), therefore these peaks are more likely to be thermal degradation products or synthesis impurities of 5F-MDMB-PICA, a known issue for this compound (Norman, Walker, McKirdy, *et al.,* 2020).

The MJA6 peaks at retention times 23.8 and 24.2 minutes however did not have 5F-MDMB-PICA as the top hit on the libraries, with the mass spectrum of the peak at 23.8 minutes (Figure 2.7) primarily identified as piperidin-4-ol,1,1-dimethylethyl-3-methyl-4-phenyl-, cis with a match score of 628 from the NIST 2.0 library. This compound was dismissed upon manual comparison due to predominantly only having similarity in the base peak. 5F-MDMB-PICA was the fourth potential identification in the list from the in-house MS library with a match score of 603, again a poor match (NIST Mass Spectrometry Data Center, 2008), however with more similarity in the major mass spectrum peaks present than the first match and therefore indicating that the compound was likely to be a thermal degradation product or synthesis impurity. Finally, the mass spectrum for the peak at 24.2 minutes (Figure 2.8) had a top library match of 5-[cyano(5-methoxycarbonylpyrrolidin-2-ylidene)methyl]-3,4-dihydro-2H-pyrrole-2-

carboxylic acid, methyl ester, match score 607, which also has the same 232 base peak but no other major mass spectrum peaks were shared when compared in the NIST 2.0 library. On the other hand, 5F-MDMB-PICA was the second match with a match score of 603 and had more similarity in mass spectrum peaks, as shown when comparing Figure 2.8 and **Error! Reference source not found.** (the reference for 5F-MDMB-PICA from Cayman Chemical Company (2016)), therefore indicating presence of a similar compound, such as a thermal degradation product or synthesis impurity of 5F-MDMB-PICA.

Figure 2.5: MS spectrum for MJA5 at 23.7 minutes

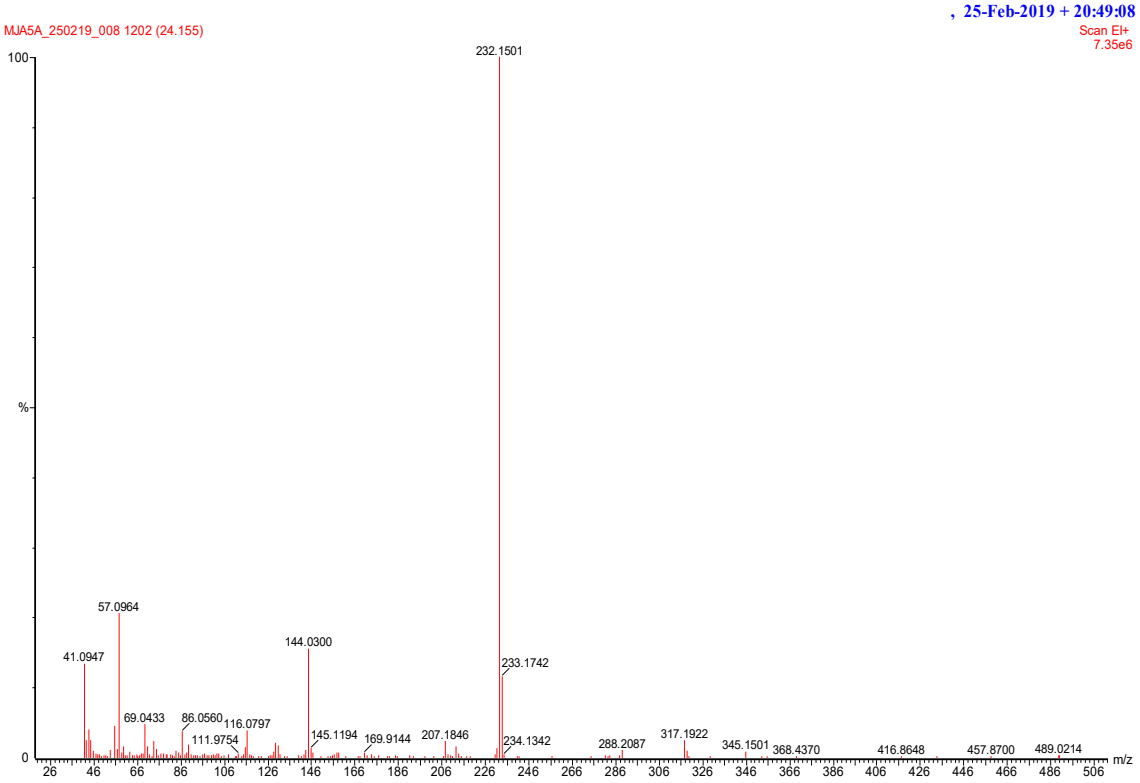


Figure 2.6: MS spectrum for MJA5 at 24.2 minutes

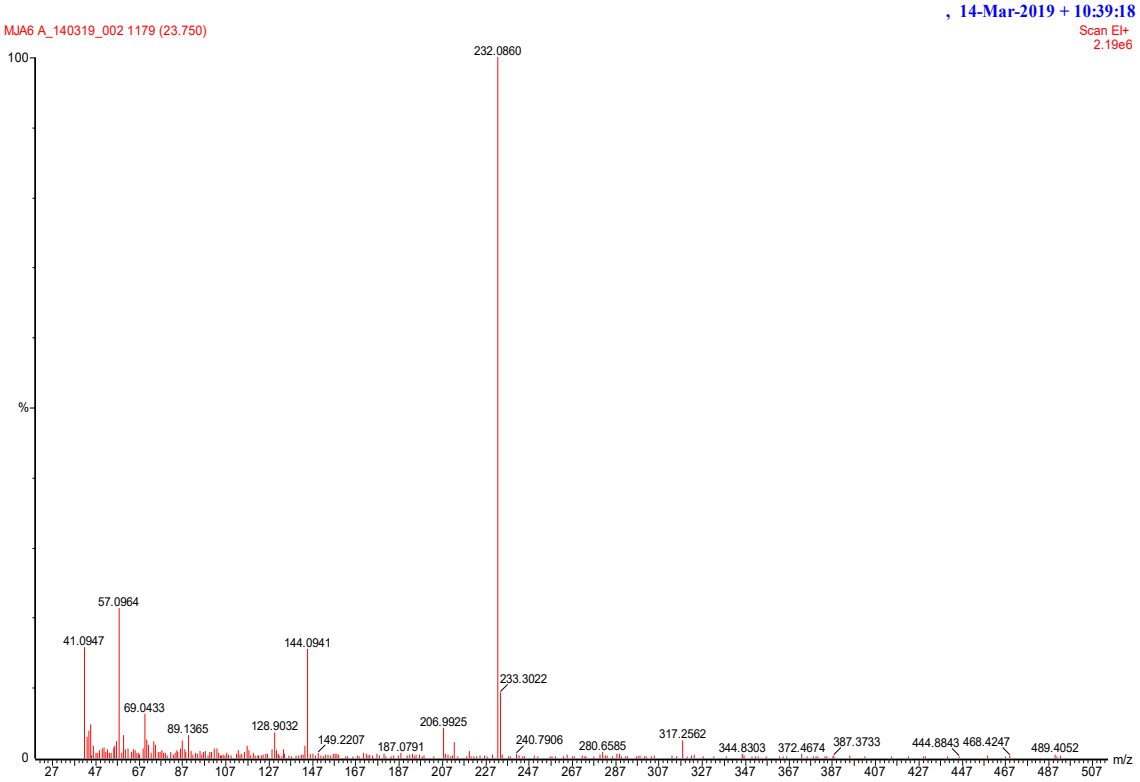


Figure 2.7: MS spectrum for MJA6 at 23.8 minutes

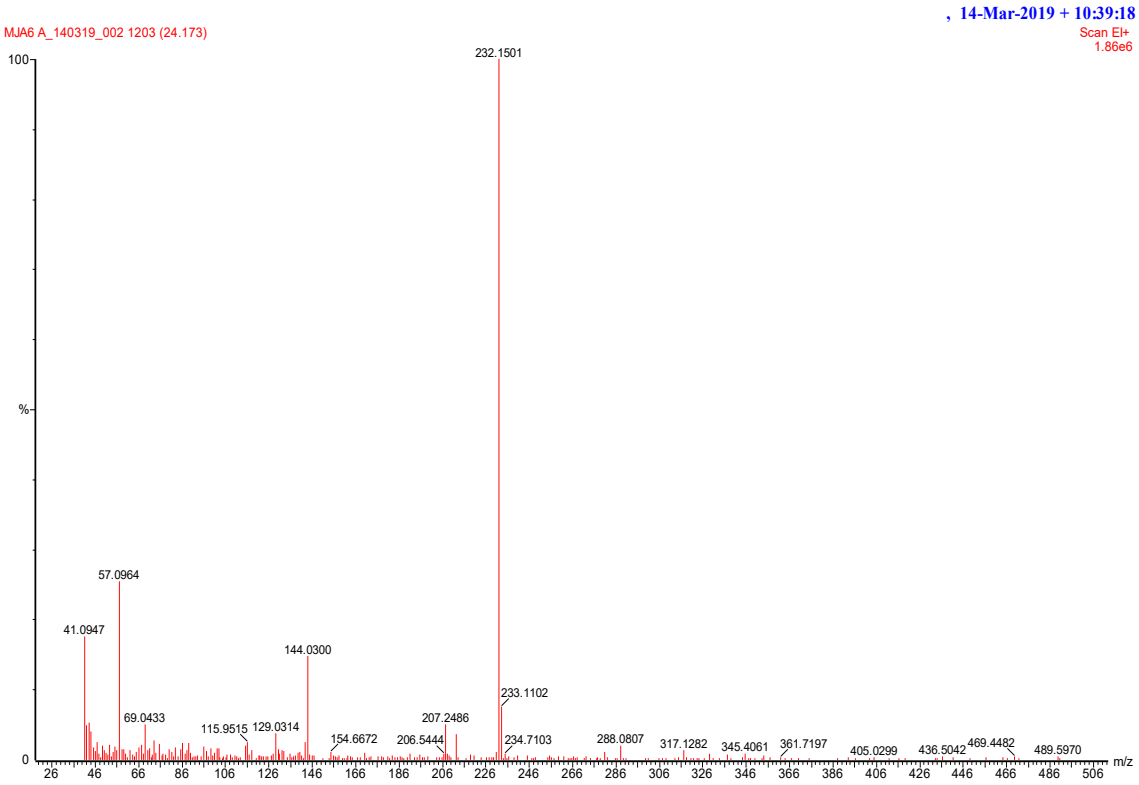


Figure 2.8: MS spectrum for MJA6 at 24.2 minutes

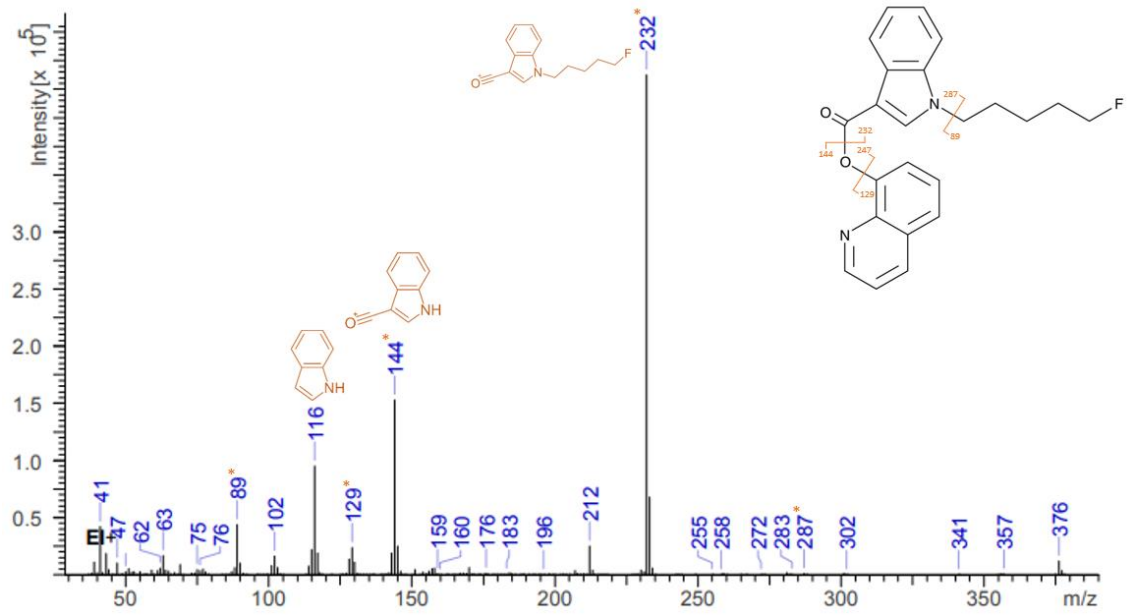


Figure 2.9: MS spectrum for 5F-PB-22 from SWGDRUG (2013b) annotated by the author

With the purchase of the LC-MS instrument in September 2019, focus turned to method development to ensure samples could be analysed using the technique. MJA5 was chosen to assess whether the sample preparation Method 2 and the instrument operating conditions (Table 2.5) developed from Ford and Berg (2016) would be

suitable. The combination of the sample preparation method and instrument operating conditions was deemed successful, with the resultant chromatogram shown in Figure 2.10. Furthermore, MJA5 was utilised as the first sample on the LC-MS to verify the identification generated through the GC-MS result by comparing to the accurate mass and the inference determined by comparing accurate mass entered into the in-house PDCL produced using the in-house synthetic cannabinoid Excel spreadsheet and information from ChemSpider .mol files. The accurate mass determined was given to four decimal places alongside a 98.59% match score, and the isotope distribution was a reasonable match, increasing the confidence in the GC-MS identification of 5F-MDMB-PICA (see Figure 2.11).

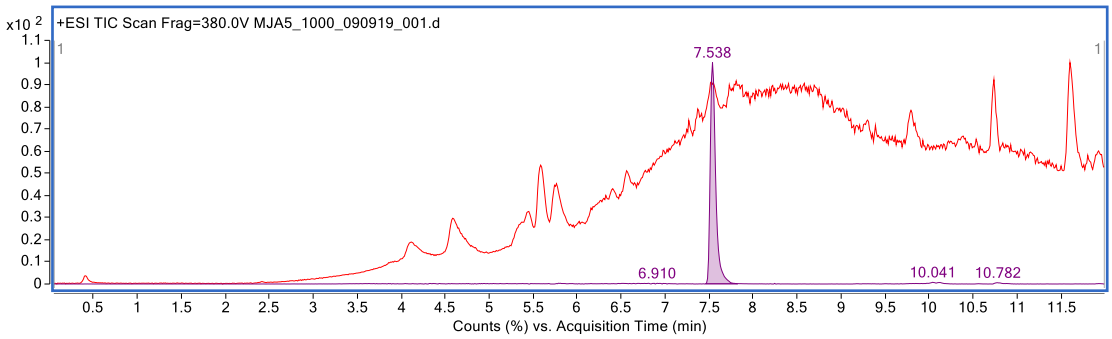


Figure 2.10: Total ion chromatogram (red) for MJA5, and extracted ion chromatogram (purple) for 5F-MDMB-PICA

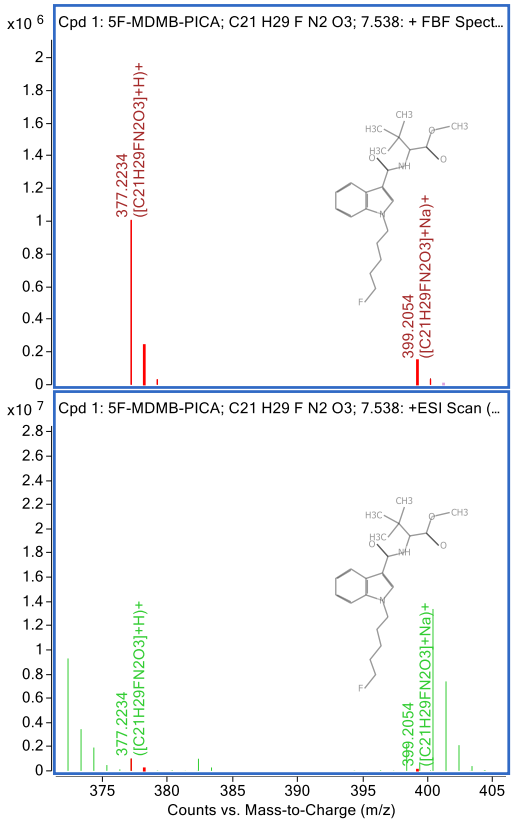


Figure 2.11: 5F-MDMB-PICA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL and MJA5 5F-MDMB-PICA spectrum below. Predicted isotope distribution marked in red

To further increase confidence in the identification of 5F-MDMB-PICA, FTIR was also used to analyse MJA5. FTIR was utilised due to its selective structural determination (SWGDRUG, 2019), plus MJA5 had already been analysed using two chromatographic techniques which determined that the sample appeared to be quite pure, therefore there was no extra considerations needed with using a non-separative technique.

The MJA5 sample was analysed using the Perkin Elmer Spectrum 2 instrument which did not have a library with synthetic cannabinoids included. To combat this, research was dedicated to identifying key functional groups present from the chemical structure of the compound in the spectrum gained (Figure 2.12). The key functional groups present in the synthetic cannabinoids encountered were labelled from assignments from various sources (Bell, 2006; Heriot Watt, 2023; Housecroft and Constable, 2006; Merck, 2023; Thermo Fisher Scientific Inc, 2008), with the colour scheme shared across Figure 2.12. The secondary amide peak is shown on the carboxamide linker labelled in pink, the sp^3 dog-ear shaped peaks for the CH_3 are labelled in dark green and the ester group can be seen in mustard. In terms of the fingerprint region for 5F-MDMB-PICA, this has only been tentatively assigned, however the peak at approximately 1466 cm^{-1} (labelled navy) is indicative of the CH_3 asymmetric deformation and CH_2 scissoring, potentially from the alkyl chain (Thermo Fisher

Scientific Incorporated, 2008). Furthermore, the peak labelled with an orange ring is indicative to the *tert*-butyl group and the purple circle, for the peak at 749 cm^{-1}, indicative of the ortho-benzene from the indole (Thermo Fisher Scientific Incorporated, 2008). Furthermore, similar peaks were seen between Figure 2.12 and Figure 2.13, which is the reference spectrum for 5F-MDMB-PICA produced by the Response project (Response, 2017).

It is worth noting that the secondary amide peak (pink), the sp^3 peaks (dark green) and the ester group (mustard) were present in all the synthetic cannabinoids analysed throughout the research.

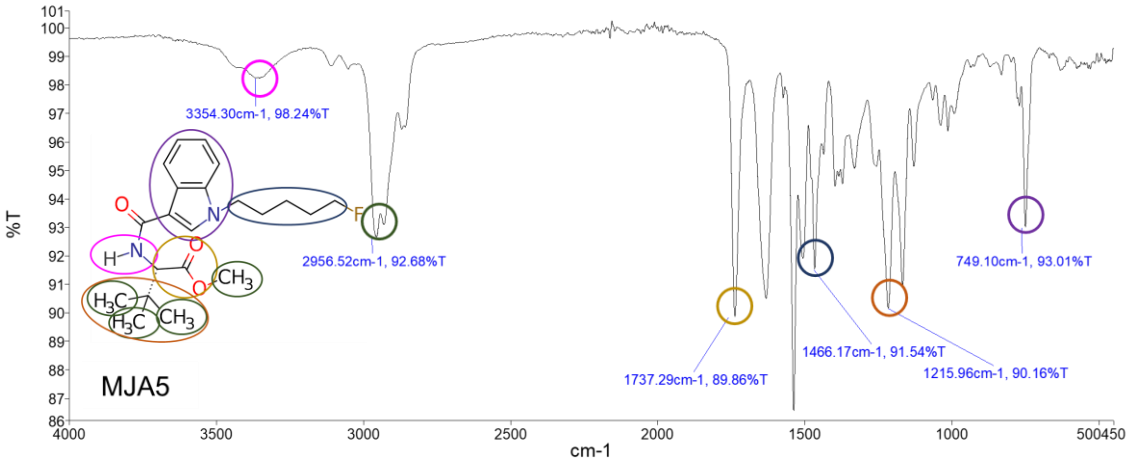


Figure 2.12: FTIR spectrum for MJA5 with correlating colour coordination

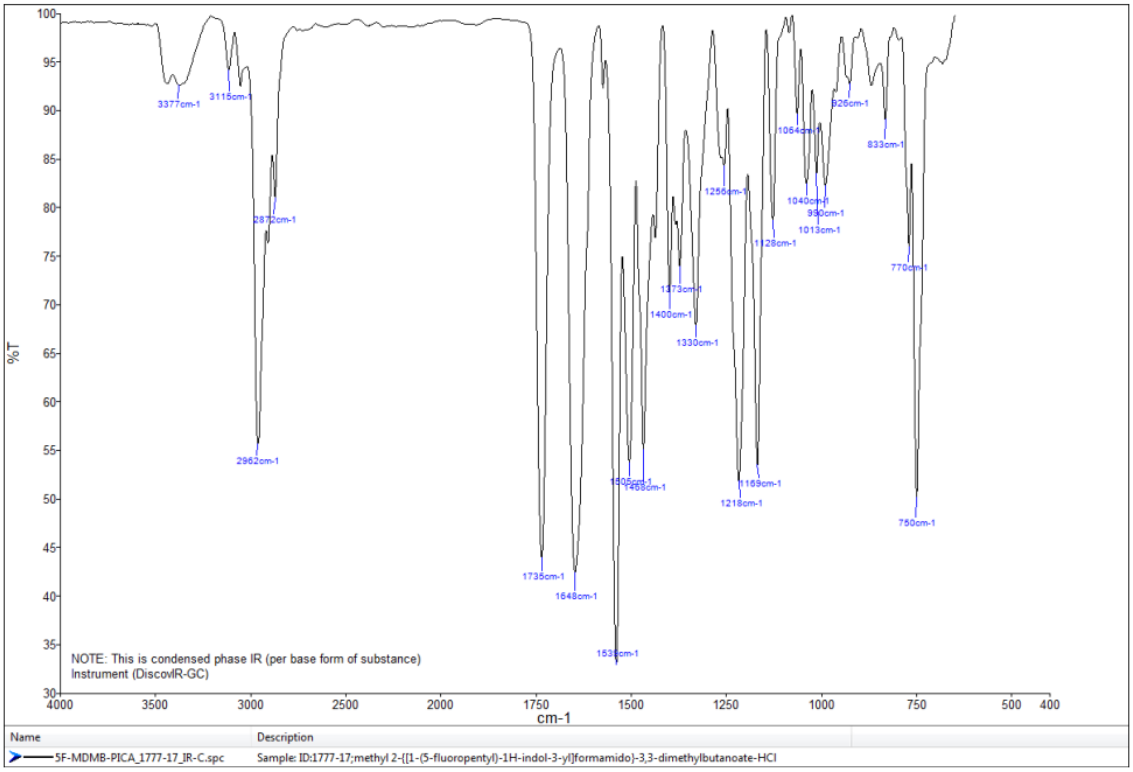


Figure 2.13: 5F-MDMB-PICA spectrum from Response (2017)

5F-MDMB-PICA was first registered by early warning systems in 2016 (WHO, 2019) and was identified in MJA5 and MJA6 between March 2019 and November 2019. Norman *et al*., (2021) noted the popularity of 5F-MDMB-PICA in Scottish and German prisons until the end of 2020, consistent with when MJA5 and MJA6 were seized and analysed, yet it is still featured in prevalence data in 2022 (NPS Discovery, 2022), showing that the popularity of the drug has allowed it to prevail over multiple years despite being under Schedule II of the 1971 Convention on Psychotropic Substances since November 2020.

MJA3

MJA3, a homemade birthday postcard, was submitted due to an Itemiser 3E® peak between 9-10 ms and featured a strong sweet odour, indicating that the paper had been interfered with and therefore could be concealing a substance. When analysed *via* GC-MS, two peaks were present within the chromatogram. The very small peak at 19.63 minutes (as shown in Figure 2.14) was indicative of being 5F-MDMB-PICA after being compared to the MJA5 and MJA6 mass spectra (Figure 2.15), to the 5F-MDMB-PICA in-house MS library entry from MJA6 with a 757 match score, and compared to the Cayman Chemical Company (2016) reference spectrum (**Error! Reference source not found.**).

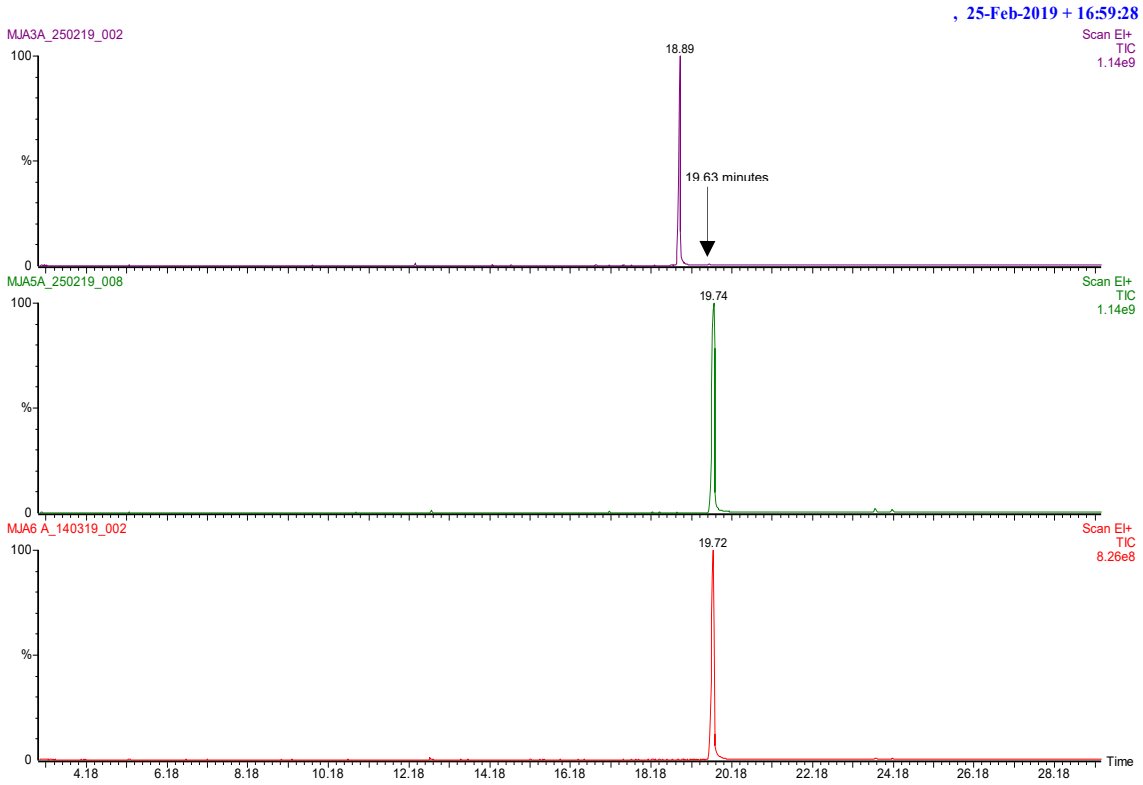


Figure 2.14: GC chromatogram for MJA3 (purple), MJA5 (green) and MJA6 (red) showing peaks at approximately 19.7 minutes retention time (with additional labelled retention time for MJA3)

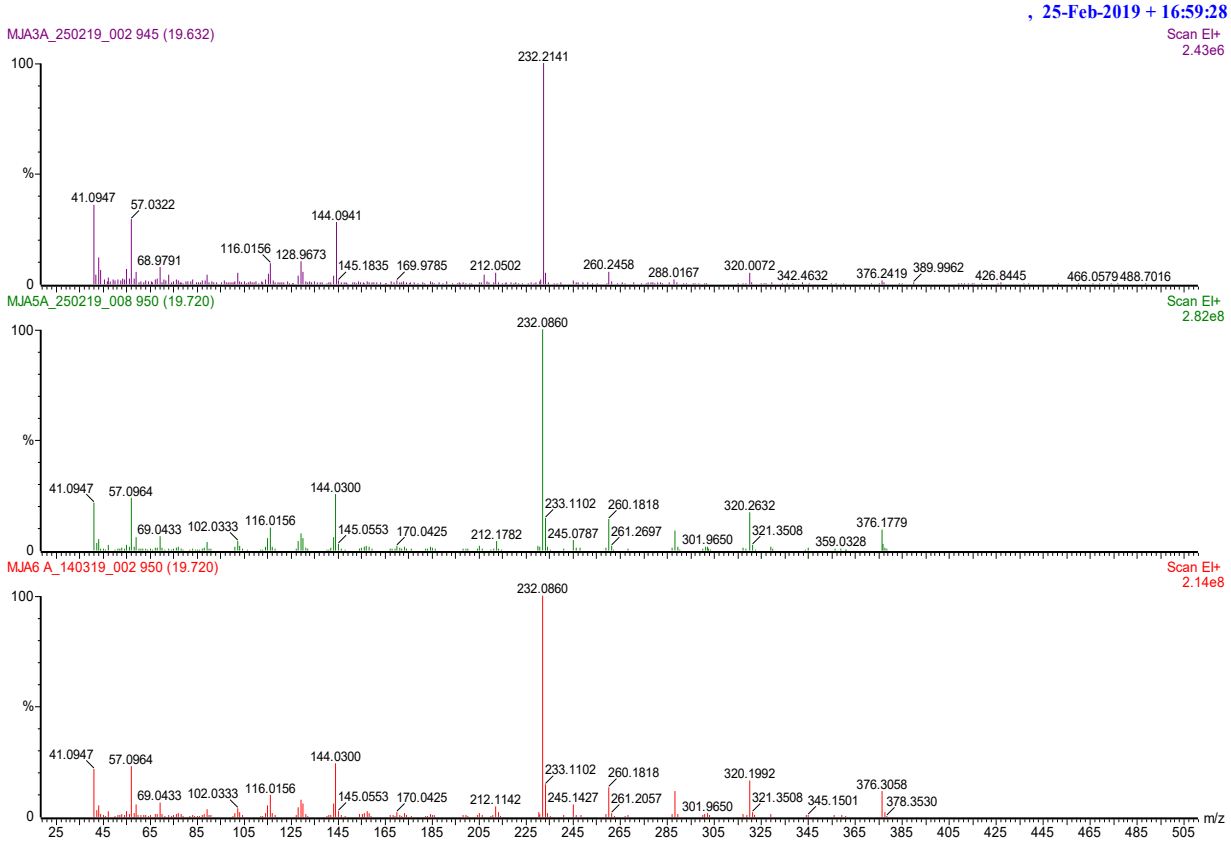


Figure 2.15: MS spectra for MJA3, MJA5 and MJA6 at approximately 19.7 minutes retention time

The major peak at 18.89 minutes, as shown in Figure 2.14, was then focused upon. Although a mass spectrum was able to be produced (Figure 2.18), it was not able to be identified initially through library searches of the NIST 2.0, online tools such as base peak and molecular ion searches on the Cayman Chemical Company GC-MS Drug Identification Tool (Cayman Chemical Company, 2022a) or manually checking online resources with reference spectra at the time of analysis. Therefore, focus was turned to the use of NMR for structural elucidation of the compound and to other online resources.

Distortionless Enhancement by Polarisation Transfer (DEPT) experiments were used to enable assignment of the carbon peaks in a spectrum. This technique identified three carbon functional groups, methines, methylenes and methyl groups, through analysis at mutually exclusive angles (DEPT 45°, 90° and 135°) to aid in determining the bond inferences (Jacobsen, 2016). The spectrum for MJA3 can be seen in Figure 2.16, with the tetramethylsilane peak (internal reference) seen at 0 ppm and the deuterated chloroform at 77 ppm. Structural inferences were indicated through DEPT angle changes and interactions with the surrounding electronegative elements dependent upon which type of carbon-hydrogen bond was present for each peak. Two CH_3 peaks were highlighted at 18.16 and 19.19 ppm due to the shielding, but a presence of a strong electronegative element nearby seemed to cause the difference in shift between the two. This suggested a presence of oxygen, and due to the two CH_3 groups being present, the first estimation was that the linked group was 1-amino-3-methyl-1-oxobutane. There was also an indication of at least four C-H bonds, which suggested the four least shielded protons (121.42 – 136.94 ppm) may be part of a benzene ring from either an indole or indazole. Four CH_2 bonds were identified at 28.98, 30.78, 46.14 and 116.14 ppm, and a potential fifth at 29.77 ppm, although this was questioned due to the low abundance as to whether it was potentially noise. At the time, there was a working theory that this could have been a cyclo-hexyl-methyl group as it was suggested that no fluorine elements were present as a result of a fluorine experiment, however there were not enough CH_2 groups to make this, so there was ongoing work to attempt to determine an alternative tail, however this was halted when the substance identification was found. The next step would have been to investigate the structure of the tail in comparison to the indole core and linker in reference to 5F-MDMB-PICA through analysis of the MS fragmentation patterns.

The quaternary carbons cannot be identified through DEPT experiments as there are no hydrogens bonded to the carbons (Jacobsen, 2016). When decoupled carbon experiments were undertaken, there were some peaks at approximately 80, 160 and

180 ppm which potentially could have been quaternary carbon peaks. However, quaternary carbon peaks are known to be shorter due to the lack of nuclear Overhauser effect enhancement (Jacobsen, 2016), plus the background noise being quite significant even after the number of scans was greatly increased, they were not included at this stage and only the carbon-hydrogen bond groups were included as identified through the DEPT. Other 1D and 2D experiments were conducted but were not required for identification.

At the same time as attempting to structurally elucidate the sample through NMR (February 2019), research was also being conducted to identify if there was potential in using posts by users and sellers of synthetic cannabinoids on Reddit.com to determine the current synthetic cannabinoids on the market and act as a potential early warning system for newly emerging synthetic cannabinoids, similar to the work undertaken by Barenholtz et al., (2021). It was hoped that there would be potential to use R to scrape subreddits like "r/noid" (a common noun for synthetic cannabinoids on the forum) or "r/researchchemicals" for names of compounds, so manual checking of the subreddits was first implemented to determine the potential before expanding to use R. MMB-022, or MMB-4en-PICA, was included in a list of synthetic cannabinoid compounds on a post by a user suggesting it was a popular synthetic cannabinoid to use and it was the only compound in the list not included in the in-house synthetic cannabinoid Excel spreadsheet. The compound name was then searched on the Cayman Chemical Company website and the MMB-022 reference spectrum (

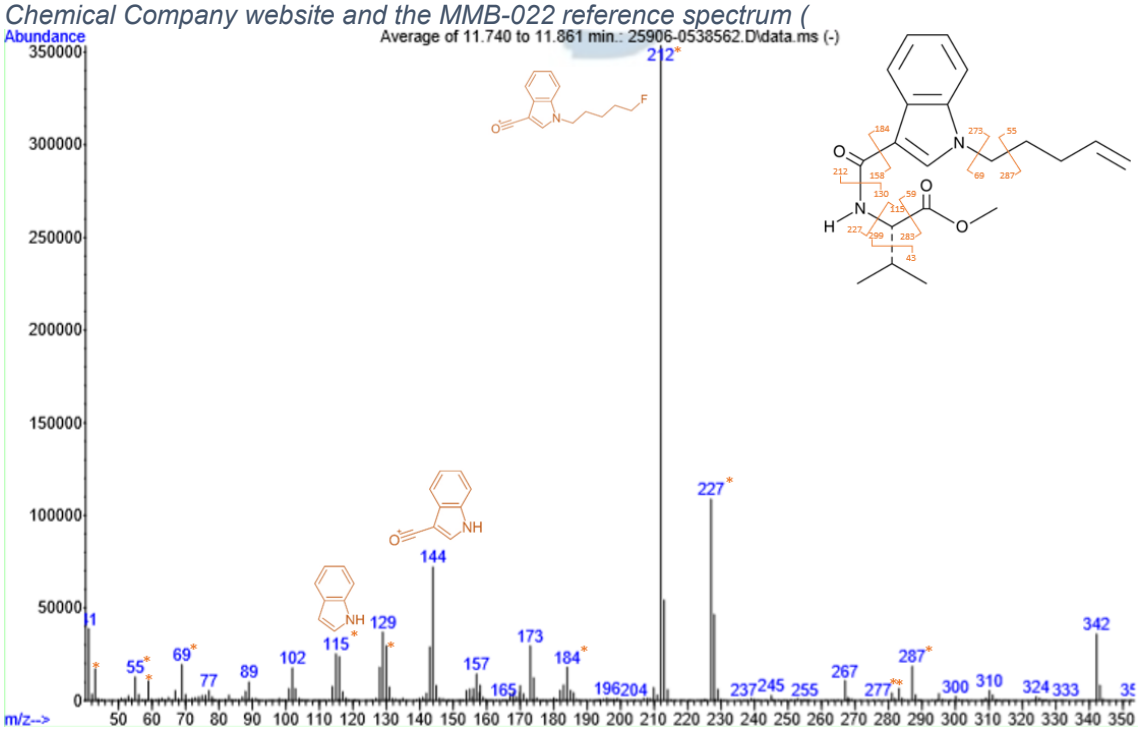
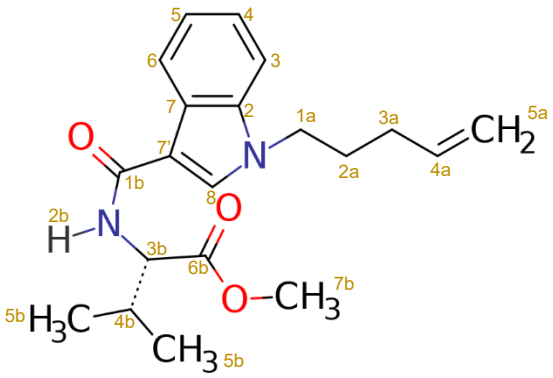


Figure 2.17) was used to compare to the MJA3 mass spectrum for the peak at 18.89 minutes (Figure 2.18) from the MJA3 chromatogram (Figure 2.14) and therefore identify the presence of MMB-022 alongside 5F-MDMB-PICA within the MJA3 sample.

Table 2.10 shows the structural inference assignments indicated from the DEPT experiments once the structure of MMB-022 was known. This highlighted that some of the estimations surrounding the structure did need work, however there was promise if the work had continued. The NMR was only needed for this sample due to the issue

with reference spectra and lack of indications through the library, however the use of NMR was extremely helpful for indications of the structure and therefore the value of the technique highlighted how it could be used in conjunction with chromatographic techniques, such as GC-MS or HPLC with the fraction collector in the future when dealing with more unknown compounds.

Table 2.10: NMR assignments for MJA3



MJA3 NMR Spectrum Assignments		
Assignments	13C{1H}/ppm	Inference
3	121.70	CH – Aromatics
4	122.56	CH – Aromatics
5	131.87	CH – Aromatics
6	136.94	CH – Aromatics
8	110.42	CH
1a	46.14	CH_2 – Straight chain
2a	30.78	CH_2 – Straight chain
3a	28.98	CH_2 – Straight chain
4a	56.95	CH
5a	116.14	CH_2
3b	120.19	CH
4b	31.81	CH
5b	18.16 and 19.19	CH_3
7b	52.26	CH_3

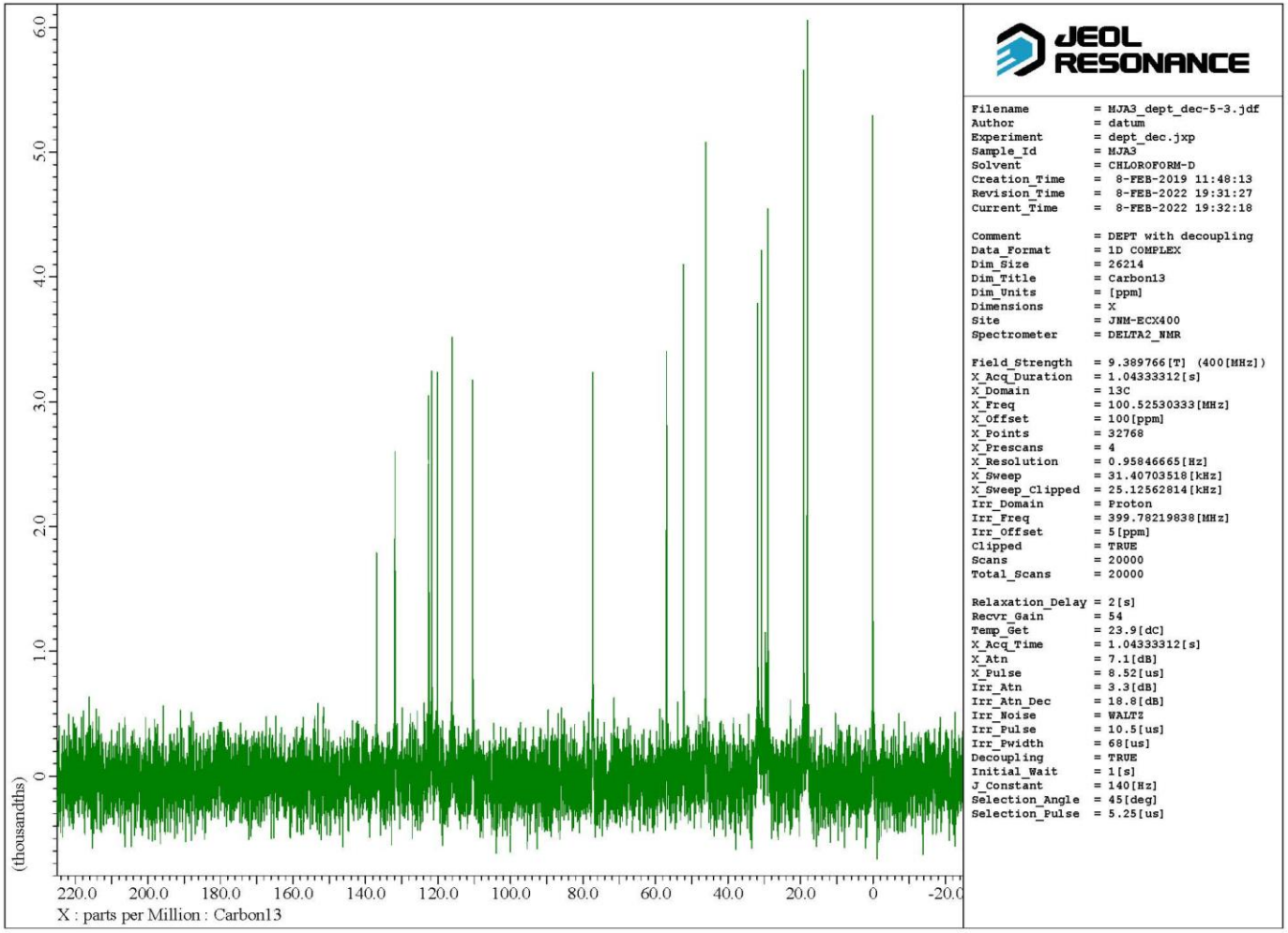


Figure 2.16: 13C{1H}/ppm (45°) NMR spectra for MJA3

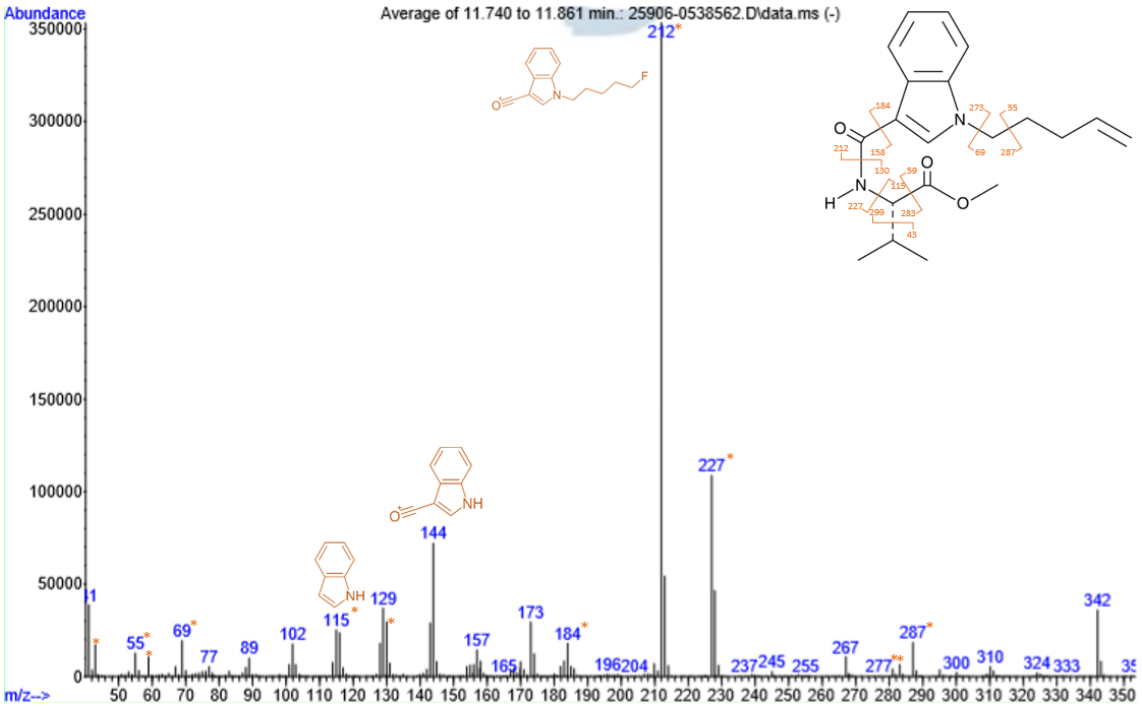


Figure 2.17: MS spectrum for MMB-022 from Cayman Chemical Company (2018a) annotated by the author

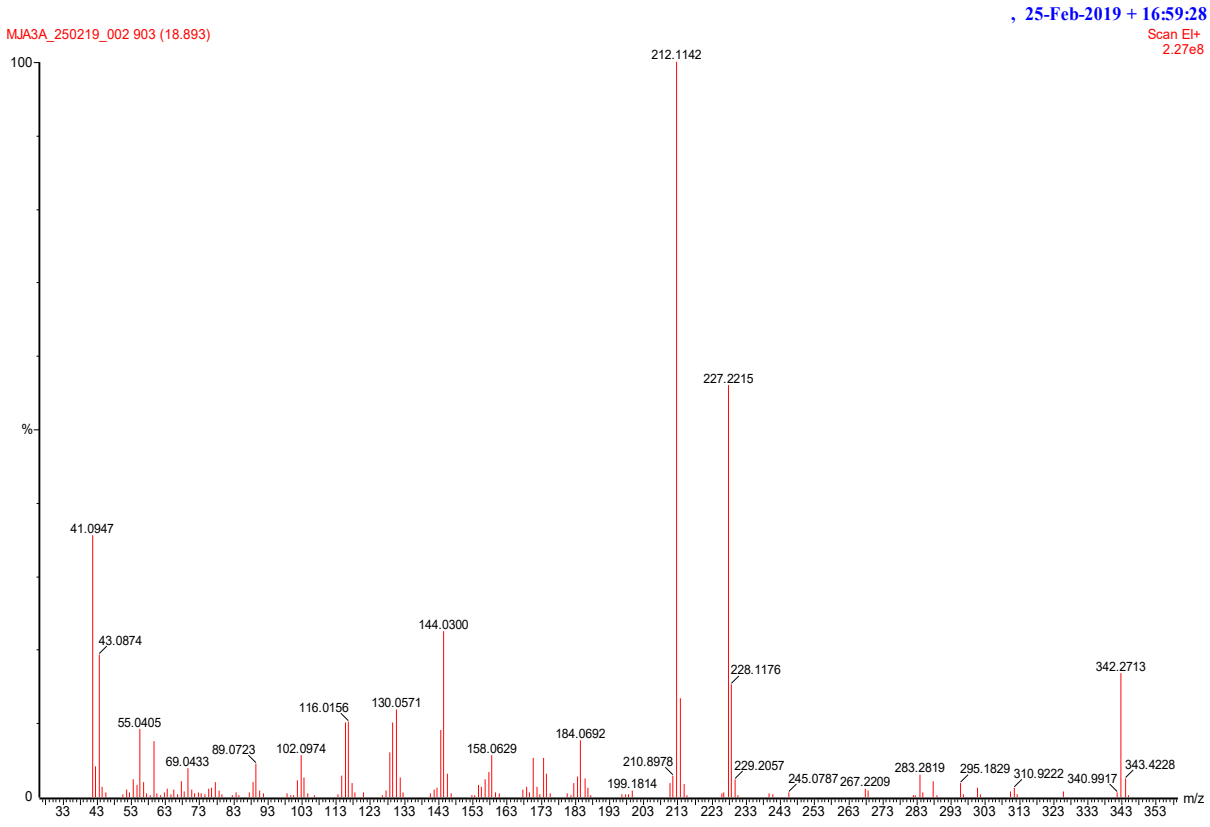


Figure 2.18: MS spectra for MJA3 at 18.89 minutes

Although structural elucidation through analysis of the fragmentation patterns was not needed for the identifications of these substances, they have been highlighted within the reference spectra to show similarities across the substances. In the case of MJA3, this may have been particularly pertinent, with similarity indicating the presence of an indole core with the peak at 116 seen, plus the linker for the peak similarity at 144 between 5F-MDMB-PICA and MJA3.

As MJA3 was a mixture of MMB-022 and 5F-MDMB-PICA, the spectrum for MJA5/5F-MDMB-PICA (Figure 2.12) was subtracted from the MJA3 (Figure 2.19) using the Perkin Elmer Spectrum IR Version 10.7.2 software on the Spectrum 2 to result in MJA3_1 (Figure 2.20), a potential spectrum for MMB-022 only. However, the two spectra are very similar, which reflects the larger abundance of MMB-022 within the compound and the low abundance of 5F-MDMB-PICA (Figure 2.14). The associated structural assignments for MJA3, MJA3_1 and MJA5 are included in Table 2.11 alongside the colour coordinated structure, highlighting the similarities such as the shared ester (mustard) and secondary amine (pink) but the inclusion of the alkene or isopropyl groups for MJA3 and MJA3_1 are not included in the MJA5 spectrum.

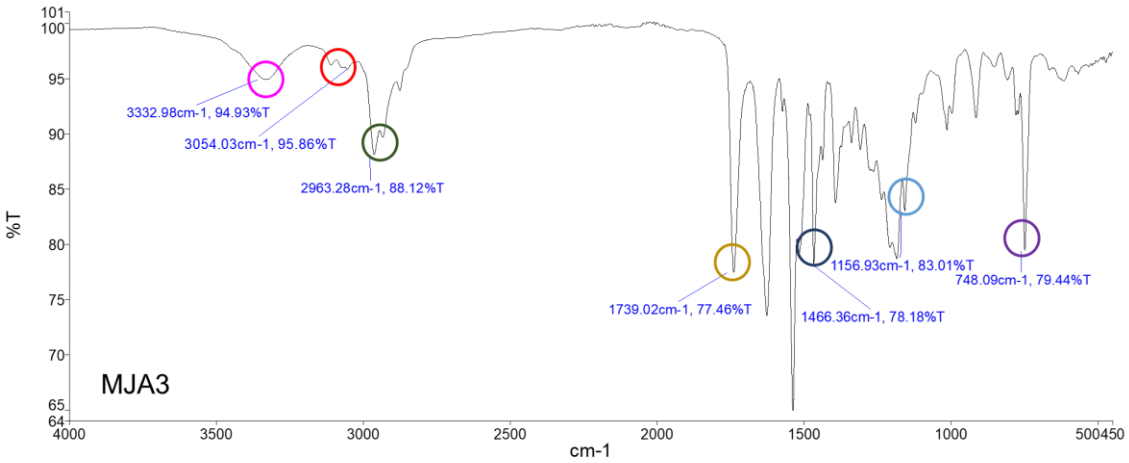


Figure 2.19: FTIR spectrum for MJA3 with correlating colour coordination

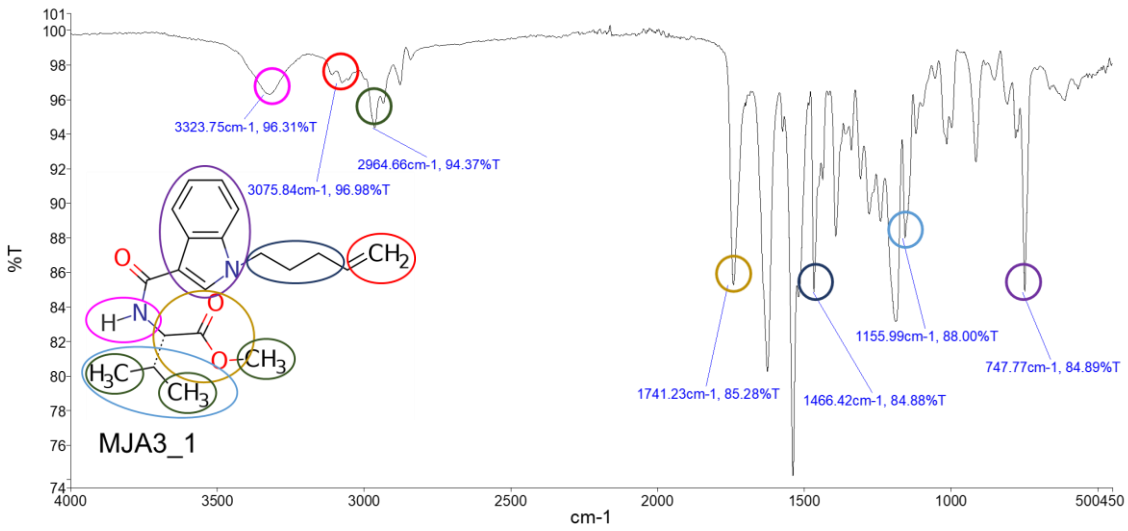


Figure 2.20: FTIR spectrum for MJA3_1, the result of the subtraction of MJA5 from MJA3, with correlating colour coordination

Table 2.11: MJA3, MJA3_1 and MJA5 indicative structural assignments and corresponding wavenumbers

		Wavenumber (cm^{-1})								Inference
Samples	MJA3	3333	3054	2963	1739	1466	-	1157	748	MMB022 and 5F-MDMB-PICA
	MJA3_1	3324	3076	2965	1741	1466	-	1156	748	MMB022
	MJA5	3354	-	2957	1737	1466	1216	-	749	5F-MDMB-PICA
	Assignments	Secondary amide N-H stretch[ab]	Alkene RCH= CH_2 C-H stretch[cd]	CH_3 (sp^3) C-H stretch[ad]	Ester C=O stretch[ad]	CH_3 asymmetric deformation and CH_2 scissoring (tentative)[e]	*Tert*-butyl CH_3 Deformati-on (tentative)[e]	Isopropyl CH_3 Deformati-on (tentative)[e]	Ortho-benzene from the indole or indazole C-H bending (tentative)[e]	

[a]Housecroft and Constable (2006), [b]Heriot Watt (2023), [c]Bell (2006), [d]Merck (2023) & [e]Thermo Fisher Scientific Inc. (2008)

MJA3 was also selected to be analysed on the LC-MS as it was identified as a mixture using the GC-MS. The total ion chromatogram can be seen in black on both Figure 2.21 and Figure 2.22, and the extracted ion chromatograms in blue highlight the in-house PCDL matched peaks using the Find by Formula function. The peak at 8.134 minutes had a 99.46% match to MMB-022 and the peak at 8.268 minutes had a 97.65% match to 5F-MDMB-PICA. For both, the library spectra and sample spectra (Figure 2.23) were compared to ensure similarity and good peak situation within the predicted isotope distribution range. Furthermore, the accurate masses were compared to those in the library and those acquired through GC-MS analysis, therefore solidifying the identification of MMB-022 and 5F-MDMB-PICA within the MJA3 sample.

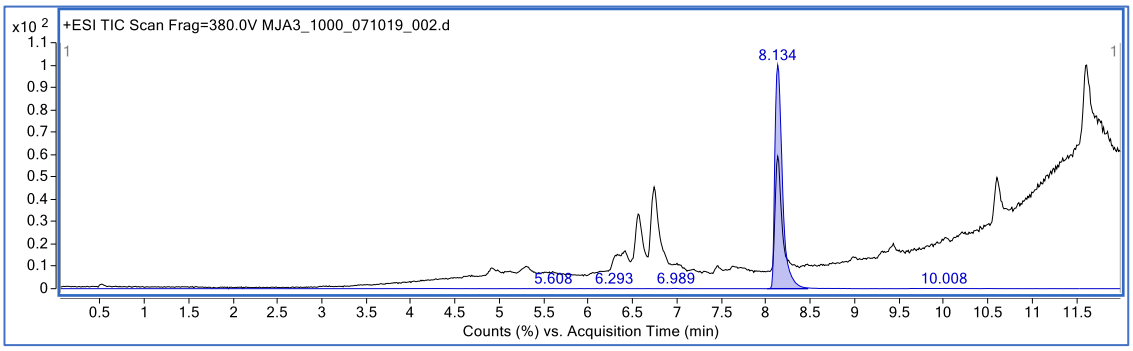


Figure 2.21: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (blue chromatogram) for MJA3 for peak at 8.134 minutes

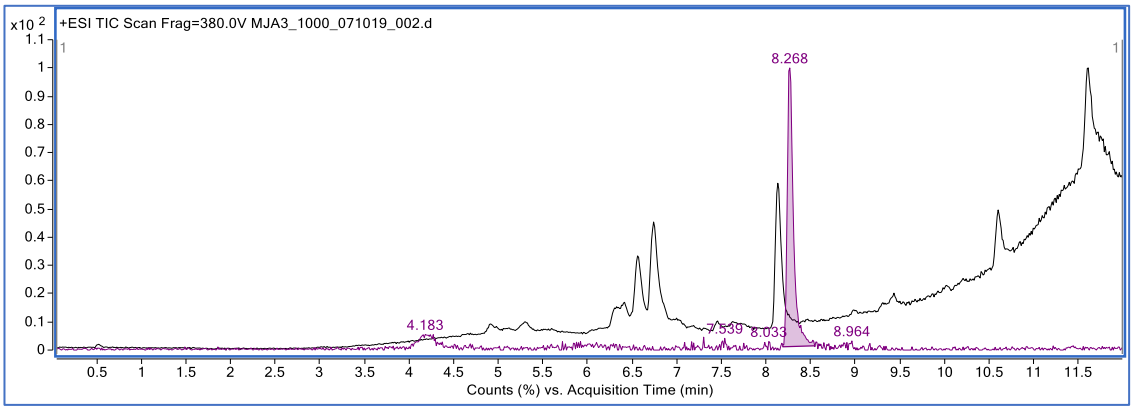


Figure 2.22: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (purple chromatogram) for MJA3 at 8.268 minutes

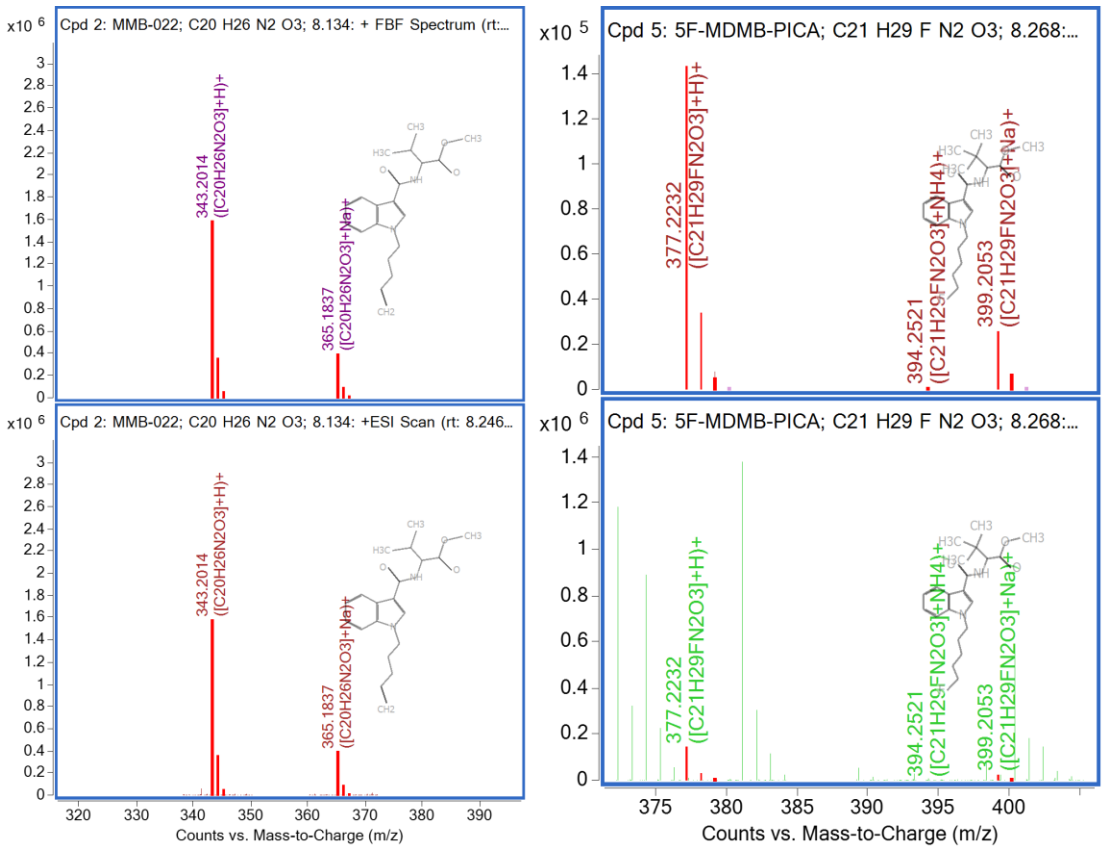


Figure 2.23: MMB-022 spectra (left) and 5F-MDMB-PICA (right) from Find by Formula (FBF) library match and MJA3 spectra below. Predicted isotope distribution marked in red

MJA7 and MJA8

MJA7 was not provided with corresponding Itemiser 3E® results at the time of submission as it was obtained outside of the usual route from the West Midlands Prisons Group, and instead given to the University for analysis from Howard Chandler, the direct contact from Rapiscan Systems Limited. Information was passed on to state that the sample had been tested on a prison Itemiser 3E® during a training session and did not trigger alarms, but there was intelligence to suggest the paper had been used by prisoners. The sample was tested at the University after submission and drift times were recorded retrospectively. MJA7 was prepared using sample preparation Method 2 and analysed using GC-MS, resulting in a single chromatography peak at 17.57 minutes (Figure 2.24) and the mass spectrum for the peak is shown in Figure 2.25.

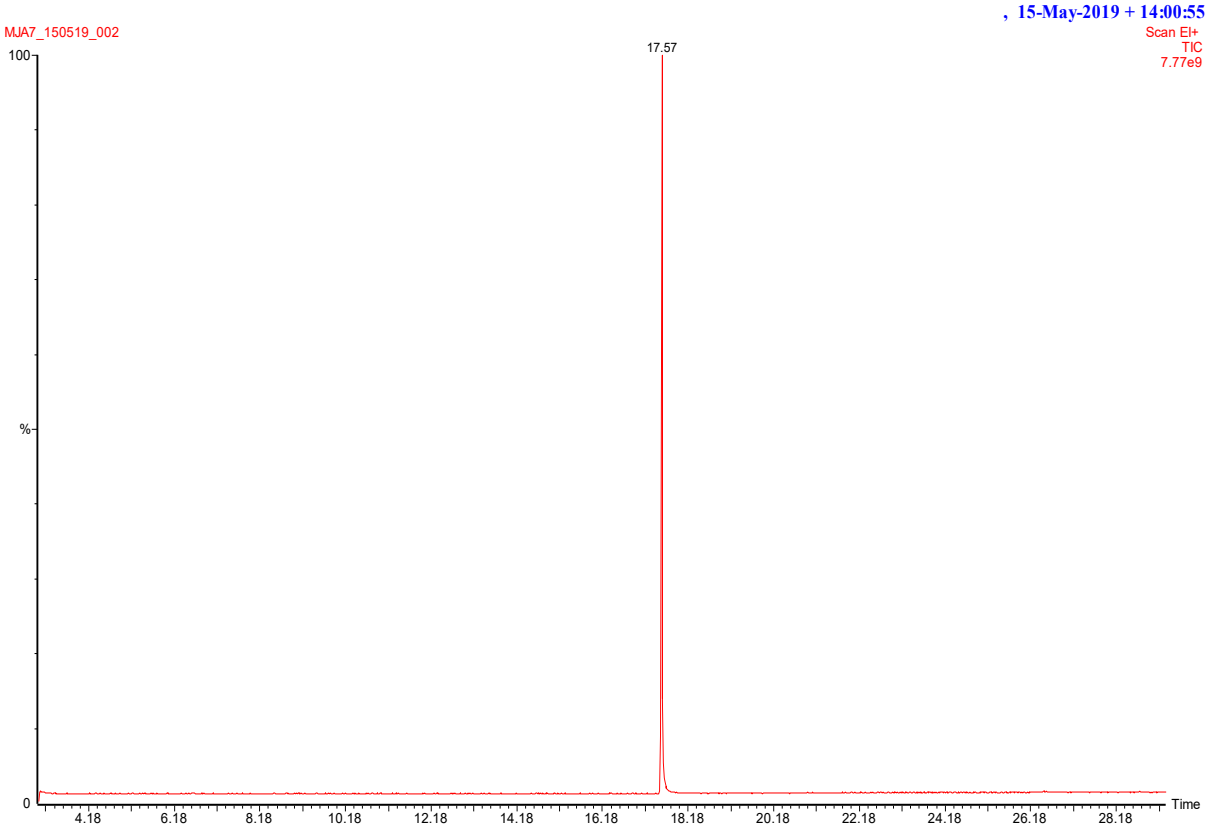


Figure 2.24: GC chromatogram for MJA7

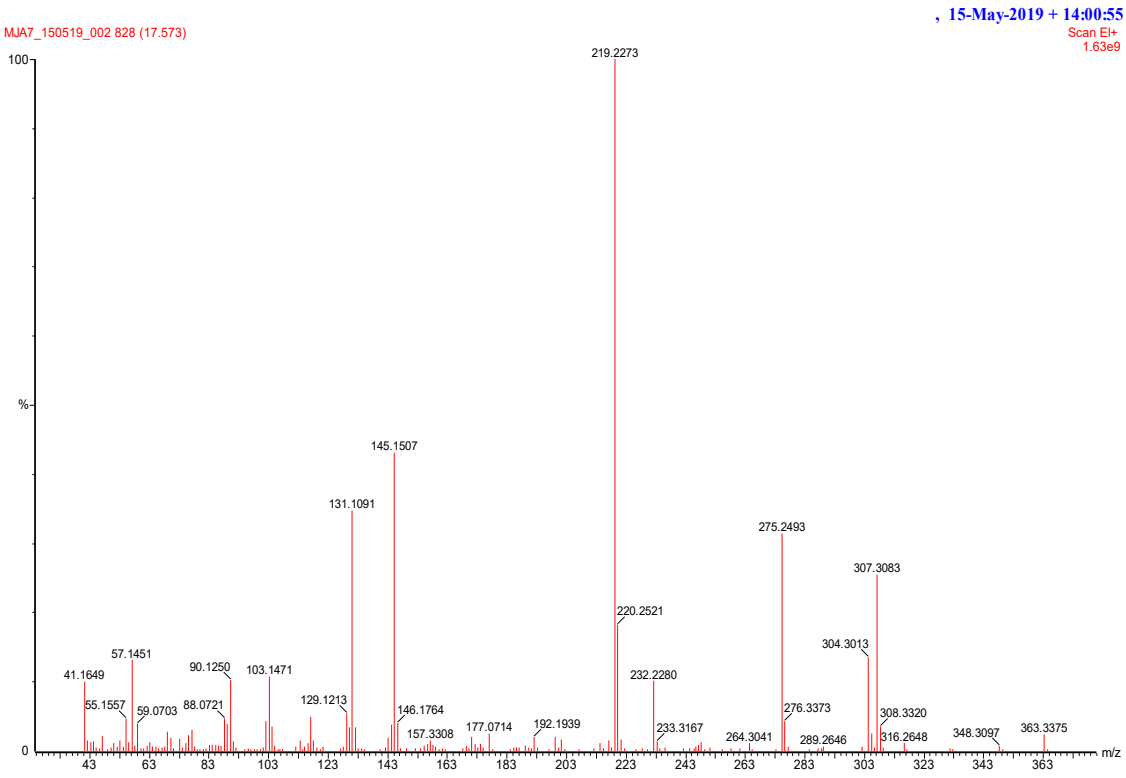


Figure 2.25: MS spectrum for MJA7 at 17.57 minutes

The NIST 2.0 library listed 8-amino-5-[S-hexylthio]-6-methoxy-2-methylquniloine as the top library hit for this sample with a 514 match score. This was considered a very poor

score (NIST Mass Spectrometry Data Center, 2008) and it may have only been allocated due to the similarity in base peak, therefore the 8-amino-5-[S-hexylthio]-6-methoxy-2-methylquniloine identification was disregarded. Focus then turned to the true identification of the compound. Communications with staff from Eurofins Forensic Services in early 2019 (Newman, 2019) highlighted a number of emerging synthetic cannabinoids being identified in judicial samples, with 4F-MDMB-BUTINACA being noted at the time as a popular compound. When the spectrum for MJA7 was produced for the peak at 17.57 minutes, this was then compared to online reference spectra for all the compounds suggested by Newman (2019), resulting in the identification of 4F-MDMB-BUTINACA through the reference spectrum from Cayman Chemical Company (2019b) shown in

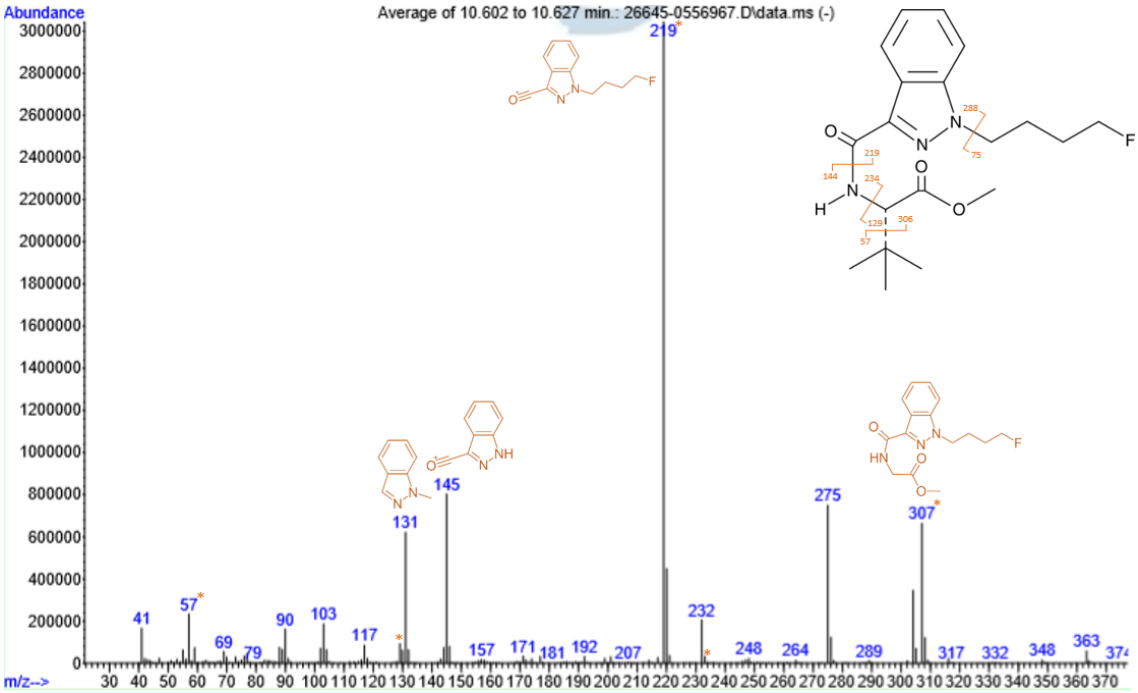


Figure 2.26 (annotated to include fragmentation information by the author). The communication with external providers showed benefits in ease of identification when there has been collaboration. Without a short-list of potential suspect compounds from Newman (2019), the time taken to find reference spectra, structurally elucidate through NMR and feed back to Rapiscan Systems Limited and HMP Featherstone could have been lengthy (as with the case of the peak at 18.86 minutes for MJA3).

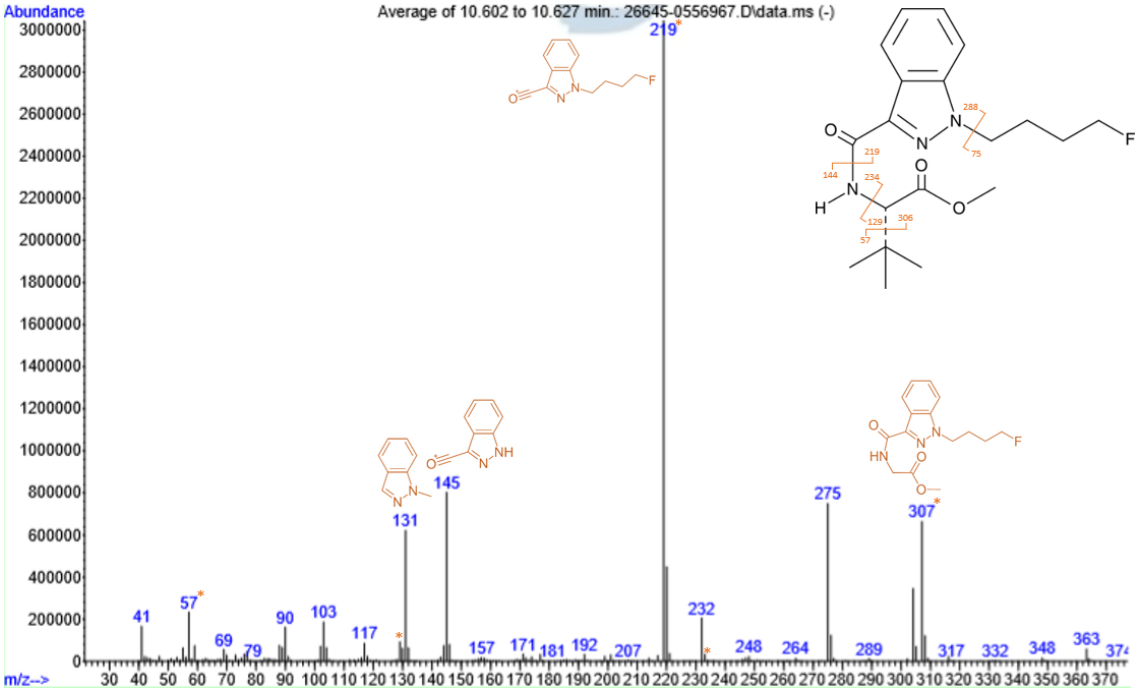


Figure 2.26: MS spectrum for 4F-MDMB-BUTINACA from Cayman Chemical Company (2019b) annotated by the author

MJA8, a small piece of paper submitted to the University, was seized from a prisoner by a dog handler after indication from a search dog. The sample had been analysed by an Itemiser 3E® at the time of submission, with a 9.099 ms time-of-flight recorded in the usual synthetic cannabinoid region. Similar to MJA7, at the time of analysis on the Itemiser 3E®, there was no substance in the library that had a similar drift time. MJA8 was analysed *via* GC-MS and LC-MS at a later date to MJA7 due to urgent turnaround times needed on a new batch of samples around the time of submission. The identification of MJA7 as 4F-MDMB-BUTINACA was fed back to Rapiscan Systems Limited representatives within four days of the submission to then urge Rapiscan Systems Limited to identify a time-of-flight definition for the compound on their Itemiser 3E®. They sought to identify a time-of-flight time for 4F-MDMB-BUTINACA, which resulted in a time-of-flight of 9.120 ms ±0.040 ms being produced in the summer of 2019. The time-of-flight recorded for MJA8 in early 2019 matches this definition.

Due to the sample being analysed after the streamlined method development process, MJA8 was prepared using sample preparation Method 4. This resulted in a single chromatography peak at 16.65 minutes, as shown in Figure 2.27, with the mass spectrum shown in Figure 2.28. The NIST 2.0 library identified the compound as 1-tert-butyl-2,4-diphenyl-1H-pyrrole with a very poor 541 match score, and the second hit was 8-amino-5-[S-hexylthio]-6-methoxy-2-methylquniloine, as seen with MJA7, but with a 516 match score. Both were assumed to have had the top two hits due to the

similarity in base peak, however both were very poor (NIST Mass Spectrometry Data Center, 2008) and therefore both identifications were dismissed. The base peak and relative molecular mass were then compared to compounds listed within the in-house synthetic cannabinoid Excel spreadsheet and major similarity was seen with 4F-MDMB-BUTINACA. Manual mass spectral peak comparison was undertaken to identify the presence of 4F-MDMB-BUTINACA, and differences in retention times were attributed to using a new GC-MS, which had a new column with different dimensions and a general drug screening temperature program (operating conditions seen in Table 2.4).

Figure 2.27: GC chromatogram for MJA8

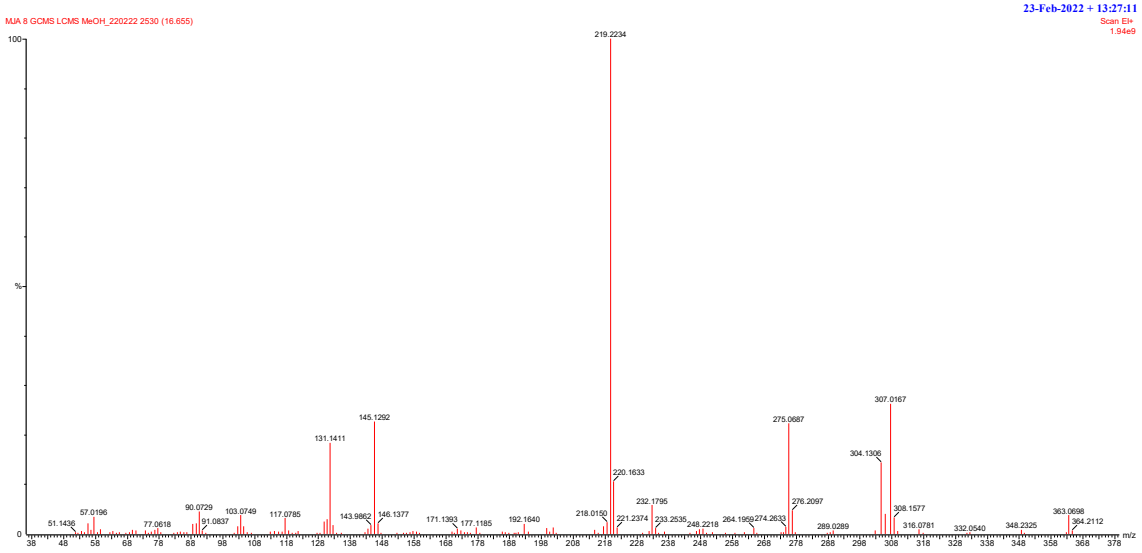


Figure 2.28: MS spectrum for MJA8 at 16.65 minutes

MJA7 and MJA8 were retrospectively analysed using the LC-MS once the instrument had been purchased and established within the laboratory. The in-house PCDL was

used to analyse the data from the LC-MS for MJA7 and MJA8 and aided in the identification of 4F-MDMB-BUTINACA, with the spectral similarity between the library spectra and acquired spectra (Figure 2.29) resulting in a match score of 98.94% and 99.18% respectively, however there was a considerable difference in retention times of the main peaks (Figure 2.30 and Figure 2.31). Although there was a peak present in all samples at approximately 8.3 minutes, the most abundant peak in MJA7 was at 0.6 minutes which was not present at all in MJA8. This led to producing a 50:50 mixture of the two samples in solution and the sample MJA7+MJA8 was analysed, as shown in Figure 2.32, with the most abundant peak at 8.4 minutes. The difference in retention time was seen to potentially arise from MJA7 originally being diluted in acetone and then reconstituted from dryness in methanol, therefore potentially having a presence of a less polar solvent present if the reconstitution was not completely from dryness. The samples were analysed on the same day with the same freshly prepared eluent and the operating conditions as outlined in Table 2.5. To investigate this issue in more detail, the samples were prepared and extracted again with methanol only and each sample, including MJA7+MJA8, was reinjected 10 times. Again, this produced the same difference in retention time but consistently high matches to 4F-MDMB-BUTINACA from the in-house library. Further work is needed to try to establish if the sample is not mixing correctly with the mobile phase by trying different sample injection methods, such as mixing the methanol sample extraction solutions of MJA7 and MJA8 with some of the mobile phase before injection. Work is also planned to compare to reference standard retention times when possible.

MJA7 was analysed using the FTIR to highlight the key functional groups present, with the colour coordinated spectrum shown in **Error! Reference source not found.**. The functional groups highlighted in Table 2.12 are very similar to those discussed for MJA5 and shown in the Figure 2.12 spectrum due to the structural similarity with the compounds; the only differences arising from the indole core and pentyl chain on 5F-MDMB-PICA and indazole core and butyl chain for 4F-MDMB-BUTINACA. The difference in the wavenumbers seen in Table 2.12 for the CH_2 scissoring (dark blue) could be due to fewer CH_2 bonds being present (Thermo Fisher Scientific Inc., 2008), however this is only a tentative identification due to the position in the fingerprint region.

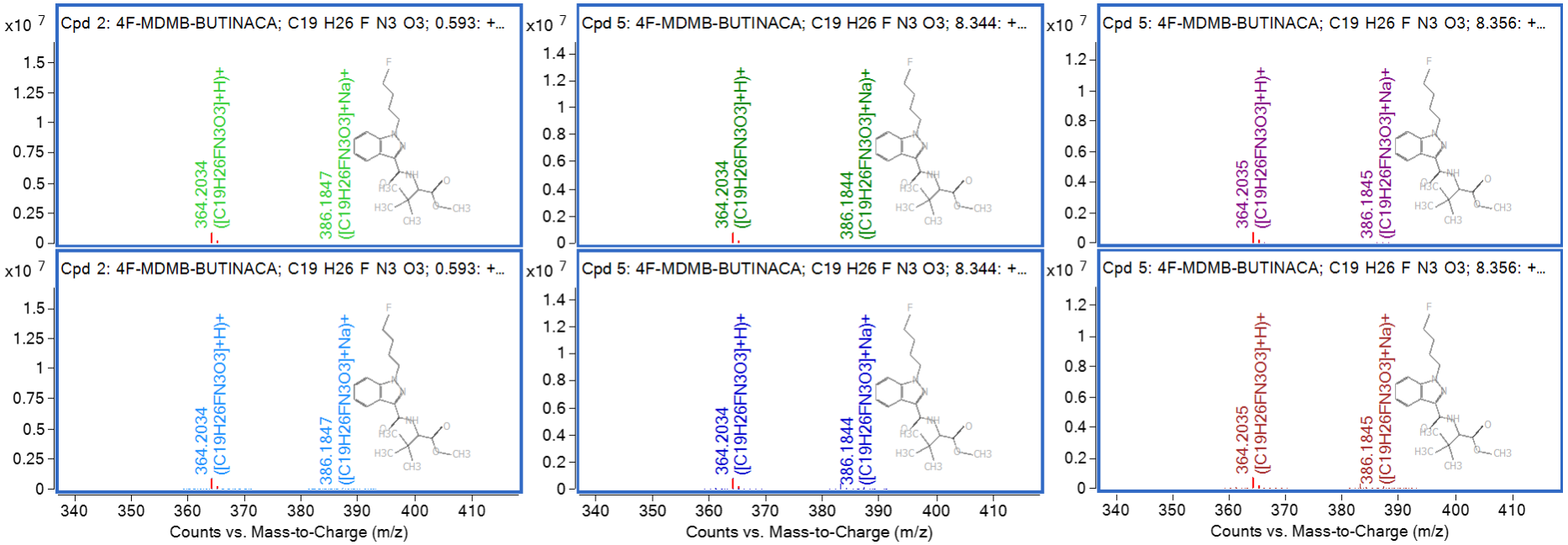


Figure 2.29: MS spectra for MJA7 (0.593 minutes), MJA8 (8.344 minutes) and MJA7+MJA8 (8.356 minutes) from left to right from LC-MS. 4F-MDMB-BUTINACA spectra from the in-house PCDL above and sample spectra below. Predicted isotope ratio marked in red.

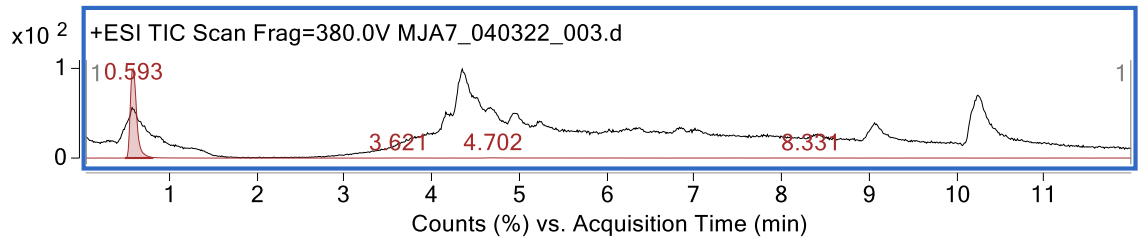


Figure 2.30: LC chromatogram for MJA7

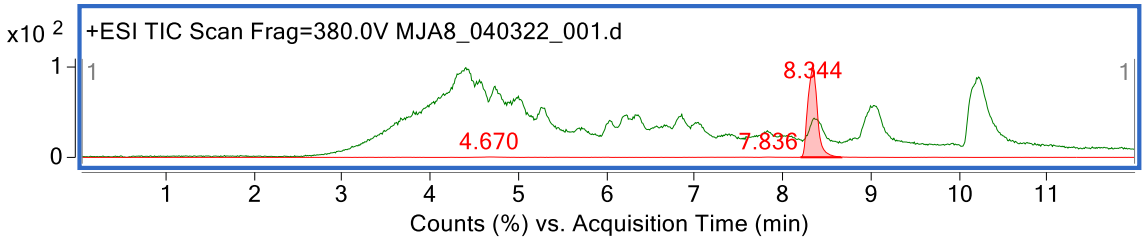


Figure 2.31: LC chromatogram for MJA8

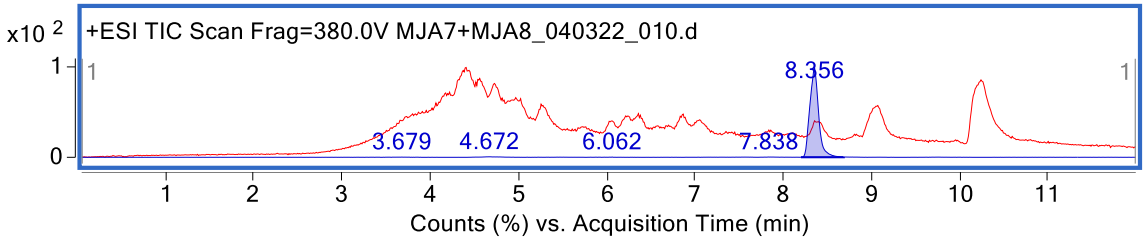


Figure 2.32: LC chromatogram for a mixture of MJA7 and MJA8

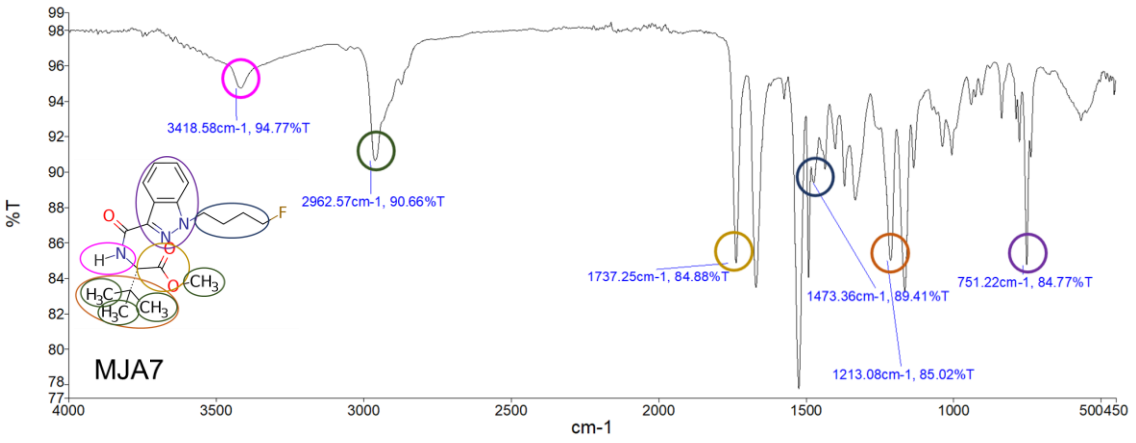


Figure 2.33: FTIR spectrum for MJA7 with correlating colour coordination

Table 2.12: MJA5 and MJA7 indicative structural assignments and corresponding wavenumbers coordination

		Inference								
Samples	MJA5	3354	-	2957	1737	1466	1216	-	749	5F-MDMB-PICA
	MJA7	3419	-	2963	1737	*1473 (tentative)*	1213	-	751	4F-MDMB-BUTINACA
	Assignments	Secondary amide N-H stretch [ab]	Alkene – RCH= CH_2 C-H stretch[cd]	CH_3 (sp^3) C-H stretch[ad]	Ester C=O stretch[ad]	CH_3 asymmetric deformation and CH_2 scissoring (tentative)[c]	*Tert*-butyl CH_3 Deforma-tion (tentative)[c]	Isopropyl CH_3 Deforma-tion (tentative)[c]	Ortho-benzene from the indole or indazole C-H bending (tentative)[c]	

[a]Housecroft and Constable (2006), [b]Heriot Watt (2023), [c]Bell (2006), [d]Merck (2023) & [e]Thermo Fisher Scientific Inc. (2008)

MJA14 and MJA17

MJA14 and MJA17 were submitted to confirm that the substance included in the alarm was the substance present, with an alarm for 5F-AKB-48 on MJA14, and an alarm for 5F-ADB on MJA17. The presence of 5F-AKB-48 on MJA14 was questioned as it was mainly prevalent as part of the third-generation synthetic cannabinoid wave (Frinculescu *et al.*, 2017). After 2016, 5F-AKB-48 became less popular, as it was not mentioned as a current new psychoactive substance in the World Drug Report 2018 (UNODC, 2018) (the first year of the research) and although seen in the first and third quarter of 2019 in Welsh prisons, it was not seen in Scottish prisons from 2018 to 2020 (Norman, Walker, McKirdy, *et al.,* 2020; Norman *et al.*, 2021). Therefore, the presence of 5F-AKB-48 in MJA14 was seen as a potential false positive that required confirmatory analysis to detect what was present. On the other hand, there was a higher likelihood of 5F-ADB being present in MJA17 due to the substance being popular around the time of submission. There were drift times at 9.165 ms for MJA14 and 9.190 ms for MJA17, suggesting a similar compound was present in both, but the library drift time for 5F-ADB was 9.255 ms ± 0.040 ms, which did not encompass MJA14, therefore Rapiscan Systems Limited needed more information on the time-of-flight definitions and the samples were sent to the University for analysis.

The samples were prepared using sample preparation Method 2 and analysed using the GC-MS, resulting in multiple chromatography peaks for both samples at very similar retention times, as shown by the overlaid chromatograms in Figure 2.34. None of the peaks for MJA14 featured the molecular ion for 5F-AKB-48, but both MJA14 and MJA17 had top NIST 2.0 library matches to 1-hexadecanol for their peaks at 12.20 minutes, with match scores of 949 and 947 respectively. Furthermore, the peaks at 13.35 minutes had the highest NIST 2.0 library match to isopropyl palmitate, with match scores of 894 and 891. These compounds may have been seen due to detergents being present when the sample has been prepared (PubChem, 2022b; PubChem, 2022c). The small peak at 13.877 minutes for just MJA14 also had a high match score to the NIST 2.0 library (934), indicating a presence of 1-heptadecanol, which is used as a flavouring agent (PubChem, 2022d) and therefore further suggested that a household product may have been soaked into MJA14.

In comparison, the peaks at 17.61 minutes for both MJA14 and MJA17 did not have a NIST 2.0 library hit with a match score above 500, therefore efforts were turned to identifying the compound. The base peaks from the mass spectra at 17.61 minutes (Figure 2.35) were compared to data saved in the in-house synthetic cannabinoid Excel spreadsheet and to the Cayman Chemical Company GC-MS Drug Identification Tool to result in an identification of MDMB-4en-PINACA due to mass spectral peak similarity

when compared to the reference spectra (

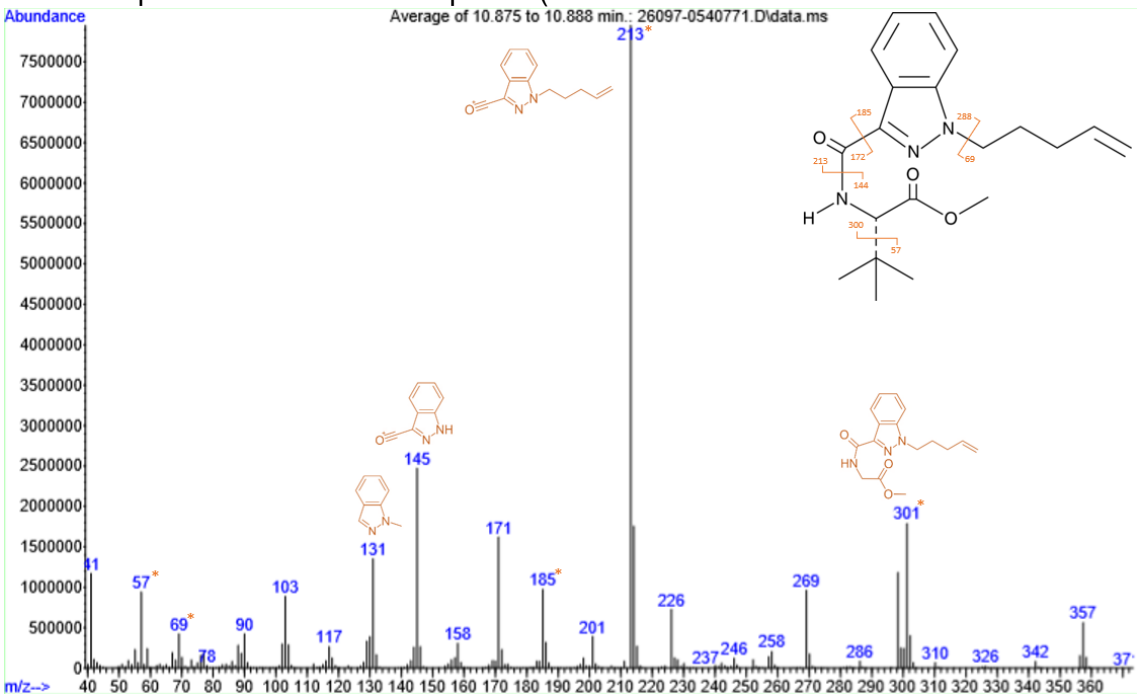


Figure 2.36) (annotated to include fragmentation information by the author).

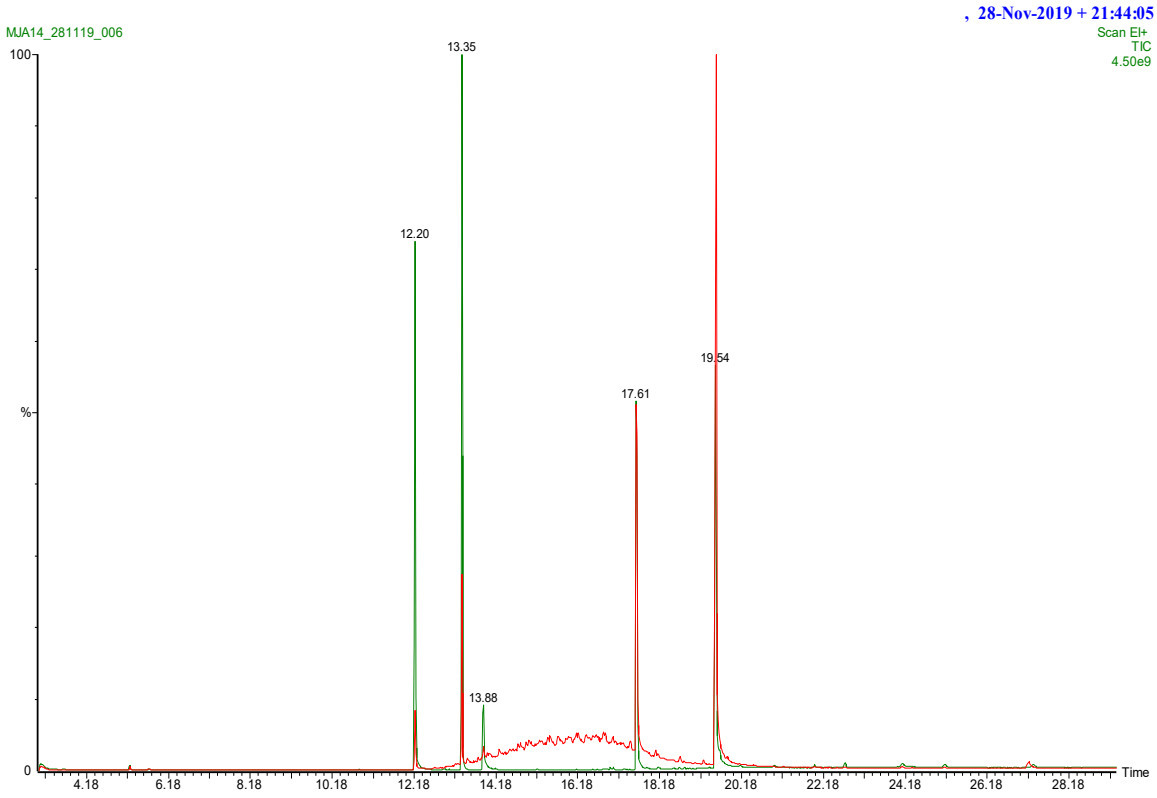


Figure 2.34: MJA14 chromatogram (green) and MJA17 chromatogram (red) overlaid to depict retention time similarity

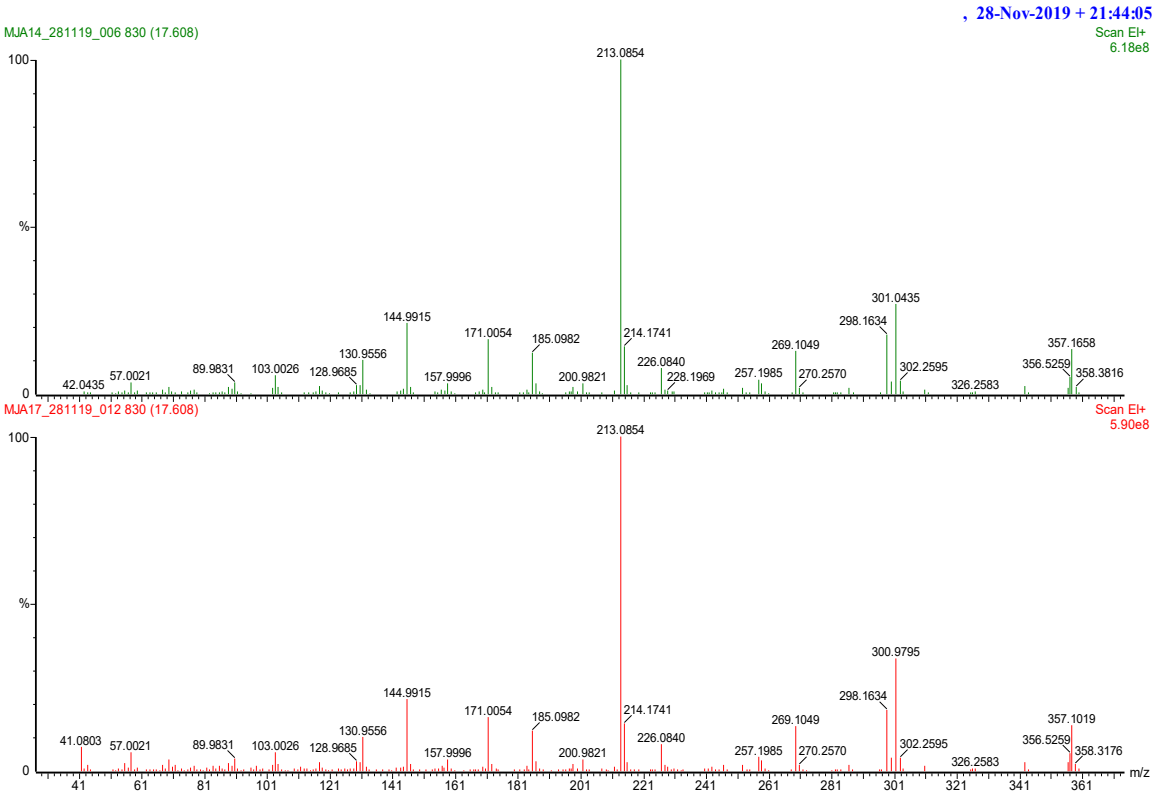


Figure 2.35: MS spectra from MJA14 (green) and MJA17 (red) at 17.6 minutes

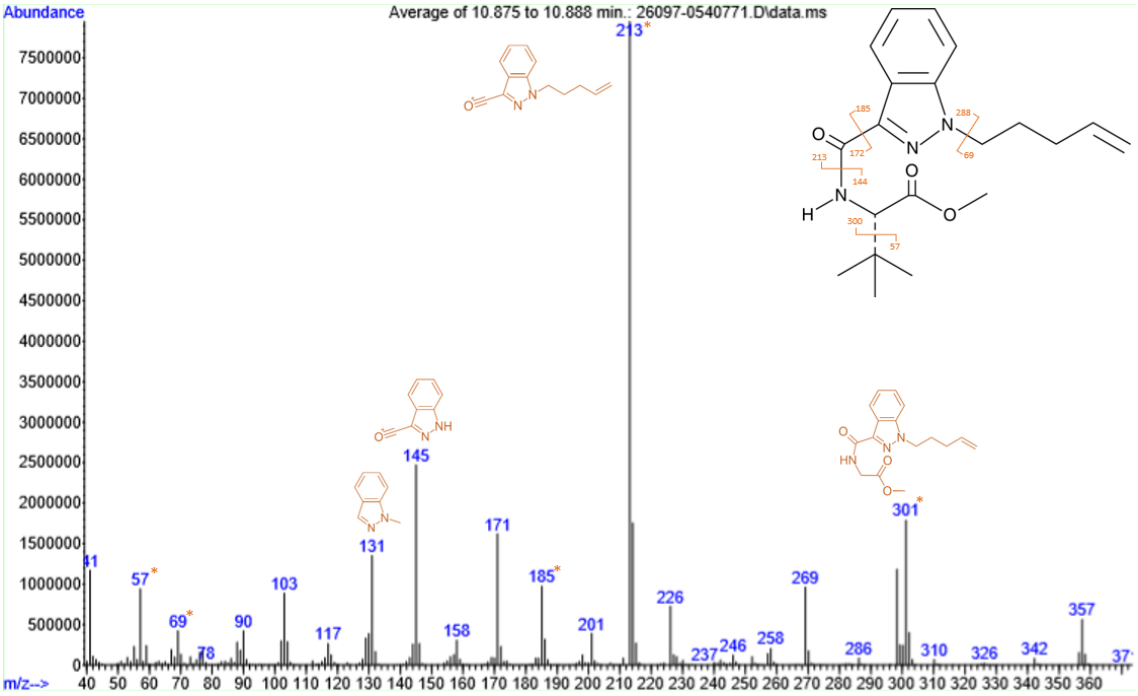


Figure 2.36: Cayman Chemical Company reference mass spectra for MDMB-4en-PINACA (Cayman Chemical Company, 2018)

The chromatography peaks for MJA14 and MJA17 at 19.5 minutes were identified using the NIST 2.0 library as they had an 867 and 851 match score to the MJA6

version of 5F-MDMB-PICA saved in the in-house MS library. They were considered good library matches and the spectra (Figure 2.37) was compared to the 5F-MDMB-PICA reference spectra in **Error! Reference source not found.**.

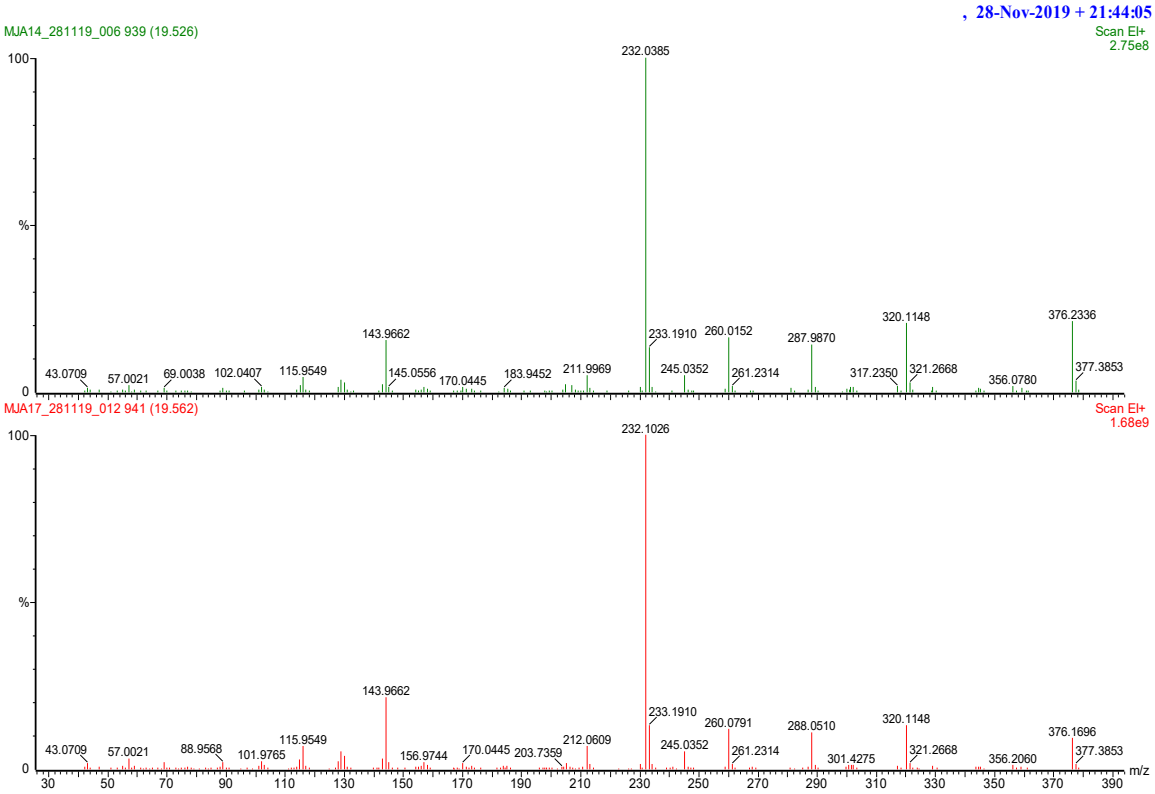


Figure 2.37: MS spectra from MJA14 (green) and MJA17 (red) at 19.5 minutes

Notably, although 5F-MDMB-PICA was already present on the Itemiser 3E®, neither MJA14 nor MJA17 triggered an alarm. This was later found to be due to an issue with the definition (the substance alarm parameters) on the Itemiser 3E®, which was investigated after the information on these identifications was communicated to Rapiscan Systems Limited. This resulted in the definition being amended and updated on the HMP Featherstone Itemiser 3E® in January 2020 to ensure that future samples would trigger an alarm for 5F-MDMB-PICA.

MDMB-4en-PINACA did not have a definition on the Itemiser 3E® and the analysis of these samples therefore were the first to prove MDMB-4en-PINACA was being sent *via* post to HMP Featherstone and as a mixture. Mixtures for MDMB-4en-PINACA are highlighted as common by Norman, Walker, McKirdy, *et al.,* (2020), with 73% of MDMB-4en-PINACA prison paper samples encountered during their work being mixed with another synthetic cannabinoid. Information of the drift times recorded was fed back to Rapiscan Systems Limited to conduct further research into the correct definition for MDMB-4en-PINACA to add to the library. Due to the chemical similarity of MDMB-4en-

PINACA and 4F-MDMB-BUTINACA, as shown in Figure 2.38, the time-of-flight range for both of these compounds was amended by Rapiscan Systems Limited to encompass both compounds, resulting in one definition on the library to cover both and hopefully increase the chance of disrupting the amount of both substances entering the prisons as these compounds are still proving to be popular. Considering the analysis of MJA14 and MJA17 was conducted in 2019, NPS Discovery (2022) outlined in their Q2 trend bulletin that MDMB-4en-PINACA proved to still be one of the most popular synthetic cannabinoids in the United States of America in 2022 and 4F-MDMB-BUTINACA had a resurgence in 2022, after initially losing popularity post 2019.

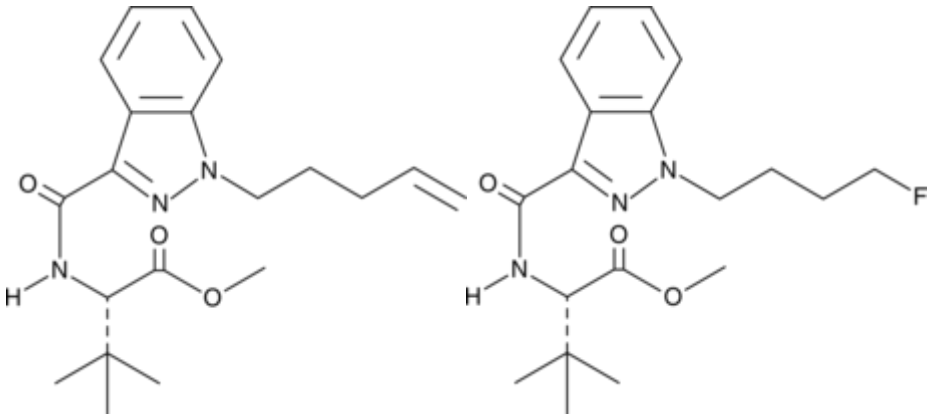


Figure 2.38: Structure diagrams of MDMB-4en-PINACA (left) and 4F-MDMB-BUTINACA (right)

MJA14 and MJA17 were analysed using LC-MS, after the installation of the instrument, to support the identification of MDMB-4en-PINACA and 5F-MDMB-PICA from the GC-MS, and the indicated presence of 5F-AKB-48 and 5F-ADB from the Itemiser 3E®, using the in-house PCDL. The chromatograms are shown in Figure 2.39, Figure 2.40, Figure 2.42 and Figure 2.43, with the respective mass spectra and Find by Formula results shown in Figure 2.41 and Figure 2.44. MJA14 was also analysed using the FTIR, and the results are discussed alongside MJA40.

Table 2.13: LC-MS match scores for MJA14 and MJA17 to in-house PCDL

Sample	5F-MDMB-PICA match score (%)	MDMB-4en-PINACA match score (%)
MJA14	97.23	99.50
MJA17	97.65	99.47

If 5F-AKB-48 had been present in MJA14, and if 5F-ADB has been present in MJA17, the acetone extraction method as part of Method 2 should have been sufficient to successfully extract the compounds, as medium polar to non-polar solvents, including acetone, are suggested for the extraction of synthetic cannabinoids (UNODC, 2013; UNODC, 2020b).

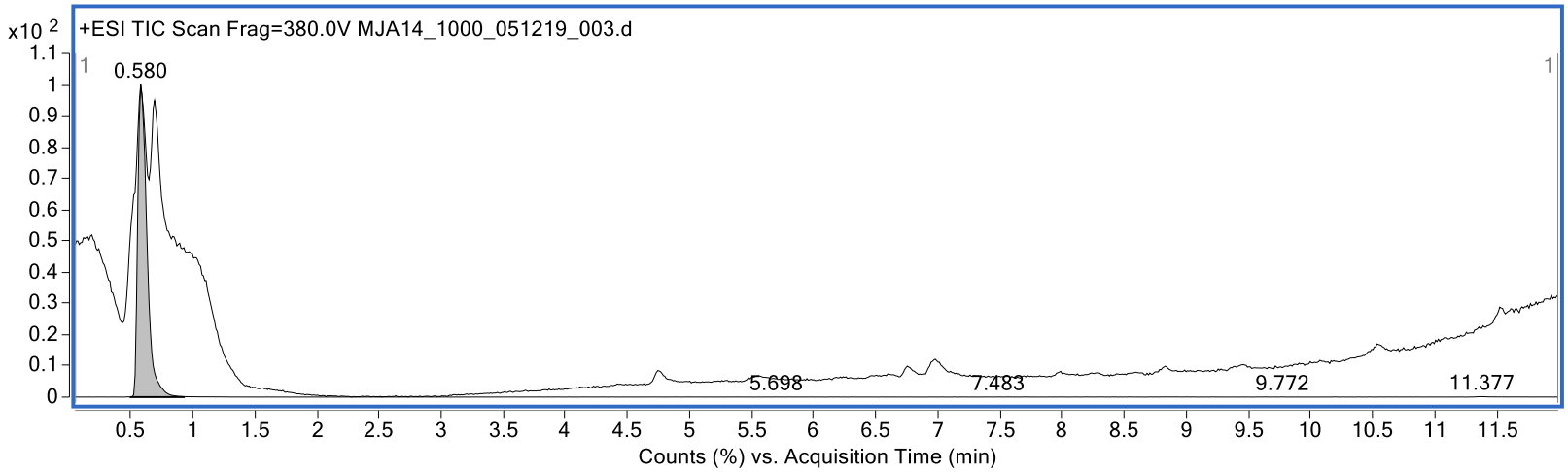


Figure 2.39: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (grey chromatogram) for MJA14 at 0.58 minutes

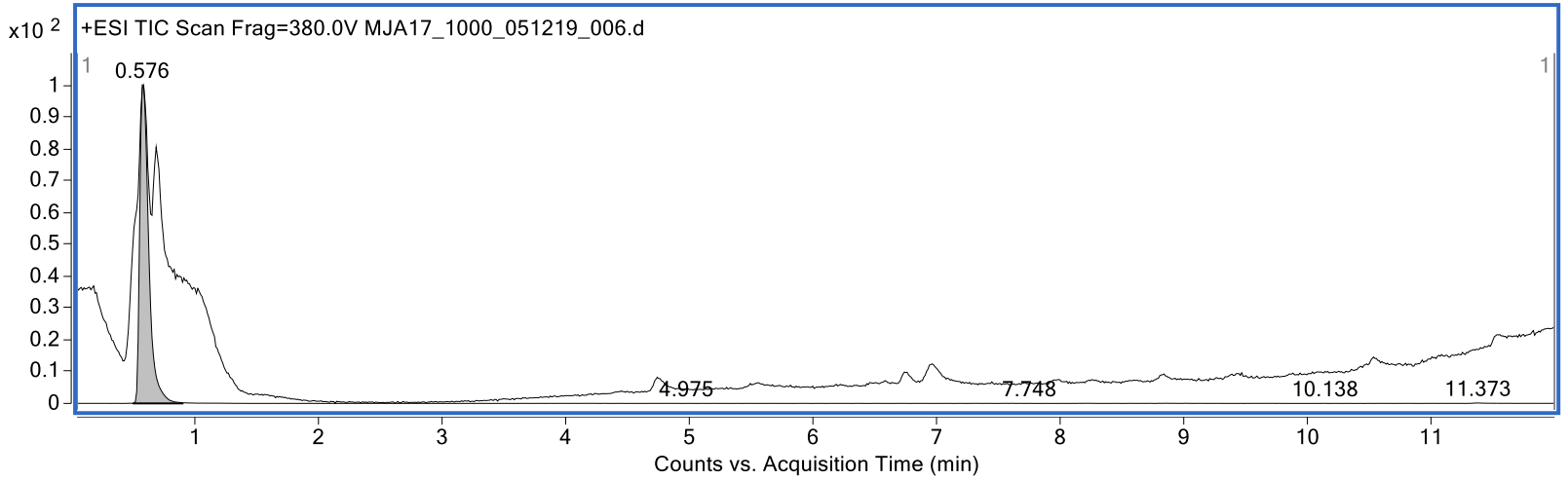


Figure 2.40: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (grey chromatogram) for MJA17 at 0.58 minutes

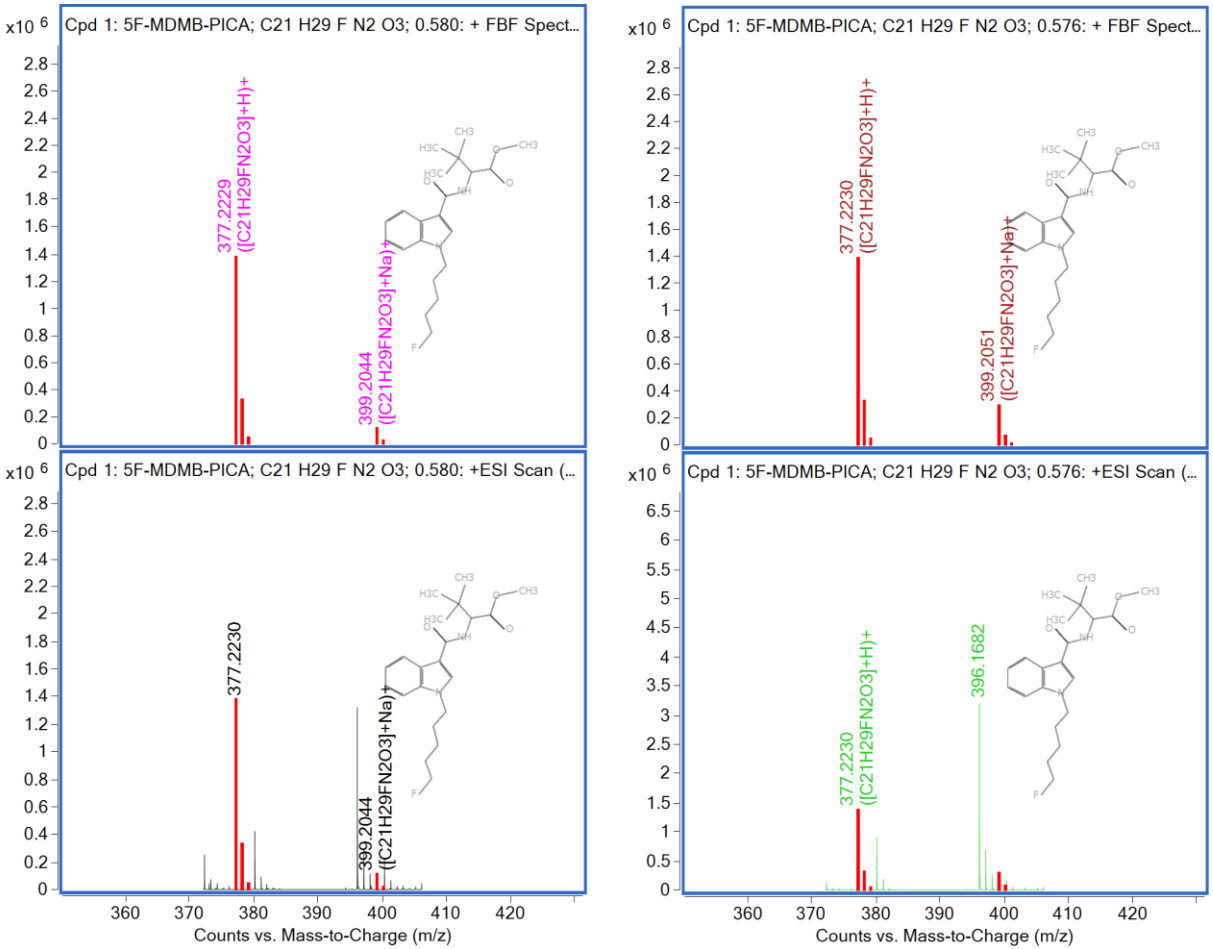


Figure 2.41: 5F-MDMB-PICA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above MJA14 (left) and MJA17 (right) 5F-MDMB-PICA spectra below. Predicted isotope distribution marked in red

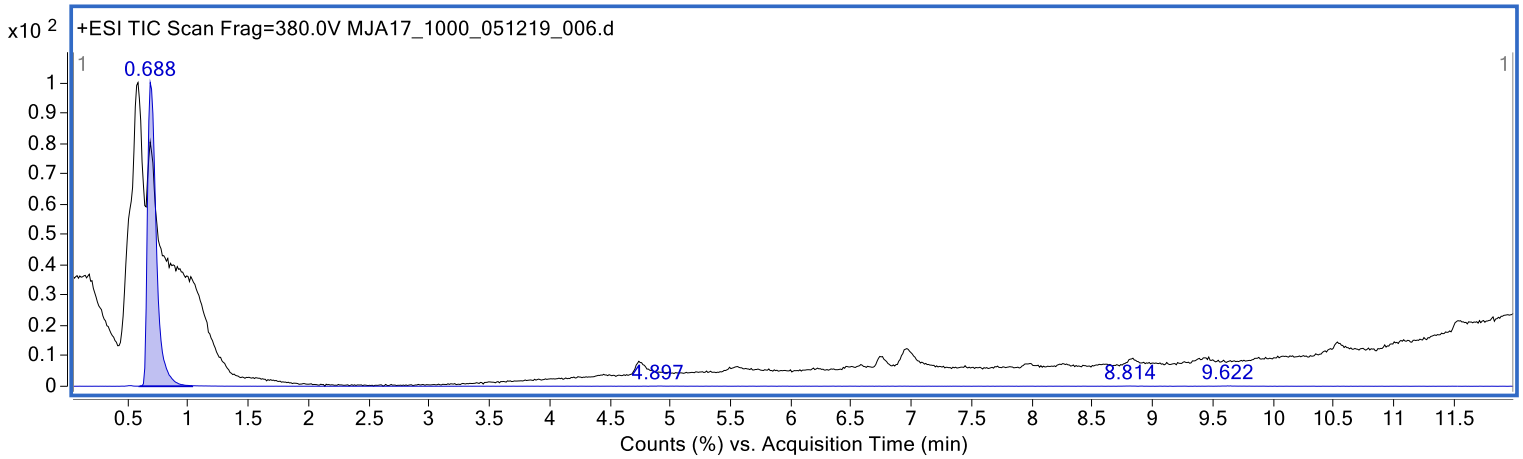


Figure 2.42: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (blue chromatogram) for MJA17 at 0.68 minutes

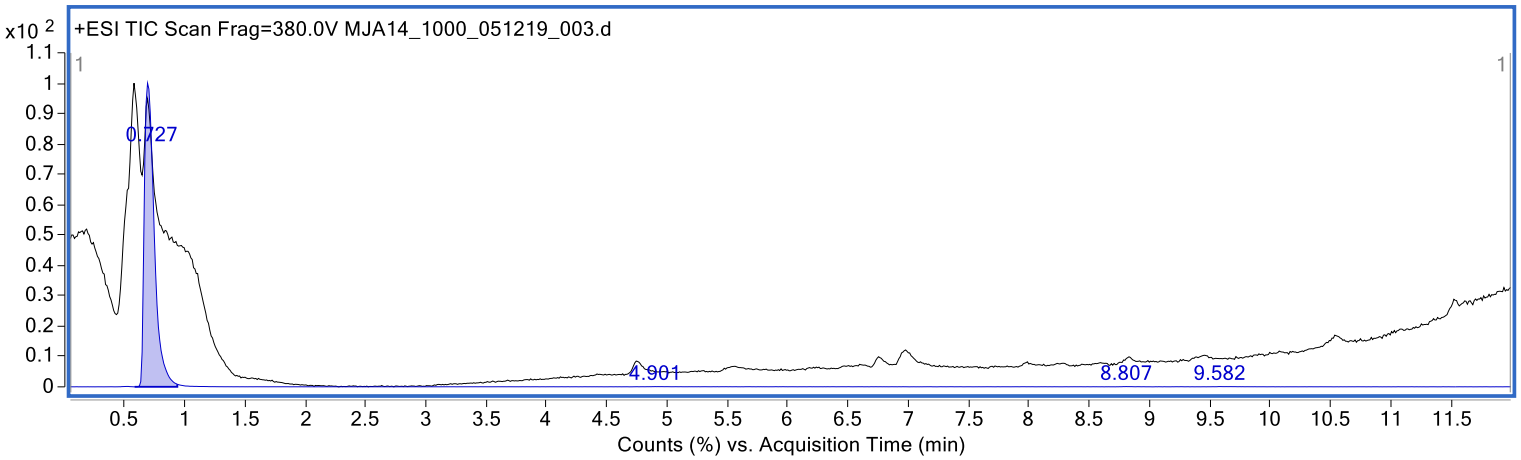


Figure 2.43: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (blue chromatogram) for MJA14 at 0.72 minutes

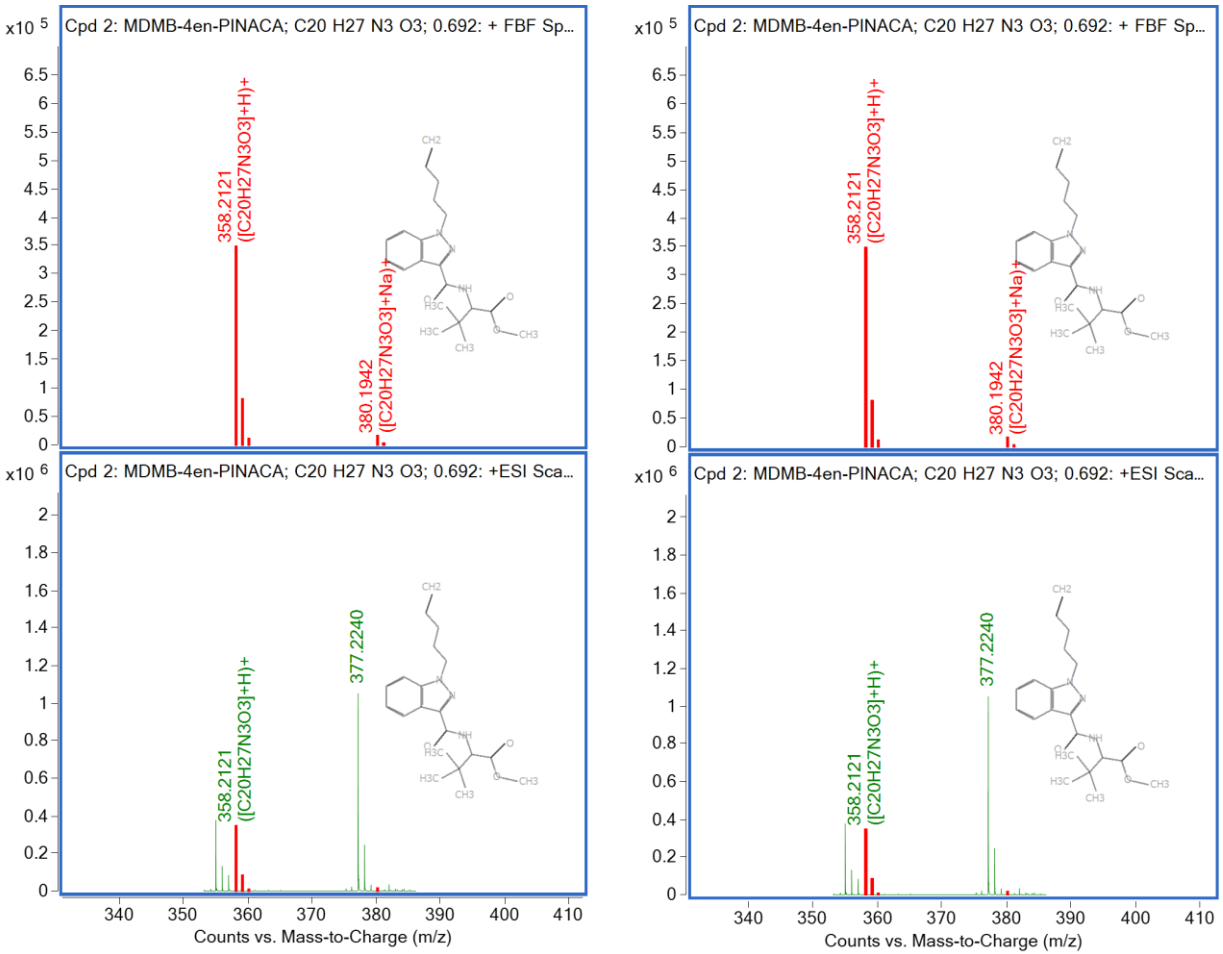


Figure 2.44: MDMB-4en-PINACA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above and MJA14 (left) and MJA17 (right) MDMB-4en-PINACA spectra below. Predicted isotope distribution marked in red

MJA38

MJA38 was one of the samples that did not originate from a West Midlands prison but had been sent to the University for analysis through liaison with the West Midlands Prison Group after they were given the sample from a dog handler working at HMP Isle of Wight. MJA38 was a Tupperware box which had been found during a search of a prison bathroom and contained multiple contraband items, including suspected tobacco, cannabis and herbal synthetic cannabinoid wraps alongside multiple scraps of lined paper. An Itemiser 3E® result printout had been provided to indicate the presence of MMB-FUBINACA, 5F-ADB/MMB-FUBINACA (through the use of the combined library definition Spice +, which was a definition created to encompass both MMB-FUBINACA and 5F-ADB) and ADB-FUBINACA, however it was not clear in the continuity documentation which item within the box had been tested using the Itemiser 3E®. Confirmatory identification was only conducted for the paper due to the primary aims of the research and linking to the Itemiser 3E® results, but the other samples were retained for future investigation.

The scraps of paper were separated from the rest of the sample and one piece without inked writing was selected for analysis to reduce the chance of ink interference. The paper was then prepared using solvent extraction Method 4 and analysed using GC-MS and LC-MS. The chromatogram featured only one large peak at 19.17 minutes as shown in Figure 2.45, and the mass spectrum for the peak is shown in Figure 2.46. Initially the spectrum was compared to the NIST 2.0 library, but as all compounds had a match score of below 500, efforts were turned to identifying the compound through the in-house synthetic cannabinoid Excel spreadsheet. The relative molecular mass for the sample was searched and the recorded base peaks compared, resulting in an initial indication of MMB-FUBINACA. Manual comparison to a reference spectrum (

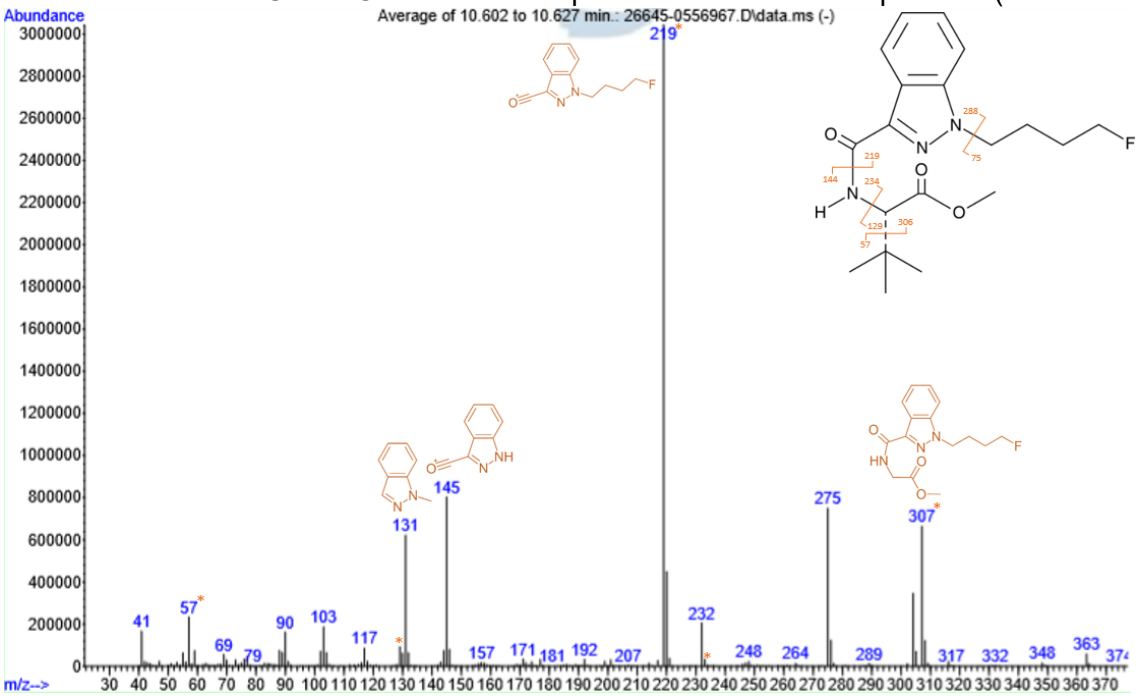


Figure 2.26) was then undertaken to determine similarity and identify the presence of MMB-FUBINACA within the sample. The high abundances for both the 109 and 253 peaks were recorded in the in-house synthetic cannabinoid Excel spreadsheet as 109/253 for the base peak, and therefore MMB-FUBINACA was quickly identified as a likely candidate due to this unusual feature within the spreadsheet and amongst spectra for the relative molecular mass on the Cayman Chemical Company GC-MS Drug Identification Tool (Cayman Chemical Company, 2022a). An annotated version including fragmentation information of the MMB-FUBINACA reference spectra can be seen in

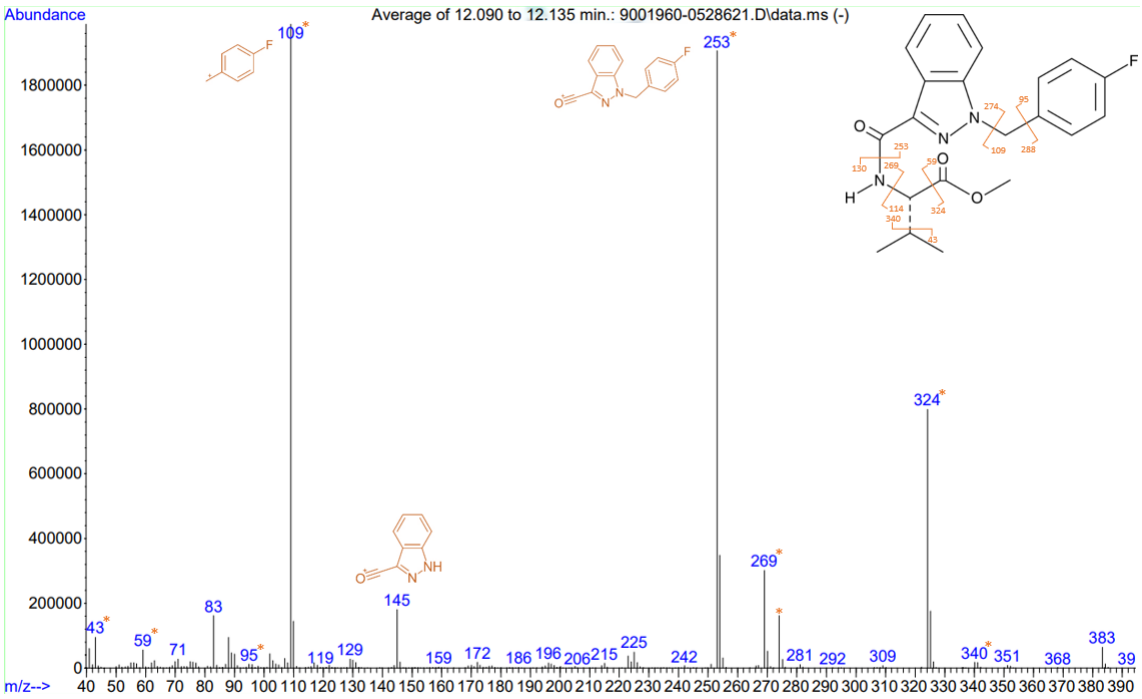


Figure 2.47.

At this stage, there was strong evidence to suggest the presence of MMB-FUBINACA between the results from the GC-MS and the Itemiser 3E®, however there was no presence of another compound within the chromatogram as there was only one peak, indicating there was no presence of ADB-FUBINACA within the sample. The presence of ADB-FUBINACA could have been contamination from the suspected herbal synthetic cannabinoid sample within the Tupperware as some of the herbal sample was loose within the box alongside the paper wraps, although there has been no analysis on the herbal sample to date to verify this potential reasoning.

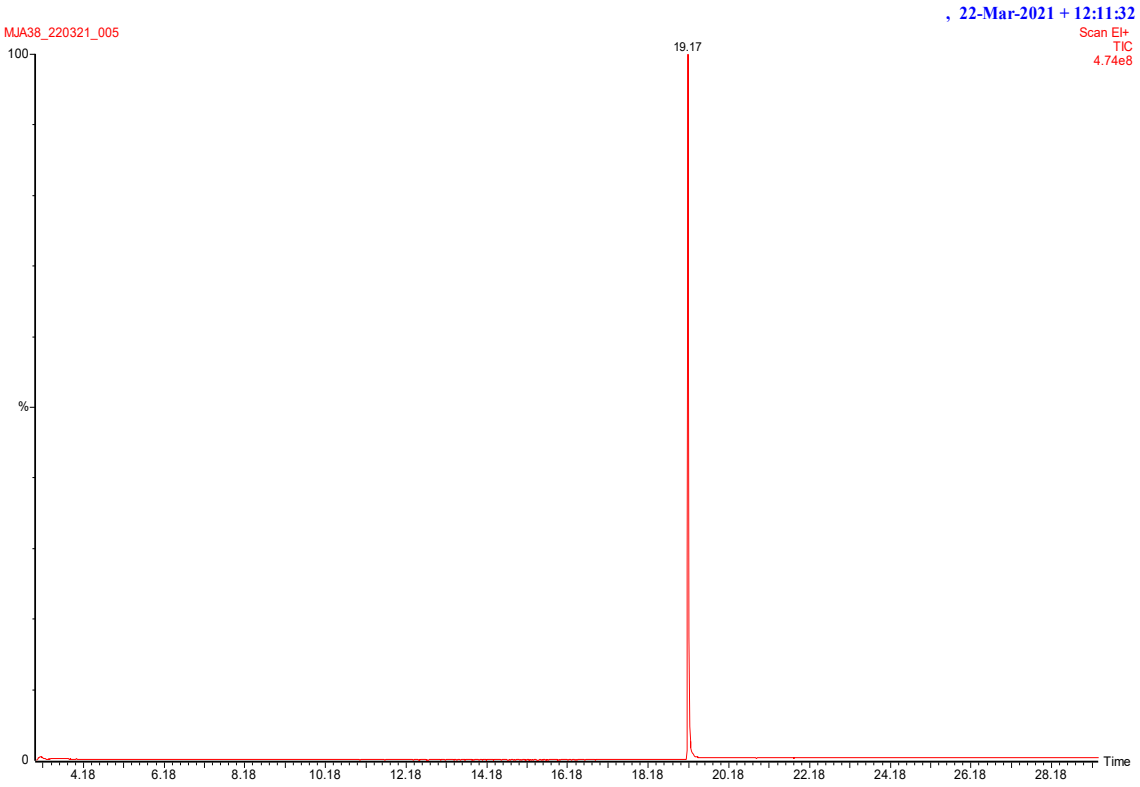


Figure 2.45: GC chromatogram for MJA38

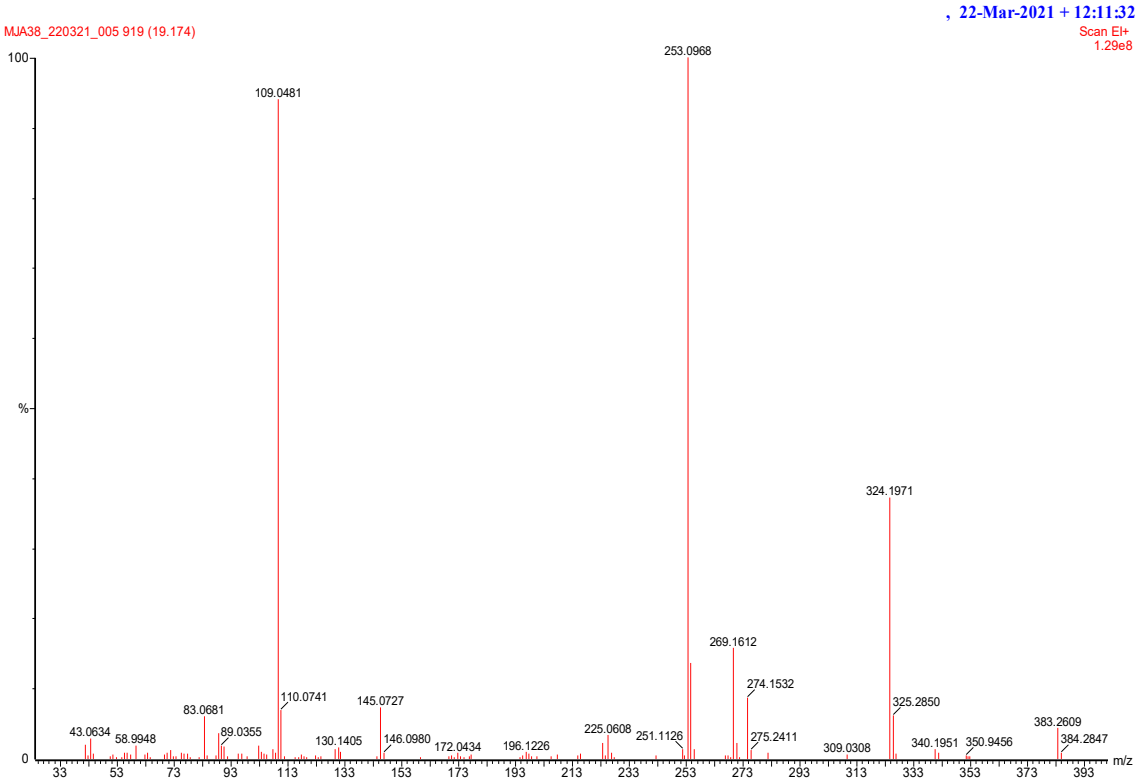


Figure 2.46: MS spectrum for MJA38

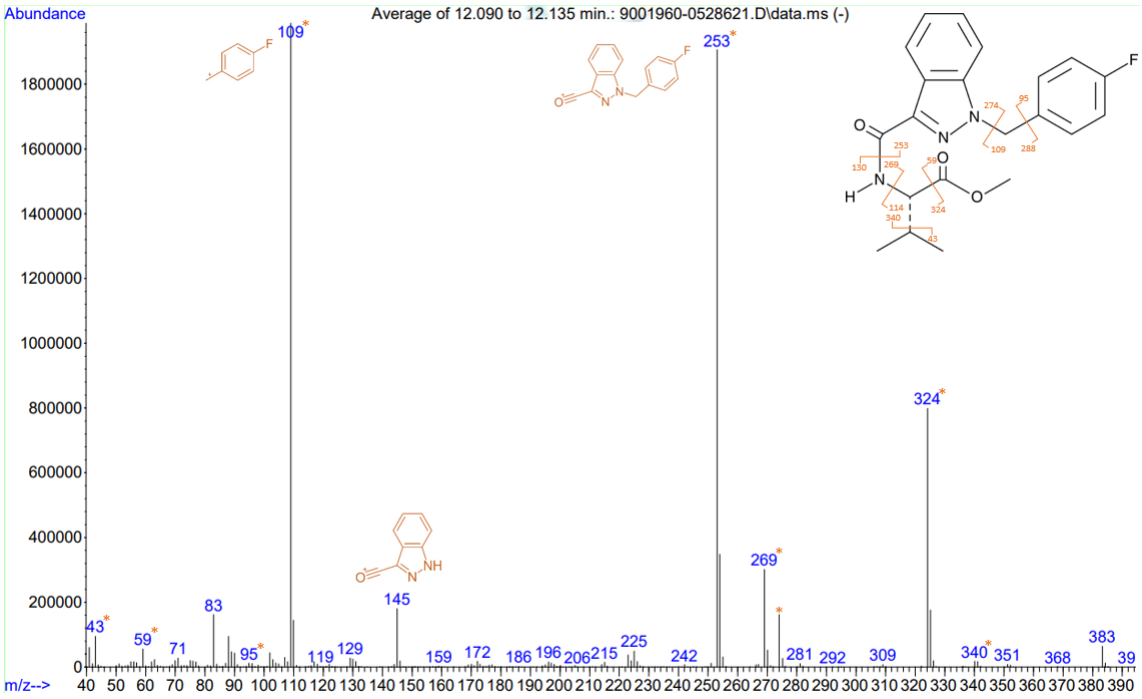


Figure 2.47: Cayman Chemical Company reference mass spectra for MMB-FUBINACA (Cayman Chemical Company, 2018b)

The sample was then analysed using the LC-MS to verify the identification made by the Itemiser 3E® and GC-MS of MMB-FUBINACA. The sample was prepared using sample preparation Method 4 and analysed to produce the chromatogram shown in Figure 2.48, with the extracted ion chromatogram shown in blue after the application of the in-house PCDL using the Find by Formula feature. In terms of the mass spectrometry results, MMB-FUBINACA had a 99.53% match to the spectrum acquired for the peak at 0.61 minutes, resulting in the spectra shown in Figure 2.49.

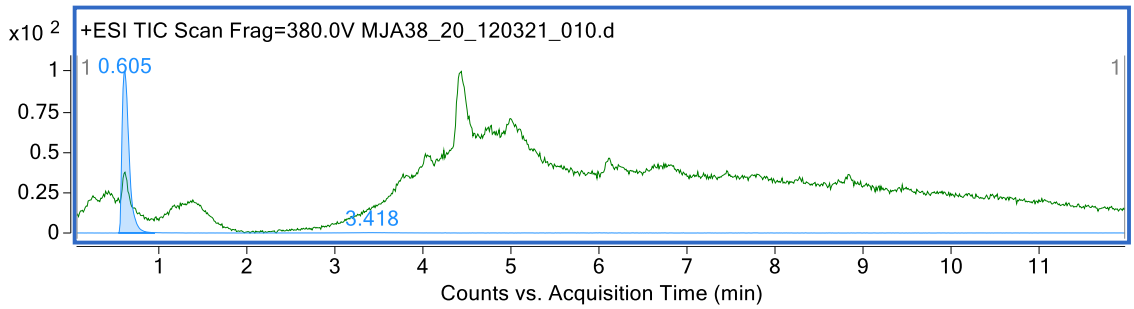


Figure 2.48: Total ion chromatogram (green chromatogram) and extracted ion chromatogram (blue chromatogram) for MJA38 at 0.61 minutes

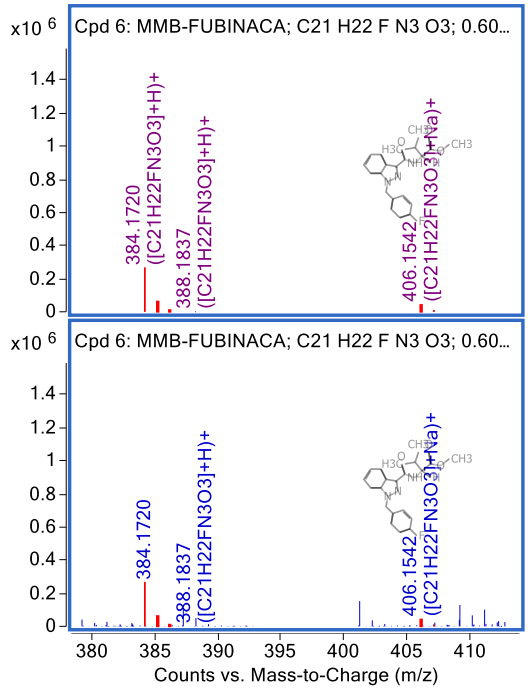


Figure 2.49: MMB-FUBINACA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above and MJA38 MMB-FUBINACA spectrum below. Predicted isotope distribution marked in red

MJA38 was also analysed using FTIR to highlight indicative functional groups within the compound. Alongside the amide, CH_3 (sp^3), ester and CH_3 asymmetric deformation and CH_2 scissoring seen in all the compounds analysed, there is the peak at 1172cm^{-1} in the spectrum shown in Figure 2.50, which was tentatively assigned to be due to the isopropyl group (Thermo Fisher Scientific Inc., 2008) circled in light blue on the colour coordinated structure. As well as the tentative identification of the 750 cm^{-1} ortho-benzene from the indazole, there is the tentative identification of the para-distributed benzene ring peak at 820 cm^{-1} from the tail of MMB-FUBINACA (Thermo Fisher Scientific Inc., 2008), as shown in light green in Figure 2.50.

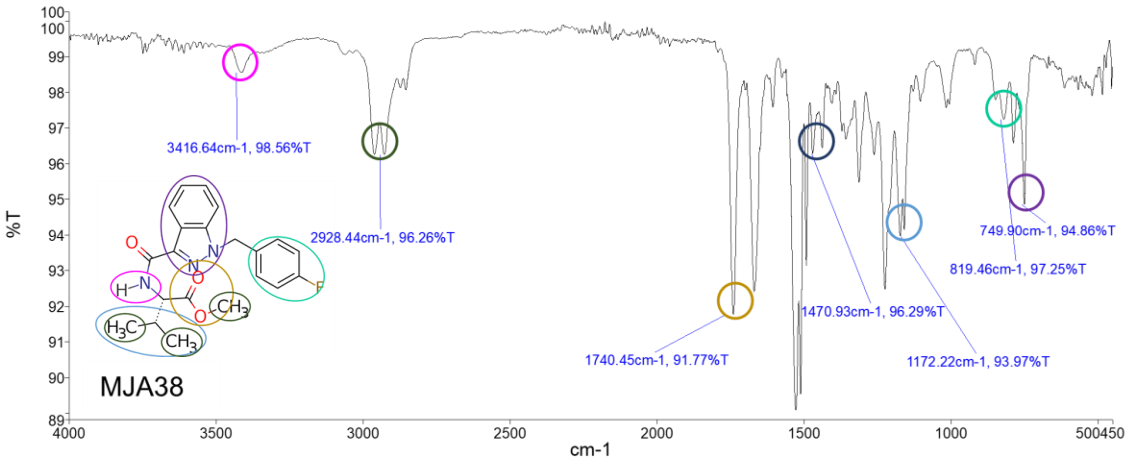


Figure 2.50: FTIR spectrum for MJA38 with correlating colour coordination

MMB-FUBINACA, otherwise known as AMB-FUBINACA, was banned as part of China's August 2018 legislation change and therefore prevalence internationally declined in the following year (Norman *et al.* 2021). The sample was seized in January 2019, which correlates with the timeline considering the sample would have been prepared in advance before sending it in, however the dog handler who seized the sample did not pass on the sample to the West Midlands Prisons Group until February 2021, therefore resulting in the sample being analysed at the much later date of March 2021. This delay highlighted the importance of timely intelligence-based testing being available to all prisons. Information from this seizure was shared with the staff at the West Midlands Prisons Group to feed back to the original dog handler who found the sample.

MJA40

MJA40 was submitted for confirmatory testing to the University after consistent indication of 4F-MDMB-BUTINACA by the Itemiser 3E® and signs of tampering. Five of the 19 pages had an accompanying Itemiser 3E® print out with a positive indication for 4F-MDMB-BUTINACA, and all featured a waxy appearance and sweet, talcum powder like smell, with some pages featuring heavy staining to the point of looking opaque. The sample was split as follows: MJA40a-e for the five pages with Itemiser 3E® print outs, MJA40f, the only one that included handwriting on the page and MJA40g, the grouped remaining pages. For MJA40a-f, 3.5 hole punches were taken from each page, and for MJA40g, 3.5 hole punches were collected randomly from the pages. All samples were extracted using the solvent extraction Method 4 and analysed on the GC-MS, with three chromatography peaks seen in each chromatogram, as shown in Figure 2.51. All samples consistently contained the same three peaks, indicating the same mixture was present throughout.

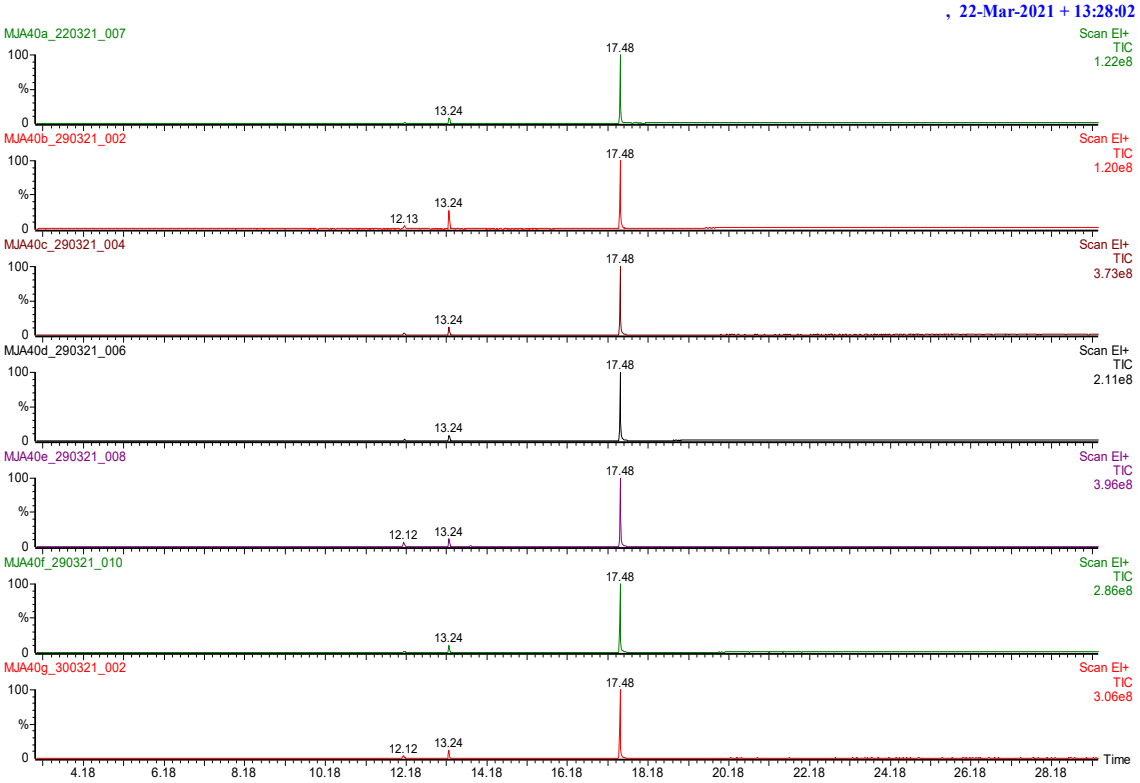


Figure 2.51: GC chromatogram for MJA40, from top to bottom, a-g

The mass spectra for the peaks at 12.1 minutes had dodecanol compounds suggested as the top hits using the NIST 2.0 library, however they all had poor match scores according to NIST Mass Spectrometry Data Center (2008). The mass spectra for the peaks at 13.24 minutes also featured a poor match score but instead for isopropyl palmitate. Although isopropyl palmitate was also seen in MJA14 alongside a decanol group in both MJA14, MJA17 and MJA47, the match scores seen here were much lower compared to those for MJA14 and MJA17.

In terms of the peaks at 17.48 minutes, the mass spectra (Figure 2.52) had no potential library matches due to poor match scores from the possible compounds in the NIST 2.0 library, so the base peak and relative molecular mass were searched on the in-house synthetic cannabinoid Excel spreadsheet and highlighted the potential of MDMB-4en-PINACA being present. As this compound had already been seen in MJA14 and

MJA17, a reference spectrum was already saved (

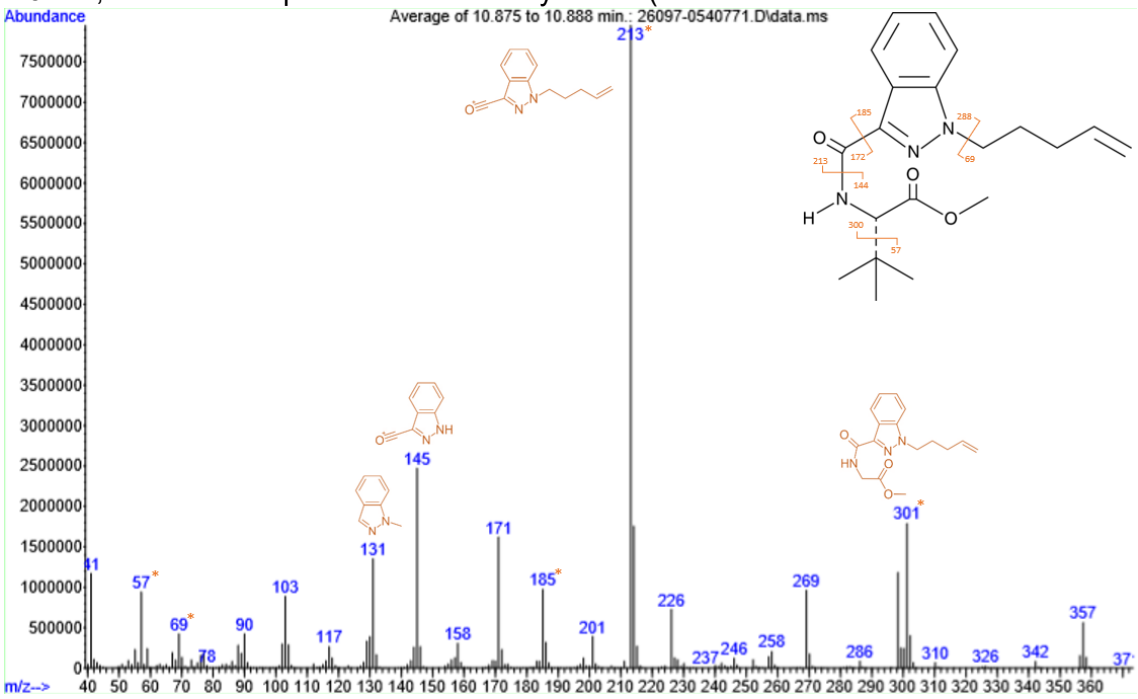


Figure 2.36), and identification of the compound was made. Furthermore, the identification of 4F-MDMB-BUTINACA by the Itemiser 3E® highlighted again that the time-of-flight definitions for that compound also span the range for MDMB-4en-PINACA, as previously discussed with MJA14 and MJA17.

To further confirm the identification of MDMB-4en-PINACA, the sample was prepared using solvent extraction Method 4 and analysed using LC-MS, resulting in the chromatogram in Figure 2.53. The chromatogram includes the extracted ion chromatogram after applying the Find by Formula feature with the in-house PCDL. The resulting spectrum (Figure 2.54) had on average, an 80% match score to MDMB-4en-PINACA when all MJA40a-g were analysed. Although both the ammonium adduct and the sodium adduct are seen in Figure 2.54, the protonated adduct is not seen and the mass spectra only included the ammonium adduct when comparing to the library. The ammonium adduct is usually much less abundant than the protonated molecule (Kruve and Kaupmees, 2017), as seen with the MJA14 and MJA17 analysis, although the ammonium adduct can be more prominent if the proton affinity is closer to ammonia (Westmore and Alauddin, 1986), as seen with this sample. The analysis did result in the correct accurate mass for MDMB-4en-PINACA and none of the compounds with higher match scores had plausible relative molecular mass results when compared to the GC-MS results. Therefore, the identification of MDMB-4en-PINACA was only classed as tentative from the LC-MS and efforts turned to also analysing the sample

with FTIR to identify the functional groups within the compound and compare to those seen with MJA14.

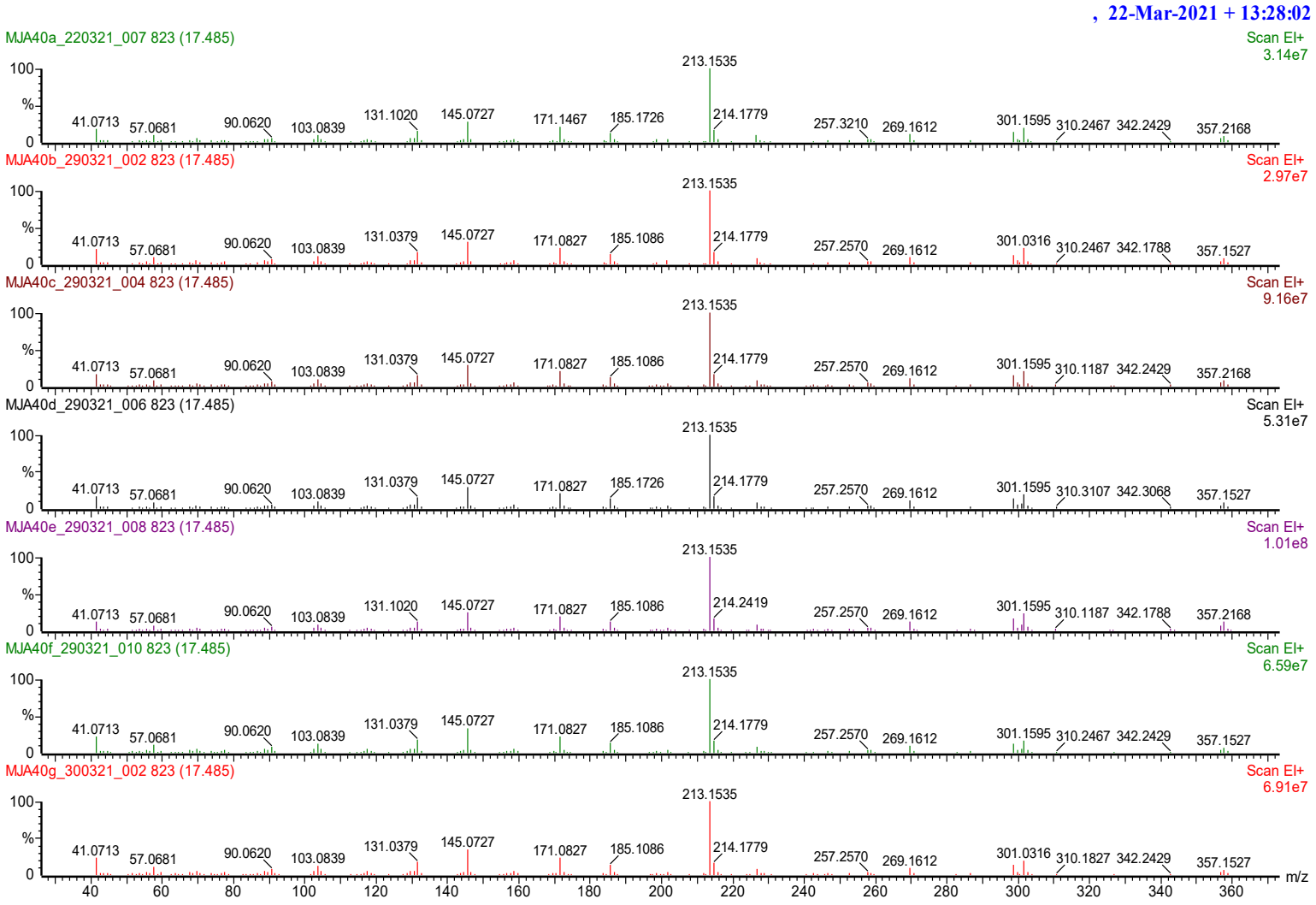


Figure 2.52: MS spectra for MJA40a-g at 17.5 minutes

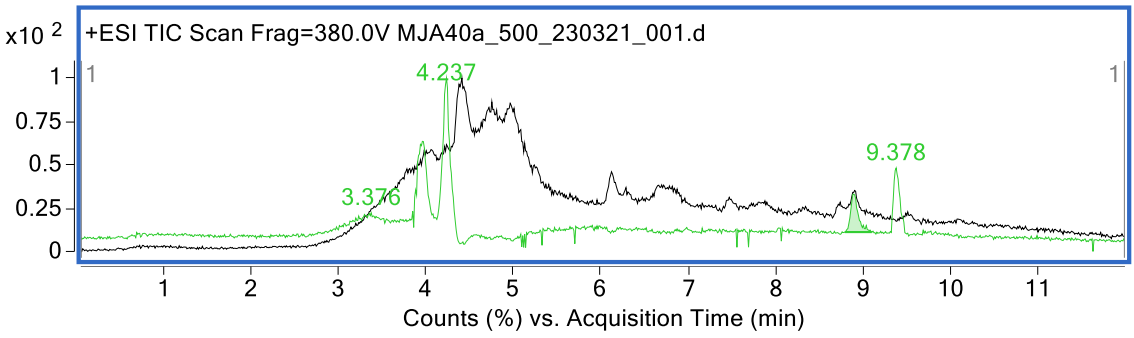


Figure 2.53: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (green chromatogram) for MJA40 at 8.9 minutes

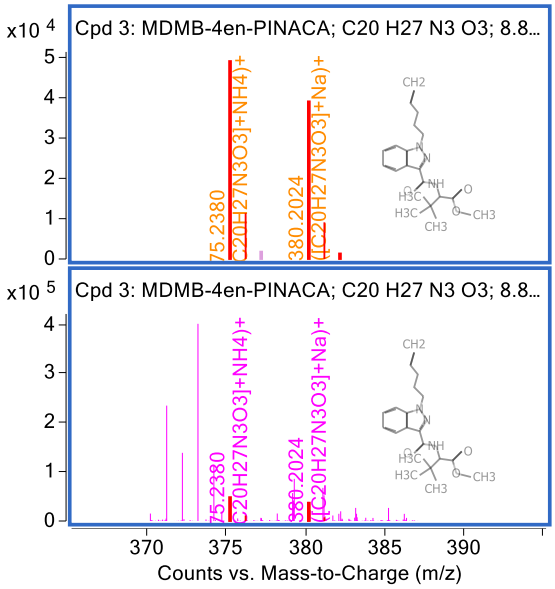


Figure 2.54: MDMB-4en-PINACA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above and MJA40 MDMB-4en-PINACA spectrum below. Predicted isotope distribution marked in red

The FTIR results showed the potential presence of peaks associated with the functional groups present in the structure of MDMB-4en-PINACA, including a peak at 3070 cm^{-1} for the alkene in the tail structure (Bell, 2006), although the peak is very weak (as shown in Table 2.14 and Figure 2.55). This peak is also present for MJA14, as shown in Table 2.14, and the reference MDMB-4en-PINACA from Response (2018) (Figure 2.56), which shows a small but sharper peak. This result supported the identification of MDMB-4en-PINACA in MJA40 despite the lower confidence of the LC-MS results.

Table 2.14: MJA5, MJA14 and MJA40 indicative structural assignments and corresponding wavenumbers coordination

		Wavenumber (cm^{-1})							Inference
Samples	MJA5	3354	-	2957	1737	1466	1216	749	5F-MDMB-PICA
	MJA14	3411	3062	2922	1737	1467	1217	750	5F-MDMB-PICA and MDMB-4en-PINACA
	MJA40	3419	3070	2918	1736	1468	1216	751	MDMB-4en-PINACA
	Assignments	Secondary amide N-H stretch[ab]	Alkene RCH= CH_2 C-H stretch[cd]	CH_3 (sp^3) C-H stretch[ad]	Ester C=O stretch[ad]	CH_3 asymmetric deformation and CH_2 scissoring (tentative)[c]	CH_3 Deformation *Tert*-butyl (tentative)[e]	Ortho-benzene from the indole or indazole C-H bending (tentative)[e]	

[a]Housecroft and Constable (2006), [b]Heriot Watt (2023), [c]Bell (2006), [d]Merck (2023) & [e]Thermo Fisher Scientific Inc. (2008)

A full table for all of the assignments can be seen in Appendix 6 – Full table for FTIR structural inferences.

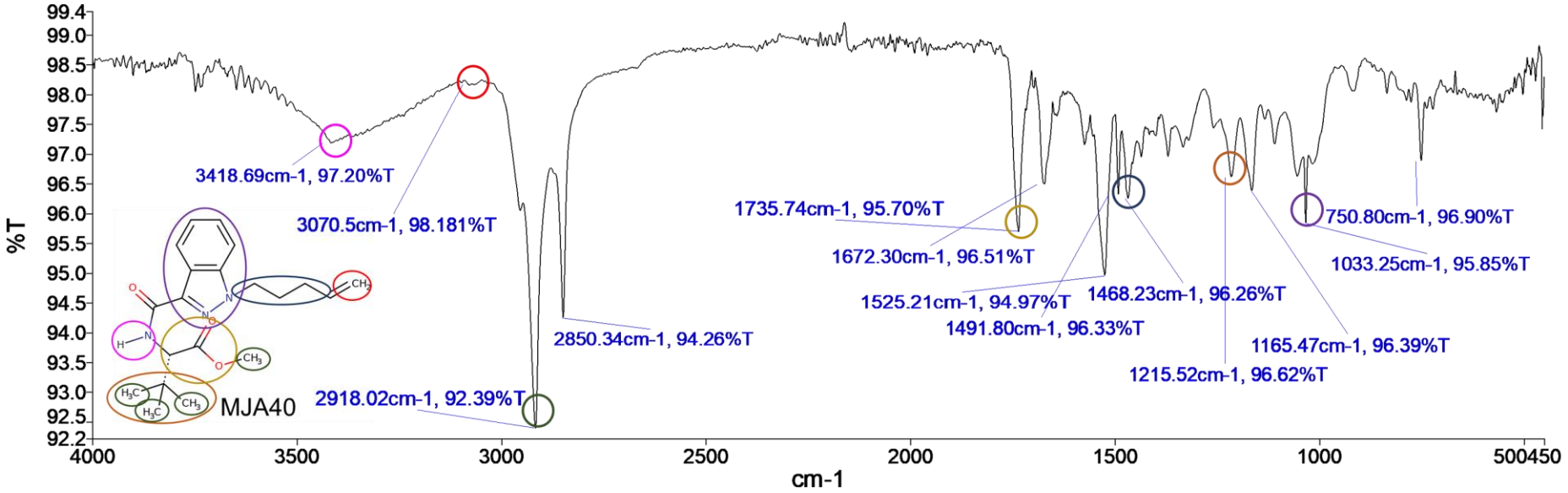


Figure 2.55: FTIR spectrum for MJA40 with correlating colour coordination

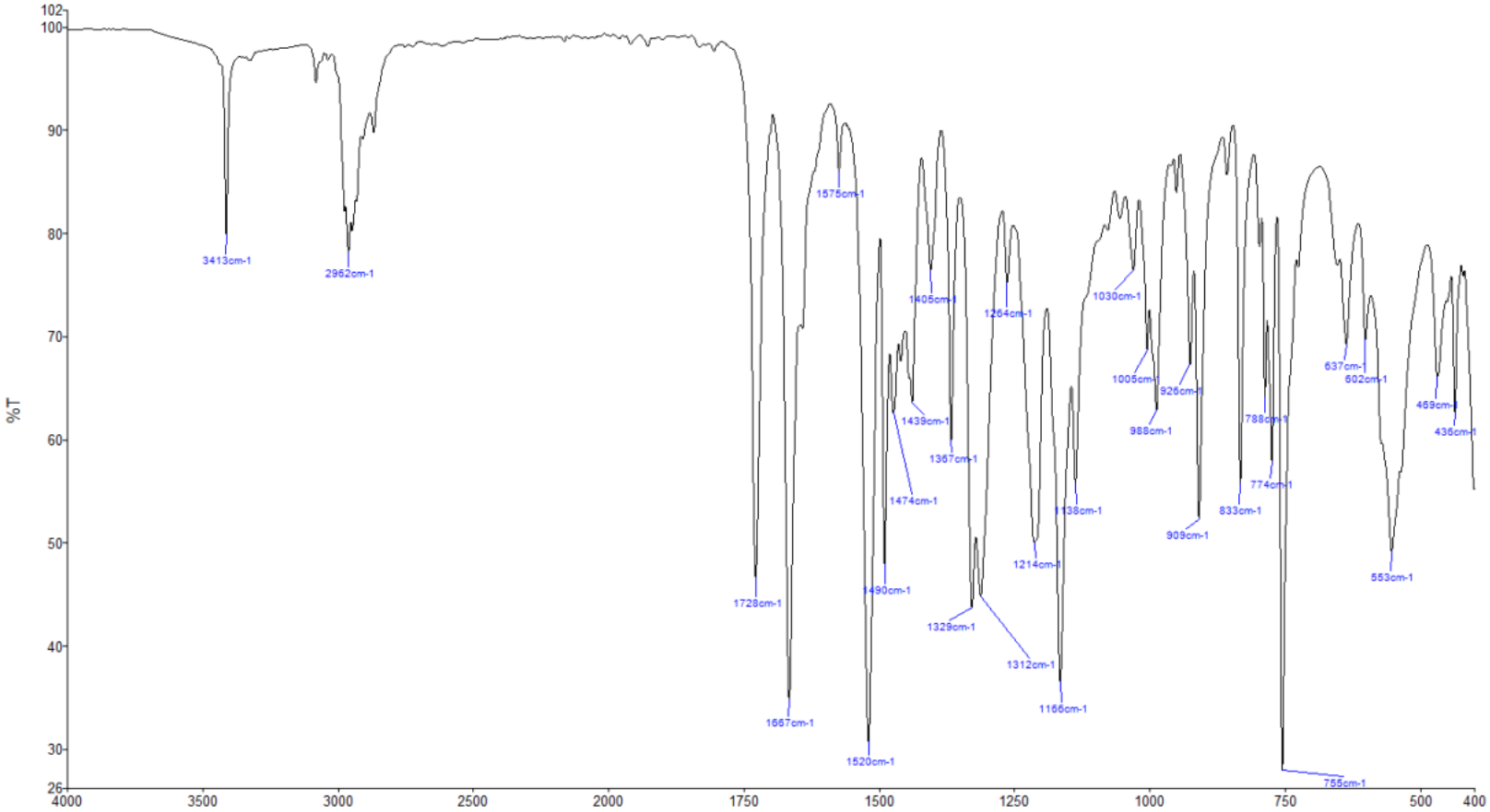


Figure 2.56: FTIR spectrum for MDMB-4en-PINACA from Response (2018)

2.3.4 Positive indications of synthetic cannabinoids from powder samples

In addition to the paper samples submitted to the University for analysis, two powder samples were also submitted due to associated intelligence regarding powder being used to prepare paper samples by prisoners. Neither had associated Itemiser 3E® results but there had been intelligence bulletins within the prison service that yellow powders could be synthetic cannabinoid powder, and as both had been found inside the prison, the West Midlands Prisons Group wanted information on the identity of the powders.

The MJA19 sample was 1.3368 g of yellow powder that had been thrown over the prison fence into a recreational area. Dissolving powder synthetic cannabinoids into a solvent to prepare paper samples is usually undertaken outside of a prison to aid in smuggling (EMCDDA, 2022), however it was suspected that in cases like this where the powder had been thrown as a package over the fence, it would be to try and circumvent the Itemiser 3E® screening as the prisoners were aware of their post being screened. The sample was weighed and prepared using sample preparation Method 5 for GC-MS and LC-MS analysis. The GC-MS analysis resulted in one very small peak on the chromatogram at 17.01 minutes, and another much larger peak at 17.59 minutes, as shown in Figure 2.57. Upon comparison to the NIST 2.0 library, match scores per mass spectra did not surpass 600, therefore the suggested compounds were dismissed, and the base peak and relative molecular mass for each were compared to those already saved on the in-house synthetic cannabinoid Excel spreadsheet. The spectra for the two peaks were very similar (Figure 2.58 and Figure 2.59); the relative molecular mass was the same for both and some peaks only differed in abundance, however there were two different base peaks, suggesting that two very similar compounds could be present. Therefore, the peak at 17.01 minutes may have been a synthesis by-product or thermal degradation product. The peak at 17.59 minutes was focused on due to the abundance, and upon comparison to the in-house synthetic cannabinoid Excel spreadsheet, was identified as MDMB-4en-PINACA, as seen in MJA14 and MJA40.

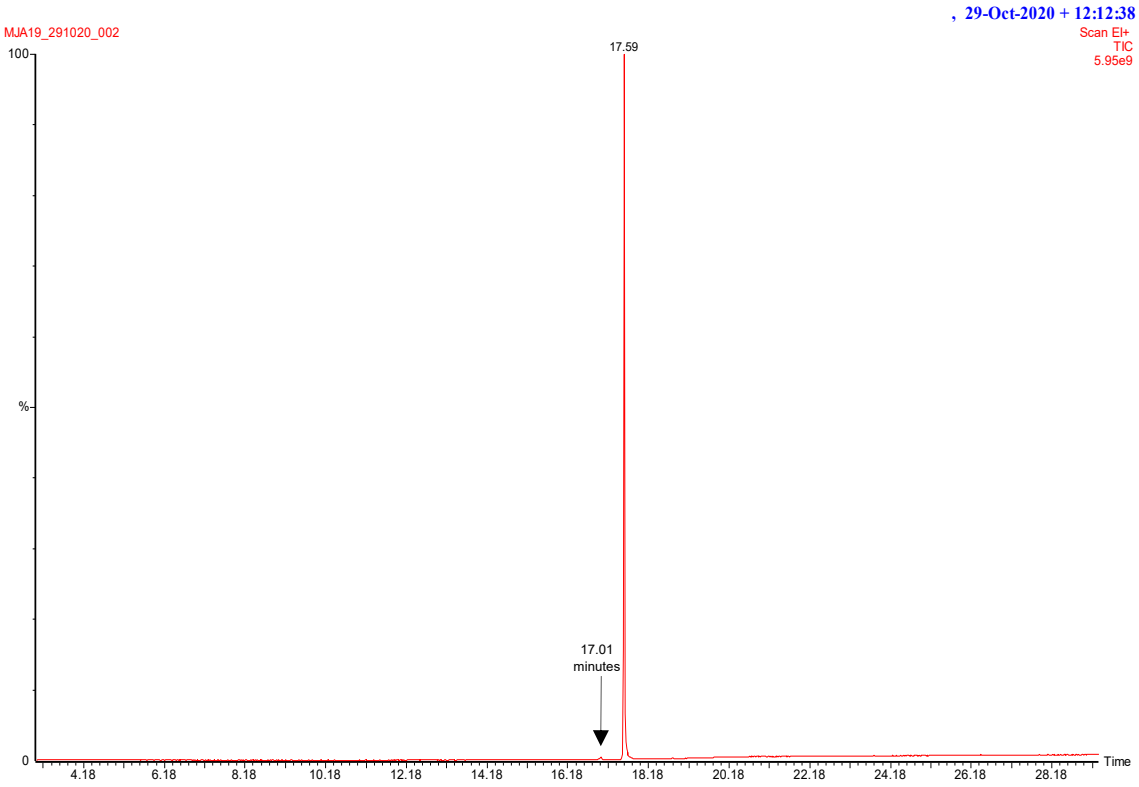


Figure 2.57: GC chromatogram for MJA19

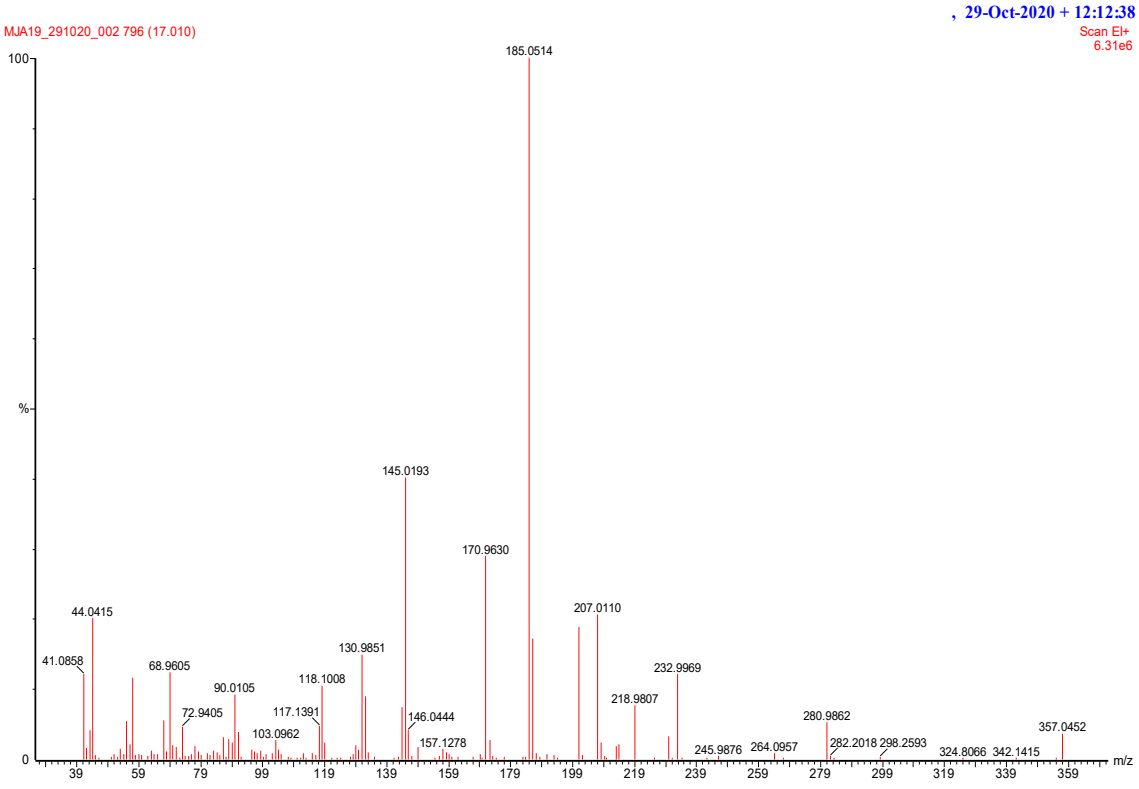


Figure 2.58: MS spectrum for MJA19 at 17.01 minutes

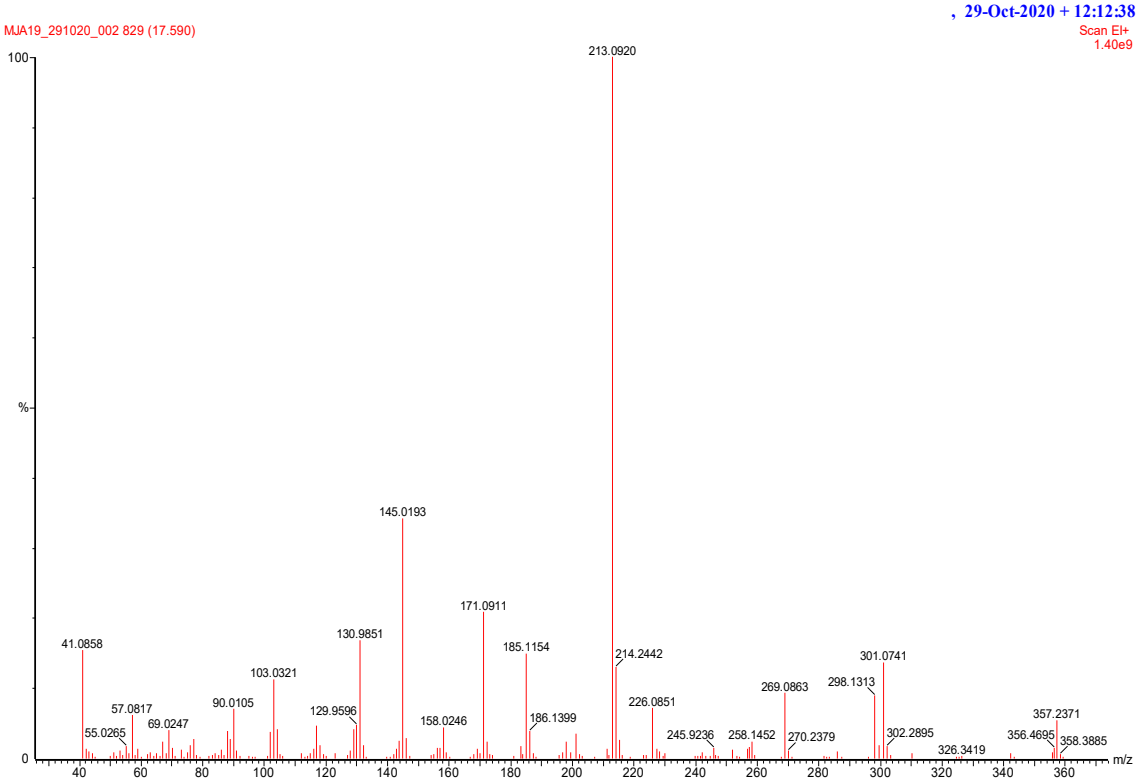


Figure 2.59: MS spectrum for MJA19 at 17.59 minutes

MJA19 was also analysed by LC-MS to verify the identification of MDMB-4en-PINACA produced through GC-MS analysis. The GC-MS sample was diluted for the LC-MS and analysed, resulting in the chromatogram seen in Figure 2.60 using the Find by Formula function aligned with the in-house PCDL, and the corresponding spectra can be seen in Figure 2.61.

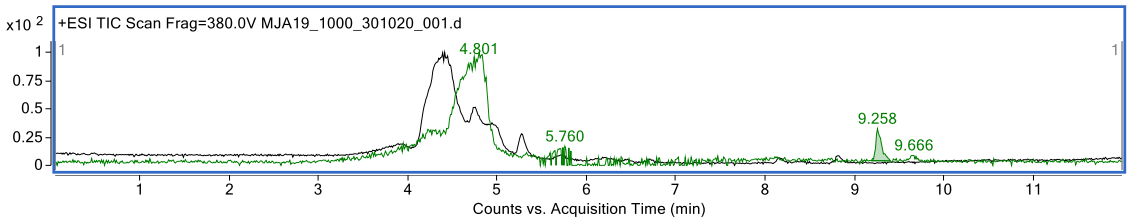


Figure 2.60: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (green chromatogram) for MJA19 at 9.3 minutes

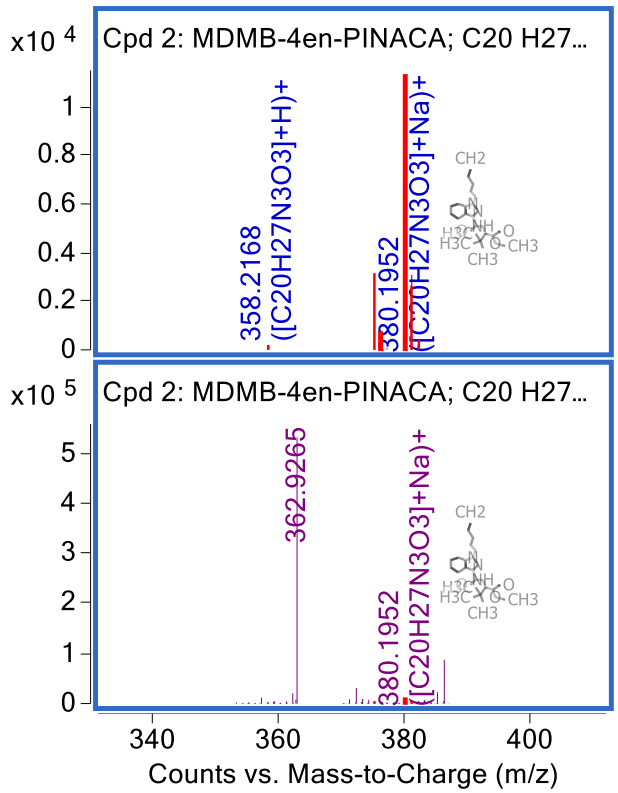


Figure 2.61: MDMB-4en-PINACA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above and MJA19 MDMB-4en-PINACA spectrum below. Predicted isotope distribution marked in red

Fortunately, the ammonium adduct was not an issue with this sample and the compound had a 90.85% match score to the MDMB-4en-PINACA library entry. This information was fed back to Rapiscan Systems Limited so they could liaise with other prisons about potential synthetic cannabinoid powders being found in prisons, plus this result was discussed with the West Midlands Prisons Group to notify them of the potential threat that was avoided as the powder could have been used to produce many paper samples. With MDMB-4en-PINACA being a highly potent synthetic cannabinoid (Krotulski *et al.*, 2020), there could have been risk to those using it if they were only familiar with lesser dosages, plus the potential risk of users mixing the synthetic cannabinoid powder with harmful liquids to dissolve them, such as using cleaning products, as prisons do not allow prisoners to own solvent or alcohol-based products.

Finally, MJA52 was submitted as a small amount (0.7778 g) of yellow powder sample that had been seized from a prisoner's cell. The sample was dissolved using sample preparation Method 5 and analysed using GC-MS and LC-MS. One chromatographic peak was produced, as shown in Figure 2.62, with a similar retention time to that shown for MJA19 (Figure 2.57). Due to this similarity in retention time, the spectrum produced was compared to MJA19, as shown in Figure 2.63, and the reference

MDMB-4en-PINACA spectrum (

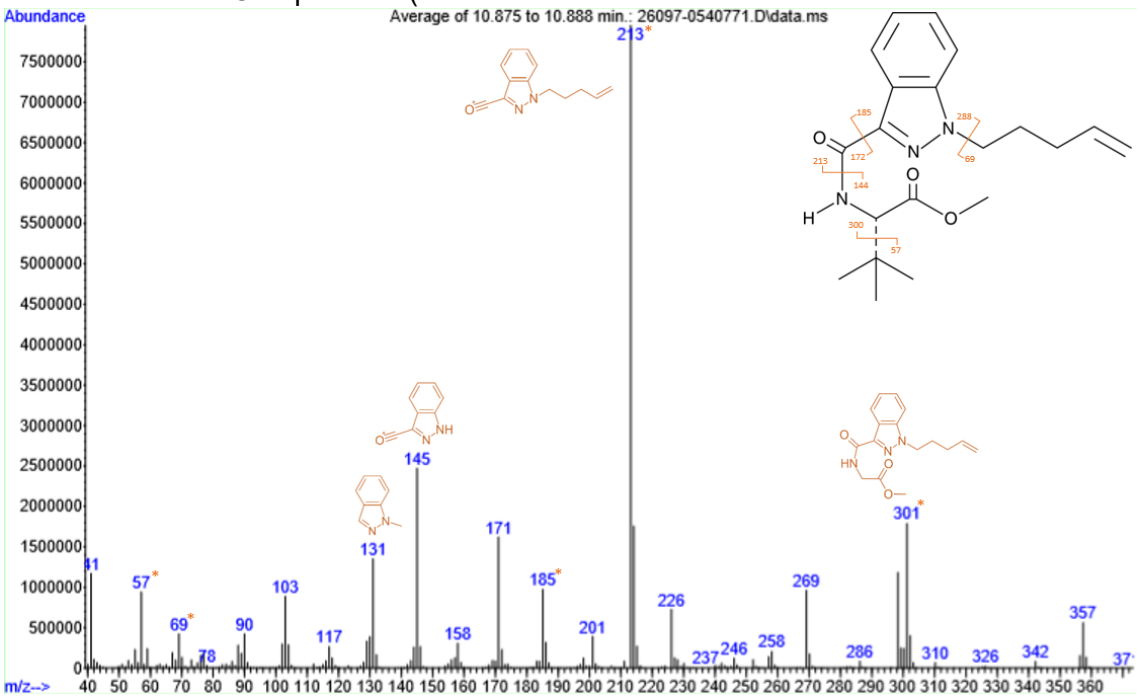


Figure 2.36) to support the presence of MDMB-4en-PINACA presence.

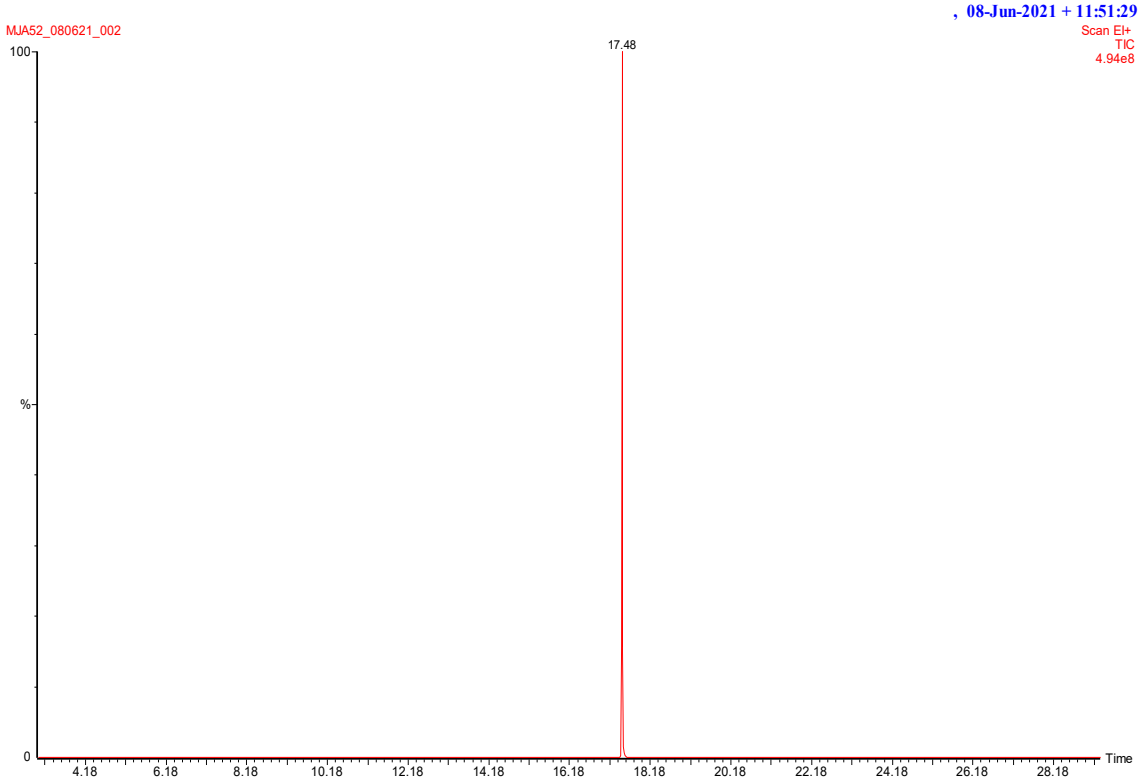


Figure 2.62: GC chromatogram for MJA52

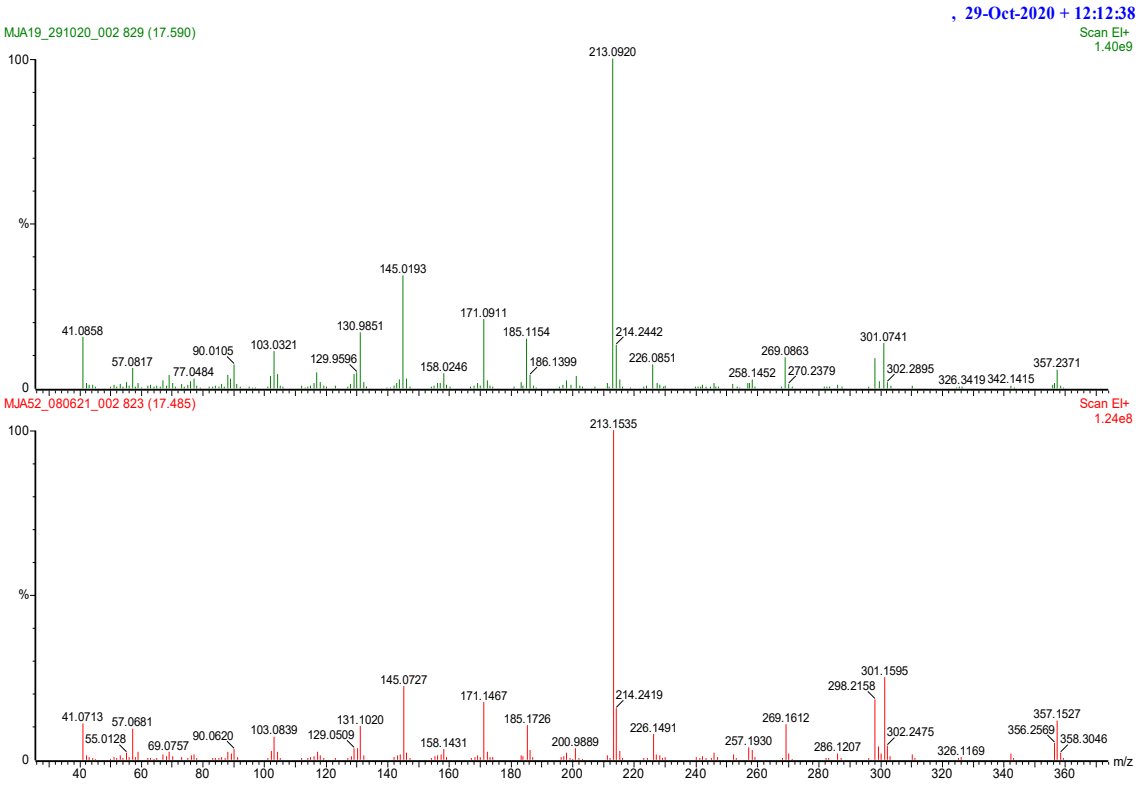


Figure 2.63: MS spectra for MJA19 and MJA52

The sample was also analysed by LC-MS, resulting in the peak at 0.672 minutes as shown in Figure 2.64 after application of the Find by Formula function with the in-house PCDL. The retention time featured is significantly different to that seen for MJA19, MJA14 and MJA40, however produced a 99.54% library match from the spectrum (Figure 2.65). A similar issue with retention time was also seen for MJA7 and MJA8 with 4F-MDMB-BUTINACA, suggesting an issue with the sample preparation method or the LC-MS eluents as consistent retention times are not being produced compared to those seen with GC-MS, where the retention time drifts have always been rational. Efforts were made to produce fresh eluent for large sample runs, however older eluents were used for one-off sample analyses, which may contribute to the difference, although in the case of MJA7 and MJA8, they were analysed sequentially.

Although accurate mass was considered suitable corroboration of the GC-MS identification, further work will have to be implemented to improve the LC-MS method and ensure consistency with the retention times. This further work would require certified reference standards to be analysed alongside these standards to identify the accurate retention time and investigate the impact of the sample injection method as mentioned previously.

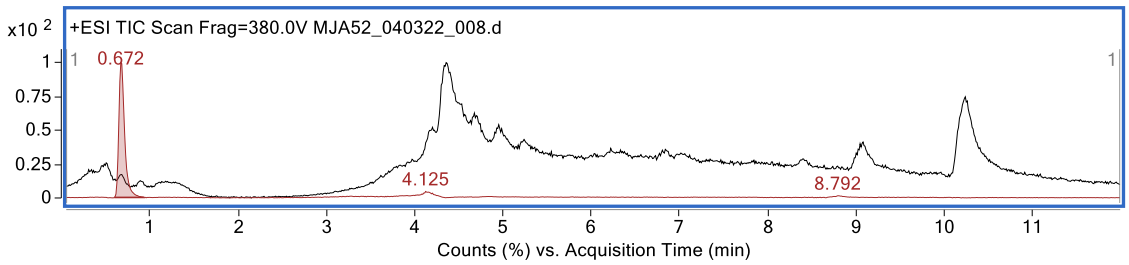


Figure 2.64: Total ion chromatogram (black chromatogram) and extracted ion chromatogram (red chromatogram) for MJA52 at 0.7 minutes

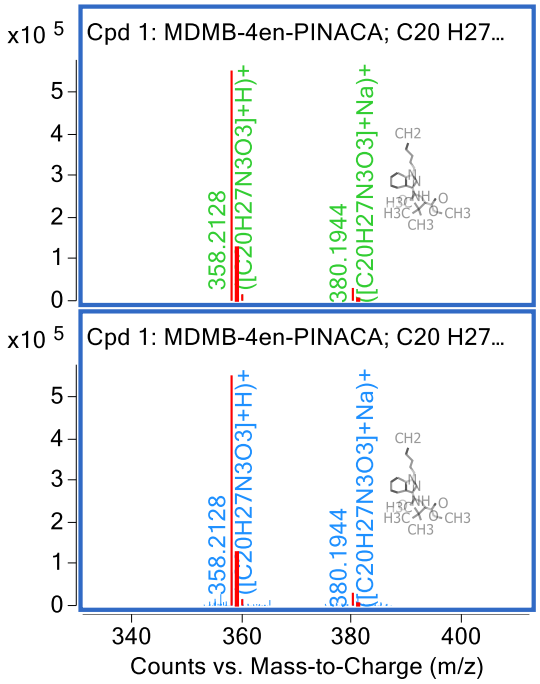


Figure 2.65: MDMB-4en-PINACA spectrum from Find by Formula (FBF) Agilent Forensic Toxicology PCDL above and MJA52 MDMB-4en-PINACA spectrum below. Predicted isotope distribution marked in red

Although certified reference standards were not used throughout this research, online reference spectra were used readily and effectively, therefore there was generally a high level of confidence in the identifications as all samples were analysed using more than one Category A or B technique as classified by the SWGDRUG (2019) guidelines.

2.3.5 Negatives

MJA1, MJA2, RANBY1 and RANBY2

MJA1, MJA2, RANBY1 and RANBY2 were prepared using Method 1, but no distinct chromatography peaks were gained using Method 1, therefore, a sample concentration step was added and MJA1, MJA2, RANBY1 and RANBY2 were analysed again to ensure that no synthetic cannabinoids were being missed by being too dilute. Method 2 resulted in larger, more defined chromatography peaks *via* GC-MS for MJA1, MJA2, RANBY1, RANBY2 and MJA4 when analysed, however the peaks were still small and not greatly resolved compared to the baseline, plus the spectra per peak did not have

characteristics seen for the synthetic cannabinoids listed in the in-house synthetic cannabinoid Excel spreadsheet in terms of their relative molecular mass (all of which have a relative molecular mass within the 300-450 range apart from Cumyl-INACA, with a relative molecular mass of 279). Furthermore, no clear identification could be made of the chemicals extracted from the sample as the match scores were around 650 or lower, therefore there was no evidence of the presence of synthetic cannabinoids.

MJA11

MJA11, a handwritten letter to a prisoner, was initially submitted for analysis due to having a peak at 9.633 ms triggering 5F-AKB-48 on the Itemiser 3E® and a sweet smell, suggesting there had been some alteration to the paper. Solvent extraction Method 2 was utilised, and the resulting solution was analysed using GC-MS. Although multiple peaks were featured on the chromatogram, as seen in Figure 2.66, none of the mass spectra had any characteristic peaks (molecular ion peak or base peak) to 5F-AKB-48 (with relative molecular mass of 383.5), suggesting a false positive.

The NIST 2.0 library indicated potential identifications for the majority of the peaks in the chromatogram, with an excellent match for Diisooctyl phthalate (947) and good matches for 1-tridecanol, 1-chloro-dodecane, ethylene glycol monododecyl ether, diethylene glycol monododecyl ether and triethylene glycol monododecyl ether (all results tabulated in Appendix 7 – NIST 2.0 Library results per peak for MJA11 GC chromatogram). Diethylene glycol monododecyl ether, lauryl glycidylether and triethylene glycol monododecyl ether were suggested compounds for multiple retention times, which is not a correct identification and suggests a similar chemical was present. This collection of these chemicals suggested the presence of a conditioner and/or a cleaning product, which may have been present to try and induce a psychoactive effect for the user, as there was intelligence to suggest common household products were being soaked into paper and smoked by the prisoners (Sherwin, 2021), or for disruptive purposes, as there was intelligence from Rapiscan Systems Limited to state that products may have been soaked into the paper with the intention to disrupt the use of the Itemiser 3E® instruments (Chandler, 2022a). Further work should be dedicated to the analysis of blank paper and card samples to produce controls, and the analysis of household products to determine if any of these have a similarity to the results seen for MJA11 and some of the other samples in this chapter.

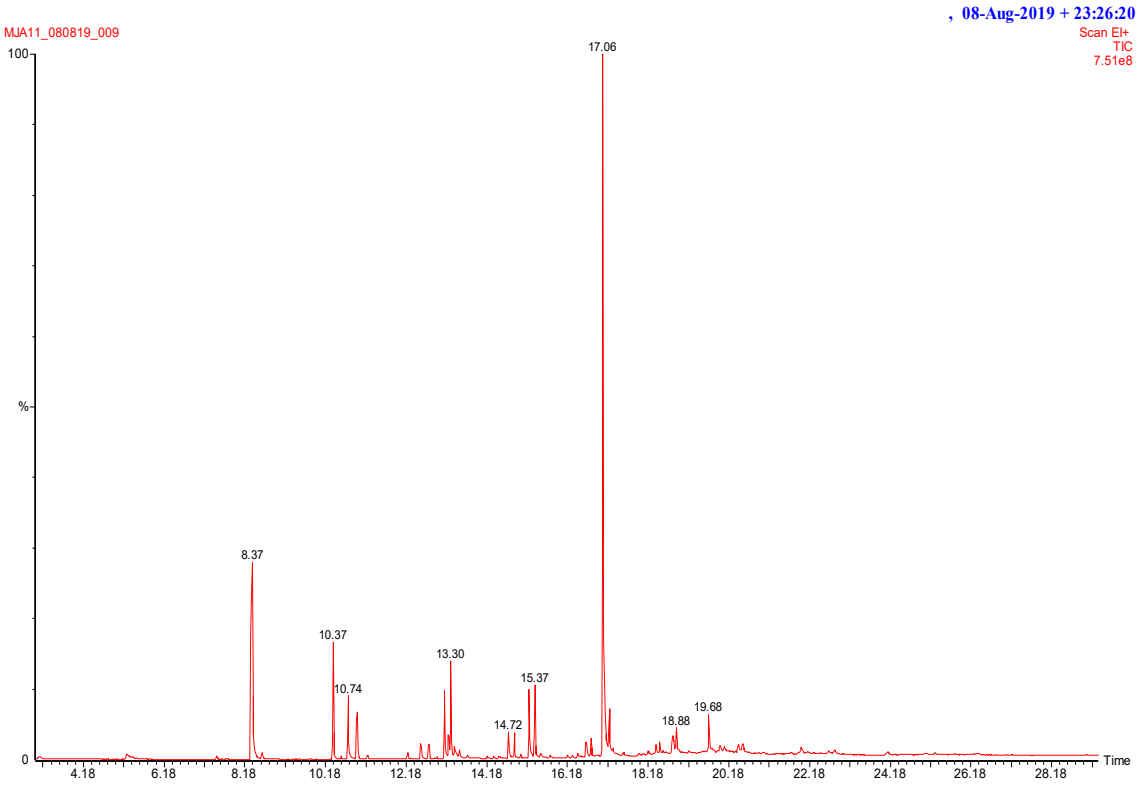


Figure 2.66: GC chromatogram for MJA11

The analysis of MJA11 coincided with the purchase and installation of the Agilent 6500 Series Quadrupole-Time of Flight Liquid Chromatography-Mass Spectrometry System and therefore was the first unknown sample to be analysed using the technique. LC-MS data interpretation did not result in any synthetic cannabinoids being identified from the in-house PCDL or any matches to drug compounds in the Agilent Forensic Toxicology PCDL. NMR analysis was performed, however the NMR spectra for MJA11 was insufficient for structural elucidation as the peaks hardly exceeded the background noise, plus the compound was a mixture, adding another layer of complexity to the interpretation. Similar to the discussion regarding 5F-AKB-48 for MJA14, if the drug had been present, the extraction and analysis procedures would have been sufficient, however there was no 5F-AKB-48 detected, therefore showing it was not present. The MJA11 sample was therefore not prioritised for further investigation due to not exhibiting sufficient evidence for the presence of a potential synthetic cannabinoid at this time but has been periodically checked against the future updates to the in-house PCDL and future research could be dedicated to determining what the false positive was for 5F-AKB-48.

MJA18

MJA18 was submitted due to the strong sweet smell and a peak between 8-10 ms from the Itemiser 3E®: 9.461 ms indicating the presence of 5F-MDMB-PICA. Although,

when the samples were extracted using acetone for solvent extraction Method 2 and analysed *via* GC-MS, no peaks were exhibited, resulting only in the baseline curve for the solvent. This was unexpected for MJA18 due to the strong sweet smell indicating tampering of the paper and the Itemiser 3E® results, however as solvent extraction Method 2 had proved successful for the extraction of 5F-MDMB-PICA in other samples (MJA3, MJA5 and MJA6), it was deemed that the compound present on the Itemiser 3E® result may have been in extremely low concentrations, a false positive or contamination from a different sample and therefore the sample was analysed by LC-MS to investigate further.

MJA18 was prepared using the methanol-based solvent extraction Method 2 for the LC-MS, as it was possible that the acetone used for the GC-MS analysis did not sufficiently extract the compound suspected to be featured on MJA18, however there was no indication of synthetic cannabinoids being present in the sample. This led to the theory that the sample could have been contaminated by another sample but on an extremely low scale, or that there could have been an issue with the sampling when analysed with the Itemiser 3E®, as the area is not a sterile laboratory environment and could have been more susceptible to contamination. The source of the odour was not identified.

Card samples

Card samples have also been encountered during the project, with four card samples submitted from HMP Featherstone in late November 2019 to analyse and identify any potential synthetic cannabinoids present. MJA12, MJA13, MJA15 and MJA16 were all cards with scratch markings on the pages and submitted for analysis due to suspicions from the post room staff, however in terms of other common characteristic features, none of the cards had an associated smell or distorted features on the card, or any peaks on the Itemiser 3E® between 8-10 ms. The samples were extracted using solvent extraction Method 2 and analysed *via* GC-MS. MJA13 and MJA16 exhibited no peaks above the baseline, which was expected due to the lack of peaks or recorded time-of-flights from the Itemiser 3E®. Chromatography peaks were seen for MJA12 and MJA15, as shown in Figure 2.67 and Figure 2.68, however neither MJA12 nor MJA15 exhibited spectral characteristics to indicate the presence of synthetic cannabinoids. MJA12 did have one peak at 10.093 minutes that was identified by the NIST 2.0 library as benzophenone, used for fragrance, UV absorption and moisturising (PubChem, 2022e), however the match score was classed as ‘fair’ (754) and none of the other peaks had match scores above 500, therefore a complete identification could not be made for this sample and it was not prioritised further due to the lack of synthetic

cannabinoid presence. MJA15, on the other hand, had one distinct peak at 11.272 minutes which the NIST 2.0 library identified with a good score as 4-methyl benzophenone, a stabilising agent for paints and coatings (PubChem, 2022f). Although the peak at 24.578 minutes was a weak match to bis(trimethylsilyl) diethyl silicate, it was inferred that this could have been due to column bleed of cyclosiloxane causing a ghost peak (eds. Dettmer-Wilde and Engewald, 2014).

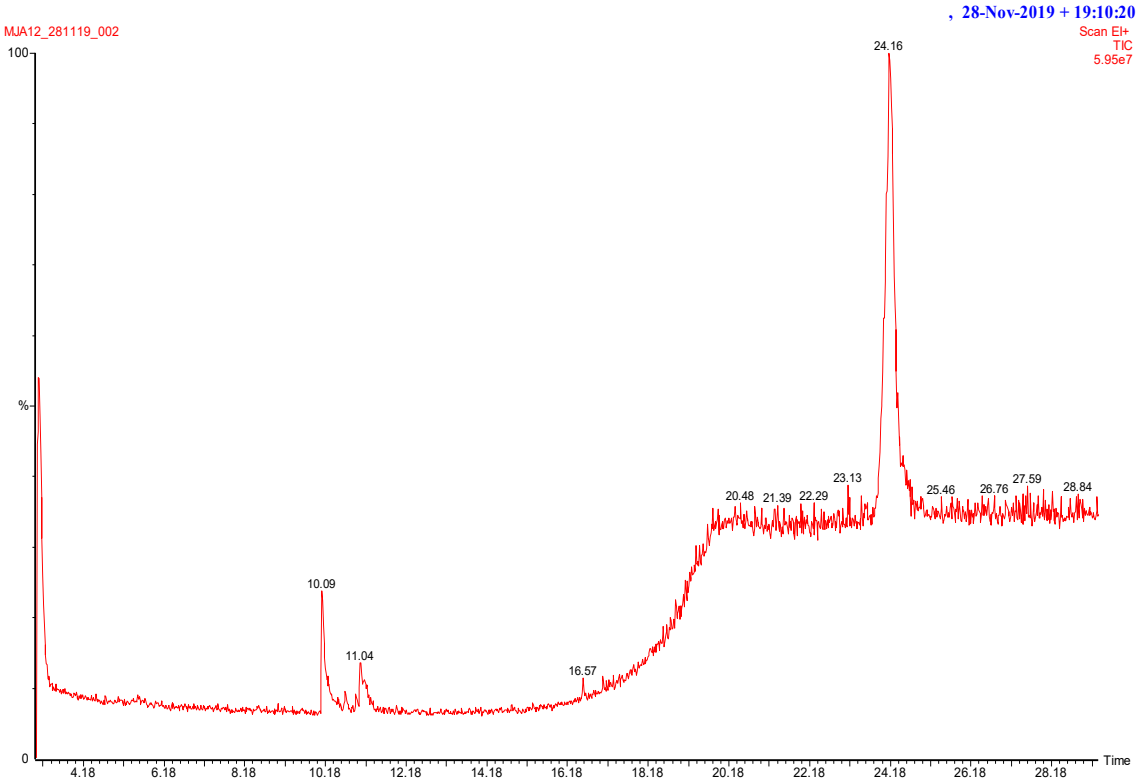


Figure 2.67: GC chromatogram for MJA12

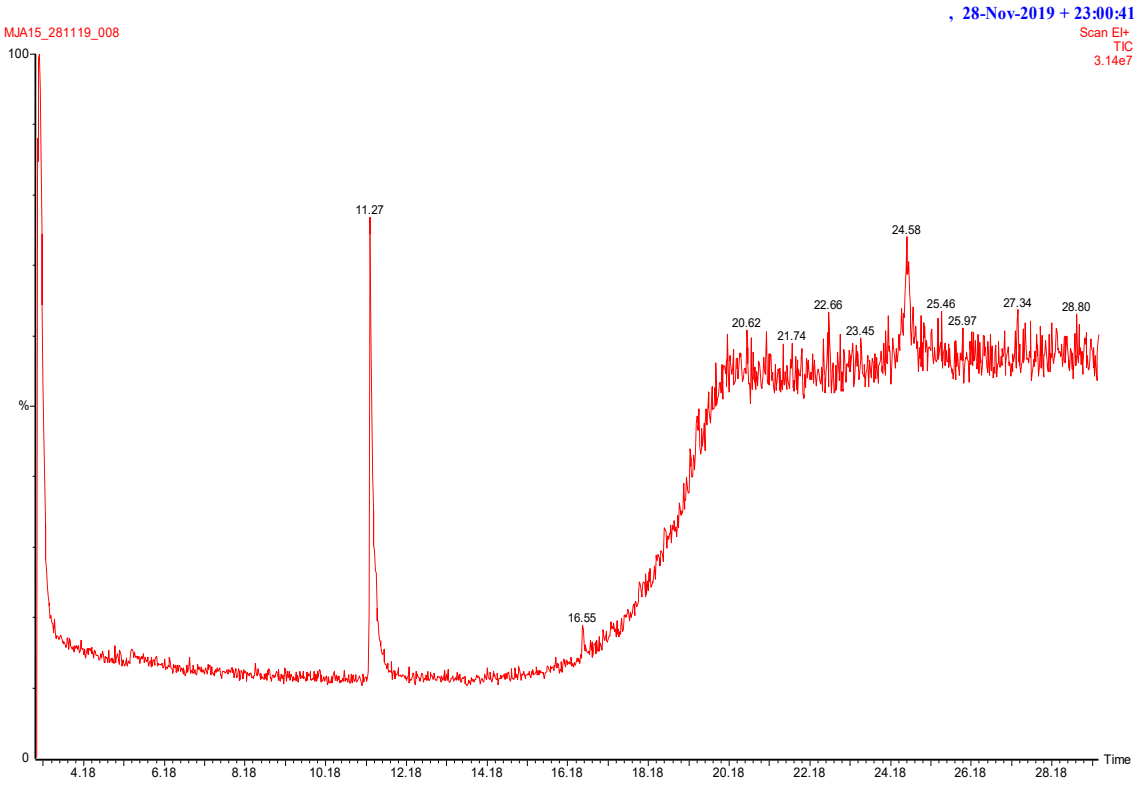


Figure 2.68: GC chromatogram for MJA15

MJA44, a Moonpig card, was submitted by HMP Stoke Heath in March 2021 with an associated Itemiser 3E® result indication to the presence of MDEA (3,4-Methylenedioxy-N-ethylamphetamine), a derivative of MDMA (3,4-Methylenedioxy methamphetamine) (Bexis and Docherty, 2006). This was investigated to rule out any traditional drug presence but was not a priority due to the lack of any indication of synthetic cannabinoid presence by the Itemiser 3E®. The sample was analysed using solvent extraction Method 4 for GC-MS and LC-MS, resulting in only a solvent baseline and therefore no indication of MDEA or any other methamphetamine salt. Although MDEA is soluble in methanol, it could have been unstable and required a derivatisation step (UNODC, 2006), however this was not pursued due to traditional drugs not being a priority within the project. It was therefore relayed back to the prison liaison that MDEA was unlikely to be present, but it was not a definitive result.

Printed pages and photographs

Another group of samples submitted were printed pages showing content from clothing websites. This was initially raised as suspicious by the intelligence team due to the similarity in the samples, with MJA29, MJA30 and MJA31 all including printed pages for tracksuits and trainers from sites such as Flannels and JD Sports and posted within a few days of each other alongside handwritten letters on lined paper. There was no sign of alteration to the images, as there was no obvious distortion to the ink or warped areas. The handwritten letters were sampled as the printed images filled most of the

paper and there may have been ink interference when screened using the GC-MS. The handwritten letter hole punches were extracted using solvent extraction Method 4 with methanol; however, no peaks were seen in the chromatogram.

MJA41, a collection of 45 photographs, was not analysed as no distortions to the photograph paper were seen and there was no obvious intelligence or Itemiser data to indicate the presence of a synthetic cannabinoid. Further work with these samples could focus on the analysis of the ink itself to determine if there would be interference from the ink.

Rule 39 samples

Rule 39 letters have also been submitted as samples to Staffordshire University for the project, however different types have been encountered. One sample, MJA42, was an obviously fake letter as it included a clingfilmed package of tobacco and blank MG11 forms amongst other pieces of paper. The sample had originally been alerted to the intelligence team as staff could feel irregularities inside the envelope and therefore suggested there was a concealment. The contents of the envelope were swabbed through a small hole in the envelope, resulting in an indication of ephedrine/pseudoephedrine and cocaine on the Itemiser 3E®, however when screened *via* GC-MS and analysed by LC-MS, there was no indication of any traditional drugs present. Ephedrine, pseudoephedrine and cocaine are freely soluble in methanol so should have been detected if present (Black *et al.*, 2007; SWGDRUG, 2005a; SWGDRUG, 2005b). The cocaine false-positive could also have been from contamination on the surface of the sample rather than cocaine being impregnated, whereas 3.5 hole-punches were taken to identify impregnated compounds by GC-MS (Norman, McKirdy, Walker, *et al.*, 2020). Furthermore, Rapiscan Systems Limited train staff to query cocaine peaks seen with the Itemiser 3E® as the surface contamination could also originate from where the sample was prepared before being sent to the prison, i.e., the paper could have been exposed to cocaine within the household it was prepared in before being posted.

The rest of the Rule 39 letters encountered were imitations of real Rule 39 letters or suspected to be real Rule 39 letters with false positives. MJA46 and MJA56 both contained printed pages, MJA46 included COVID-19 guidelines and MJA56 included advice around legal proceedings, but both had some evidence of staining on some of the pages, which raised suspicions from the prison staff that the letters were concealments. Neither MJA46 nor MJA56 had been initially screened with an Itemiser 3E® however, so there was no associated intelligence surrounding the potential presence of a drug. Samples were taken from areas of staining to aim to increase

chances of detection, however the MJA56 chromatogram only featured the methanol baseline and no peaks *via* GC-MS when using solvent extraction Method 4. This suggested that there was not any significant adulteration to the paper, that the adulteration compound was too dilute, or that a compound may have been present, but the sample was not extracted successfully using methanol. No indication of drug presence was seen *via* LC-MS analysis and comparison to the PCDLs either. Although methanol was used, there is still potential that the sample present was not soluble in the solvent, or that even though the hole punches were taken from stained areas, the sampling technique may have missed the active compound. This sample was not prioritised for further analysis *via* different extraction solvents however due to other samples taking priority.

MJA46 did however include four distinct peaks when analysed *via* GC-MS (as shown in Figure 2.69) but none of the peaks indicated a presence of a drug compound when examining the relative molecular masses and base peaks of the mass spectrum. Furthermore, the suggested matches outlined by the NIST 2.0 library were all considered 'poor' with none of the match scores above 600, suggested a compound other than a common drug or chemical may have been soaked onto the pages to have caused the stains.

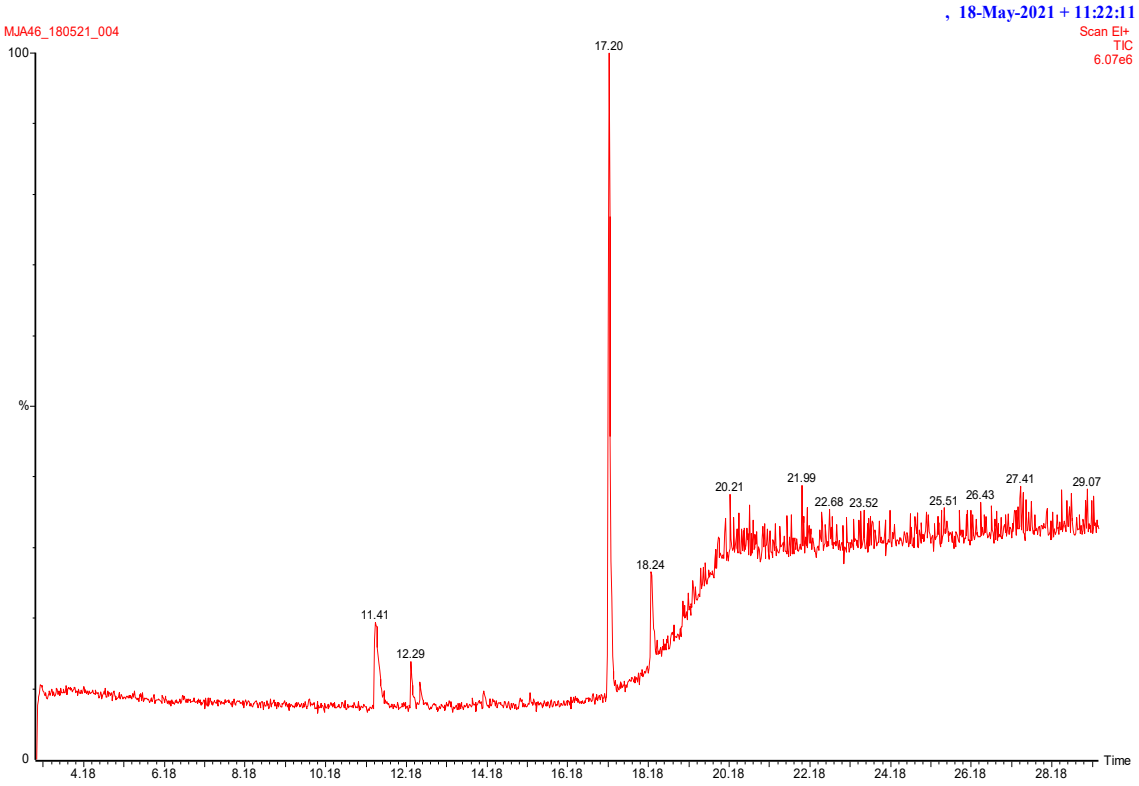


Figure 2.69: GC chromatogram of MJA46

MJA47 was submitted with associated intelligence to suggest that the samples could have been a mixture of baby oil, battery acid and toilet cleaner, a mixture suggested to induce a psychoactive effect when smoked (Sherwin, 2021), however no Itemiser 3E® results were recorded for the sample. The nine pieces of paper from MJA47 were grouped according to visual observations, resulting in MJA47a, MJA47b, MJA47c and MJA47d. Samples were taken from MJA47b and MJA47c for GC-MS due to the staining present on the samples and the resultant chromatograms can be seen in Figure 2.70. The chromatograms suggest the same substance was soaked into both sets of paper due to the similarity in peak retention times and relative intensities across the four peaks, and although the distinct peaks present did not indicate a presence of a drug, they indicated a presence of a conditioner or cleanser, as discussed and shown in Table 2.15. The split cells show the top hit first and then the top corresponding hit (library match) from the similar corresponding peaks on the other chromatogram below, which was always the second or third suggestion on the NIST 2.0 library. Further work could explore the use of the chemicals present, however the focus of the research was synthetic cannabinoids.

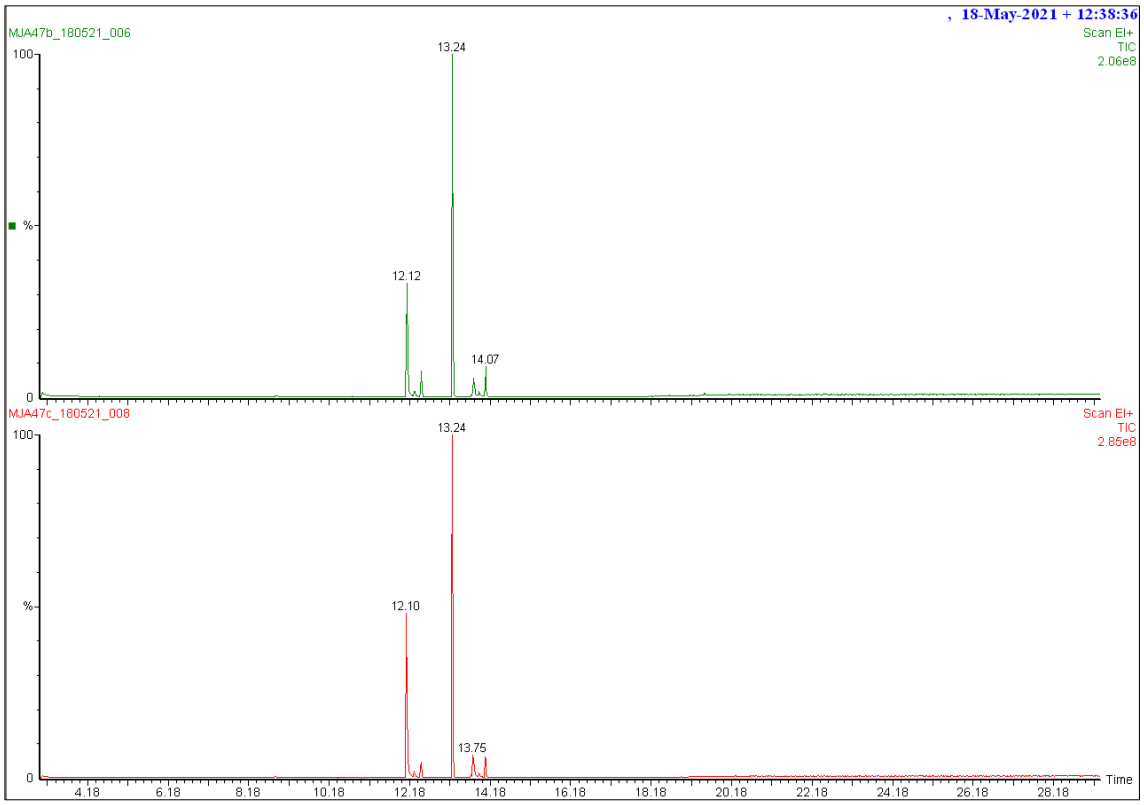


Figure 2.70: GC chromatogram of MJA47b (green) and MJA47c (red)

Table 2.15: Comparison of NIST 2.0 library results for MJA47b and MJA47c per GC chromatogram peak

MJA47b				MJA47c			
Retention time (minutes)	Name from NIST 2.0	NIST 2.0 match score	Uses	Retention time (minutes)	Name from NIST 2.0	NIST 2.0 match score	Uses
12.117	1-Tridecanol	894	Emollient, fragrance, and skin conditioner (PubChem, 2022g)	12.099	1-Hexadecanol	929	Cleanser (laundry detergent and personal hygiene), surfactant, emollient and fragrance (PubChem, 2022b)
	1-Hexadecanol	890	Cleanser (laundry detergent and personal hygiene), surfactant, emollient and fragrance (PubChem, 2022b)		1-Tridecanol	903	Emollient, fragrance, and skin conditioner (PubChem, 2022g)
12.467	Methyl palmitate	788	Emollient, flavouring, conditioner and fragrance (PubChem, 2022h)	12.469	Methyl 14-methylpentadecanoate	813	Fatty acid methyl ester, can be used in detergent (eds. Hayes, Solaiman and Ashby, 2019)
	Methyl 14-methylpentadecanoate	763	Fatty acid methyl ester, can be used in detergent		Methyl palmitate	797	Emollient, flavouring, conditioner and fragrance (PubChem, 2022h)

			(eds. Hayes, Solaiman and Ashby, 2019)				
13.243	Isopropyl palmitate	878	Antistatic, binder, conditioner for personal hygiene and solvent (PubChem, 2022c)	13.243	Isopropyl palmitate	876	Antistatic, binder, conditioner for personal hygiene and solvent (PubChem, 2022c)
13.771	1-Hexadecanol	784	Cleanser (laundry detergent and personal hygiene), surfactant, emollient and fragrance (PubChem, 2022b)	13.754	1-Docosene	830	Skin conditioner and lubricant, and in Vanilla planifolia, Hordeum vulgare (barley) (PubChem, 2022i)
	1-Docosene	782	Skin conditioner and lubricant, and in Vanilla planifolia, Hordeum vulgare (barley) (PubChem, 2022i)		1-Hexadecanol	784	Cleanser (laundry detergent and personal hygiene), surfactant, emollient and fragrance (PubChem, 2022b)
14.070	Methyl stearate	774	Emollient, flavouring, fragrance and skin conditioner (PubChem, 2022j)	14.053	Methyl stearate	798	Emollient, flavouring, fragrance and skin conditioner (PubChem, 2022j)

The MJA32, MJA33, MJA34, MJA36, MJA37 and MJA45 Rule 39 letters all had an indication of a traditional drug presence from the Itemiser 3E® results, including heroin, MDMA, MDA/4-MMC, PCP and amphetamine. Other than the Itemiser 3E® indication, there was no major suspicion for samples MJA32, MJA33, MJA34, MJA36 and MJA37 in terms of visual observations, however MJA45 was deemed suspicious as the envelope only featured the recipient and Rule 39 stamp, with no mention of the solicitor it was supposedly sent from and underpaid postage. Furthermore, when the envelope was opened, there were two printed sheets from the Police and Criminal Evidence Act 1984 covered front and back with multiple sheets of A5 lined paper, suggesting that they were being used to fill out the envelope and decrease the chances of sampling the centre pieces. Sampling therefore focused on the centre printed sheets for MJA45, and the usual representative sampling technique was used for MJA32, MJA33, MJA34, MJA36 and MJA37. Solvent extraction Method 4 with acetone was utilised for MJA32, MJA33, MJA34, MJA36 and MJA37, and MJA45 was sampled later with methanol, however no peaks were exhibited *via* GC-MS for MJA32, MJA33, MJA34, MJA36 and MJA37 and only two very small peaks exhibited in MJA45 which were inferred to have resulted from the methanol blank, as very similar retention times and mass spectra were collected for both peaks. Furthermore, no indication of a traditional drug or any drug in either PCDL was present after LC-MS analysis, therefore implied that the traditional drug indication from the Itemiser 3E® could have been a false positive of a constituent component of the letter, or contamination.

MJA43, another fake Rule 39 letter, had an indication of tramadol, nimetazepam, cocaine, 4F-MDMB-BUTINACA and ADB-FUBINACA from the Itemiser 3E® results, however upon screening by GC-MS, using the solvent extraction Method 4, there were no chromatography peaks present, only the methanol baseline mirrored from the methanol blank. Furthermore, no indication of a drug presence was seen in the LC-MS analysis, resulting in confusion surrounding the indications made by the Itemiser 3E®. The sample was compiled of 40 pages in total from various sections of the Criminal Justice Act 2003 chapters, although not sequential or complete chapters (fully outlined in Table 2.9), plus a page from InsideTime.org. To attempt to maximise the potential of drug extraction, hole punches were taken from pages which had been sampled by the Itemiser 3E® trap as it had left scratch marks on the surface of the paper, however that did not result in any indicative peaks. Potentially the indications could have been from contamination from other samples when the Itemiser 3E® sample analysis was occurring, the inks present could have caused a false positive response, or the active

compounds were not sampled, or not detected upon analysis. The representative sampling across the four corners was at first intuitive, but then was supported by other researchers doing similar or the same (Angerer, Möller and Auwärter, 2018; Antonides *et al.,* 2020; Norman, McKirdy, Walker, *et al.*, 2020) and has been sufficient for other samples, but may not have been sufficient for this sample where targeted dispensing could have occurred. However, as the time taken to exhaustively sample all 40 pages would be considerable, and as the sample had already been prevented from entering the prison, it was decided that further investigation of this sample would not be undertaken at the time. Other sampling method strategies may need to be produced for samples with a large number of pages.

MJA27 and MJA28

MJA27 was also submitted to verify the presence of synthetic cannabinoids and traditional drugs on a Rule 39 letter. All ten pieces of paper were swabbed by prison staff and the Itemiser 3E® resulted in indications for 5F-AKB-48 on eight sheets, phencyclidine (PCP) on two sheets, morphine on two sheets and finally pseudoephedrine on one. Due to the suggested presence of a synthetic cannabinoid on so many of the pages, this sample was submitted to the University for confirmatory analysis, however it was noted that there was no obvious staining or smells, and all the pieces of paper were letterhead pages for a national law firm. Upon analysis *via* GC-MS, and using solvent extraction Method 4, no chromatography peaks were seen, only the solvent baseline. 5F-AKB-48 is soluble in methanol and was analysed *via* GC-MS using methanol as an extraction method from herbal samples in previous research by the author and by others in the field (Frinculescu *et al.,* 2017), plus is a recommended solvent by SWGDRUG (2013a), so the 5F-AKB-48 should have been extracted if present using solvent extraction Method 4. Furthermore, pseudoephedrine, morphine and PCP are also all soluble in methanol (SWGDRUG, 2000; SWGDRUG, 2005a and SWGDRUG, 2005c), therefore the potential reasoning behind the lack of peaks could be that the quantities were not enough to be extracted from the paper when using solvent extraction Method 4, there was surface level contamination only or there were false positives on the paper. To further investigate and investigate the potential causes of a false positive, a branch of the law firm involved gave the West Midlands Prison Group some of their blank letterhead paper to be analysed by the University (MJA28). MJA28 was not screened with an Itemiser 3E® by the West Midlands Prison Group so a comparison of the Itemiser 3E® results could not be made, however the GC-MS results were the same, with a blank methanol solvent baseline curve for each. Both samples were also analysed *via* LC-MS and neither had any indication on the Agilent

Forensic Toxicology library for 5F-AKB-48, morphine, PCP or pseudoephedrine, further implying a false positive from the Itemiser 3E® for the MJA28 sample. Unlike MJA11 and MJA14, where there was a false positive for 5F-AKB-48 from the Itemiser 3E® and indication of a potential cleaning product upon GC-MS analysis, that was not seen for this sample.

Upon analysis of MJA58, a calendar diary with an Itemiser 3E® result peak of 10.246 ms, specific focus was turned to representative sampling due to the number of pages present, therefore samples were taken from the first page for the months January, May, August and December and extracted with solvent extraction Method 4. Once analysed using GC-MS, there were no peaks seen, only the methanol baseline, and no indication of the presence of any drug compound using LC-MS. Potentially this was due to the presence of a new type of synthetic cannabinoid as the Itemiser 3E® peak at 10.246 ms was not one of the usual synthetic cannabinoid time-of-flights and not triggering any traditional drug sample, however there could have been a substance present and it was missed from sampling. Although sampling was conducted from more than one area of the page, as suggested by Angerer, Möller and Auwärter, (2018) and Norman, Walker, McKirdy, *et al.*, (2020), organised crime groups may be very specific with the location of the impregnated area over a larger sample size to attempt to evade detection. Therefore, further work focusing on the sampling procedure for MJA43 and MJA58, plus future large sample sets, needs to be established as a priority to increase confidence that synthetic cannabinoids or other drug substances are not present within the sample, however in the meantime, seizing the sample halts any potential of a concealment reaching the prisoner, therefore still disrupting the potential of drugs entering the prisons.

MJA20-MJA26

Another group of letters that were submitted to the University at the same time from the same prison were samples MJA20, MJA21, MJA22, MJA23, MJA24, MJA25 and MJA26. All the samples had a strong sweet smell, plus MJA21, MJA23 and MJA26 featured heavy staining, which heightened suspicion of the paper being used for concealment purposes. Furthermore, MJA21 had two peaks on the Itemiser 3E® within the 8-10 ms range which suggested a potential synthetic cannabinoid presence. None of the other samples had been screened with the Itemiser 3E®. The samples were all analysed *via* GC-MS using solvent extraction Method 4. Samples MJA20, MJA22, MJA24 and MJA25 did not feature any peaks, only the curve of the methanol baseline. Samples MJA21, MJA23 and MJA26 did feature peaks within their chromatograms, plus shared similar peaks at 11.6 minutes and approximately 15 minutes (Figure 2.71).

Of the peaks featured, none of them had a match score above 700 when compared to library substances, the minimum for a fair match (NIST Mass Spectrometry Data Center, 2008), and none of the molecular ions and structural indications from the fragmentation indicated presence of a synthetic cannabinoid, so although it can be assumed that there were similar components across the samples, the substances that were present were not formally identified. To further investigate the identity of the substances present, the samples were all analysed *via* NMR and LC-MS. The NMR spectra for each compound were too noisy for structural elucidation, even after method development with the number of scans applied. On the LC-MS, the Agilent Forensic Toxicology library identified the top potential hit to be methadone. To further investigate this potential, a methadone hydrochloride standard was analysed *via* GC-MS and NMR to compare to the spectra obtained for both, however the GC retention times and resultant mass spectrum were not similar to any of the samples and there was no similarity in peak position or intensity to the proton spectra for any of the samples from the batch. The methadone hydrochloride standard was also analysed alongside samples on the LC-MS, however the chromatograms for each exhibited completely different retention times, therefore excluding methadone as a potential. There has since been intelligence from Rapiscan Systems Limited that organised crime groups have tried to disrupt the use of the Itemiser 3E® by soaking paper with oils and various household solutions in the hopes that once they are swabbed, they would negatively impact the instrument and reduce the use of them in prisons (Chandler, 2022a), so this could have been the primary purpose of this batch rather than for concealment purposes.

These investigations have raised several issues that would benefit from further work: the causes of false positives, the lack of detected substances from paper that is clearly stained and odorous, the possible motivation behind some of these evidence items and the challenge of comprehensively sampling items which are comprised of many pages.

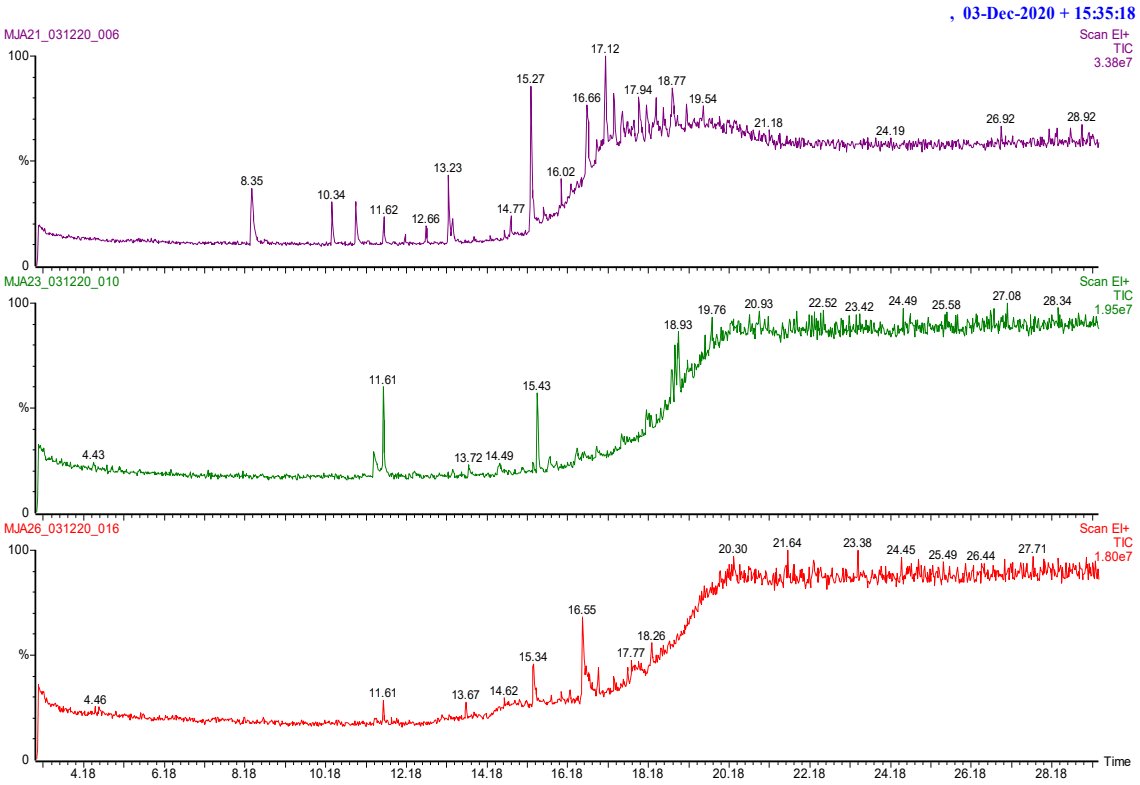


Figure 2.71: GC chromatograms for MJA21 (purple), MJA23 (green) and MJA26 (red)

2.3.6 Miscellaneous

Samples that were not categorised as paper or powder samples were classed as miscellaneous samples which encompassed the remaining 13 samples mentioned in Table 2.9. Of the miscellaneous samples, the only samples analysed *via* GC-MS were MJA9, MJA10 and MJA55. The MJA9 sample was a peaches tin with the top cut off to act like a sleeve, housing a shorter but similar diameter condensed milk tin to complete the top of the tin and leave a hollow section under the condensed milk tin. In the cavity below the condensed milk tin was some tissue paper, however the tissue had been spoiled from the condensed milk leaking. The sample was prepared using sample preparation Method 2 alongside paper samples, however upon analysis *via* GC-MS, no chromatography peaks were present. Although more analysis time could have been dedicated to determining if there was a substance on the tissue, such as using another solvent, the fact that the sample was spoiled and soon turned mouldy resulted in the sample not being further analysed. MJA10, a packet of seeds, had a positive inference for 5F-MDMB-PICA when swabbed and screened on the Itemiser 3E® alongside two other peaks between 8-10 ms, suggesting the seeds may have been soaked or coated in a synthetic cannabinoid. Solvent extraction Method 6 was used for the sample to try to extract any substances from the surface or from inside the seeds, which resulted in two main chromatography peaks once analysed by GC-MS (Figure 2.72). The MS

spectra were investigated for both to try to determine the substances present, however the NIST 2.0 library match did not exceed a 700 match score to any of the compounds (NIST Mass Spectrometry Data Center, 2008). Additionally, the relative molecular mass and base peak combination, as shown in Figure 2.73 and Figure 2.74, did not match any substance listed in the in-house synthetic cannabinoid Excel spreadsheet, or to any substance listed on the Cayman Chemical Company website or the DrugBank Online website, therefore definitively ruling out 5F-MDMB-PICA but still not identifying the compound present. Due to the sample not being paper based, it was not prioritised for further sampling, however the sample has been retained in case of any future analyses.

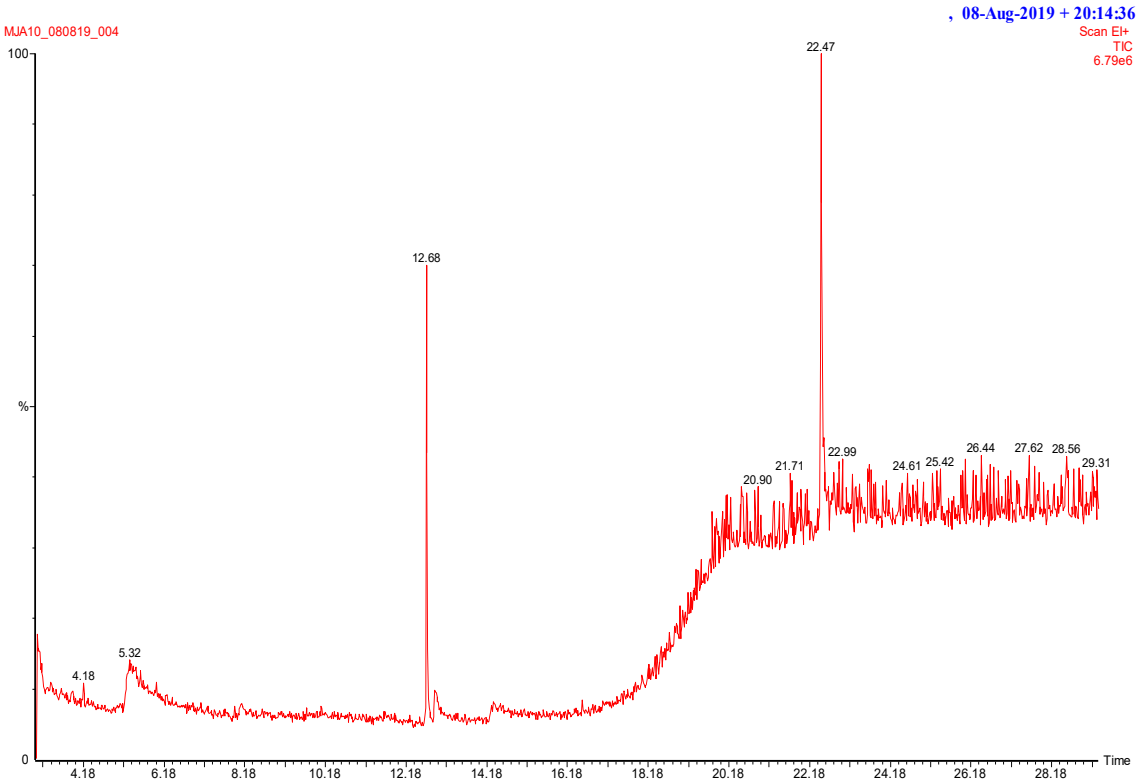


Figure 2.72: GC chromatogram for MJA10

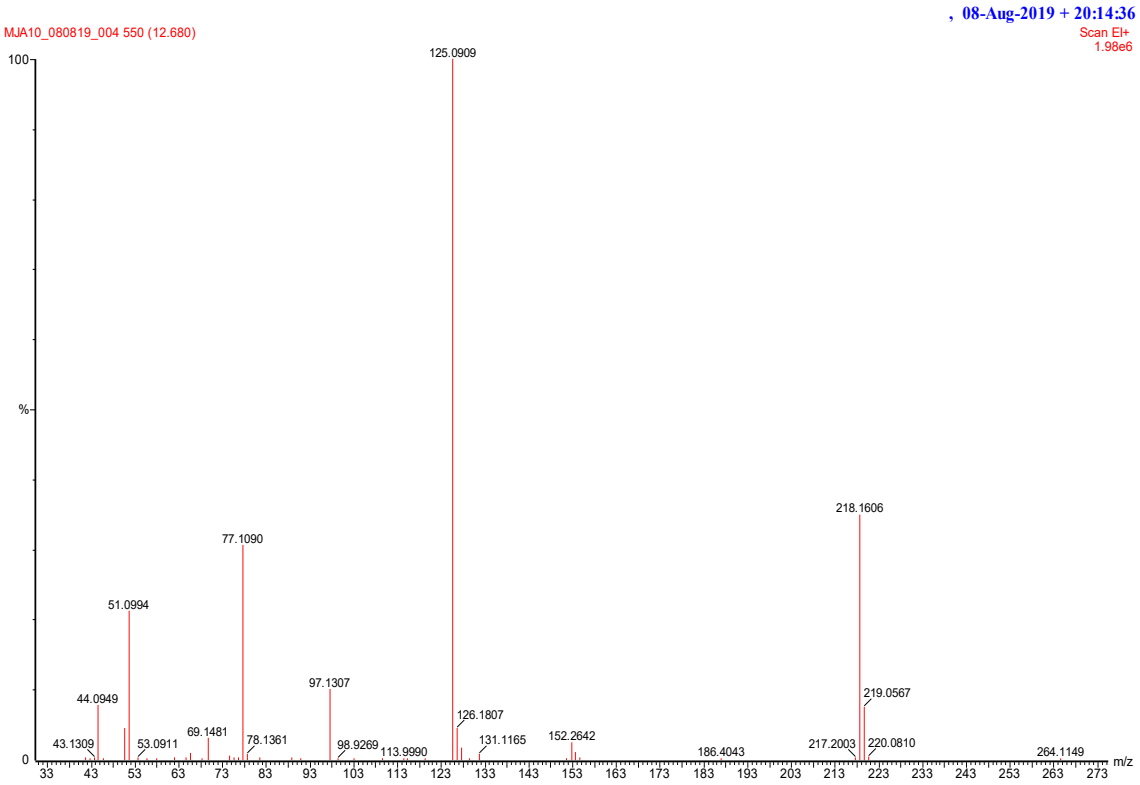


Figure 2.73: MS spectrum for MJA10 at 12.680 minutes

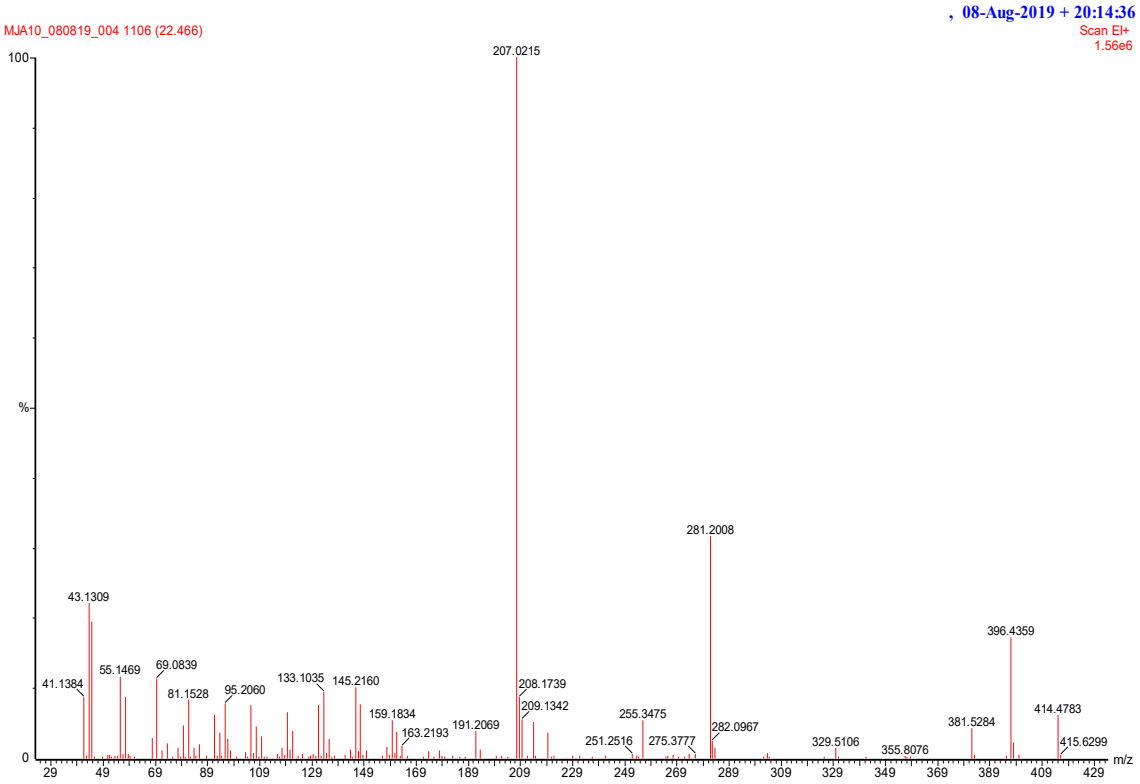


Figure 2.74: MS spectrum for MJA10 at 22.466 minutes

MJA55, a package containing 14.0135g of grey powder taken from a cleaning cupboard in a prison, was submitted to the University for confirmatory analysis due to the suspicion surrounding the find and an Itemiser 3E® peak at 9.643 ms. The sample was analysed using sample preparation Method 5 and GC-MS. This analysis resulted in one chromatography peak at 16.22 minutes, as shown in Figure 2.75, and a NIST 2.0 library hit for sertraline, a selective serotonin reuptake inhibitor (SSRI) antidepressant (National Health Service, 2022), with a match score of 688. Although this match was less than the 700 threshold for a fair match (NIST Mass Spectrometry Data Center, 2008), it did have a plausible reason to be within a prison in a hidden setting, however there were some abundance differences when comparing the mass spectra to reference spectra (Figure 2.76 and Figure 2.77).

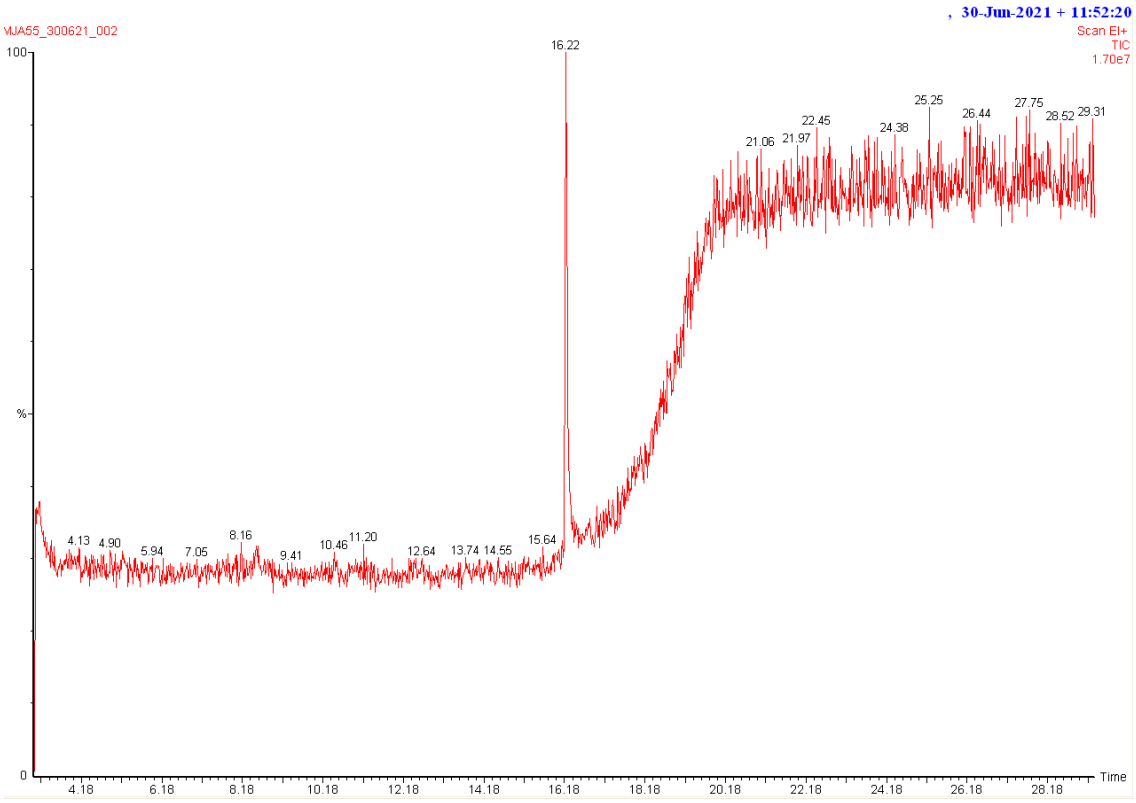


Figure 2.75: GC chromatogram for MJA55

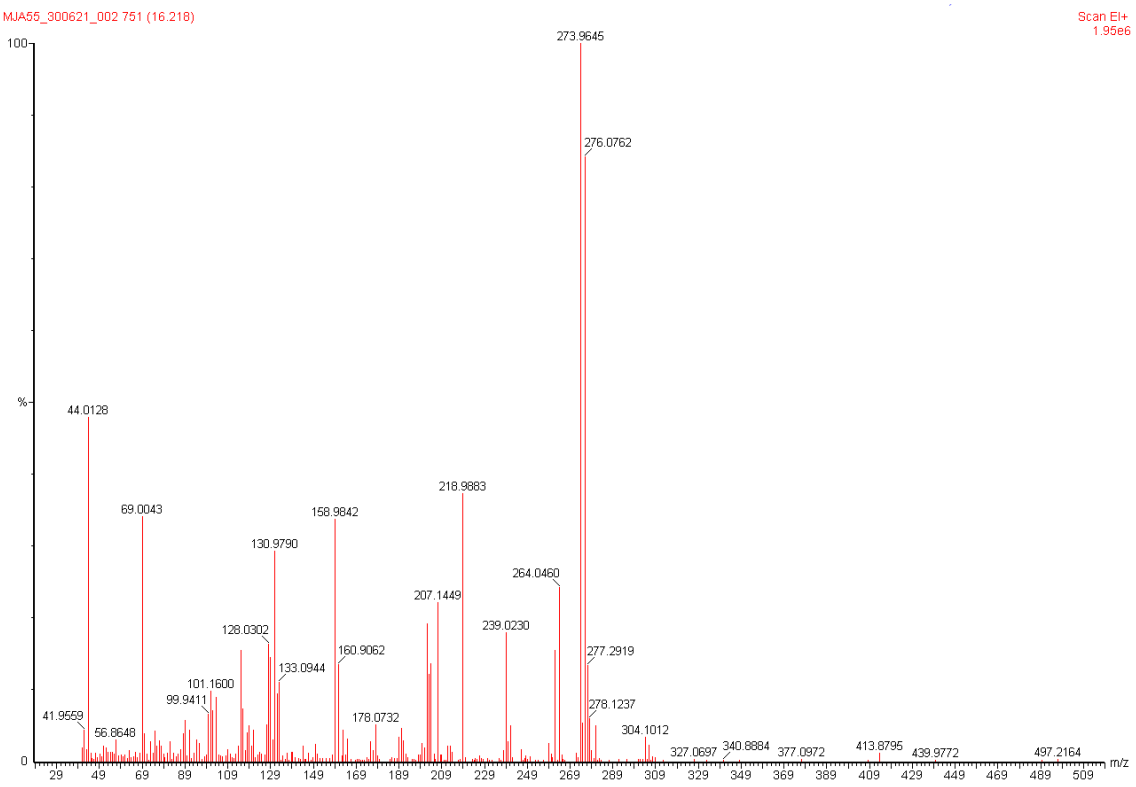


Figure 2.76: MS spectrum for MJA55

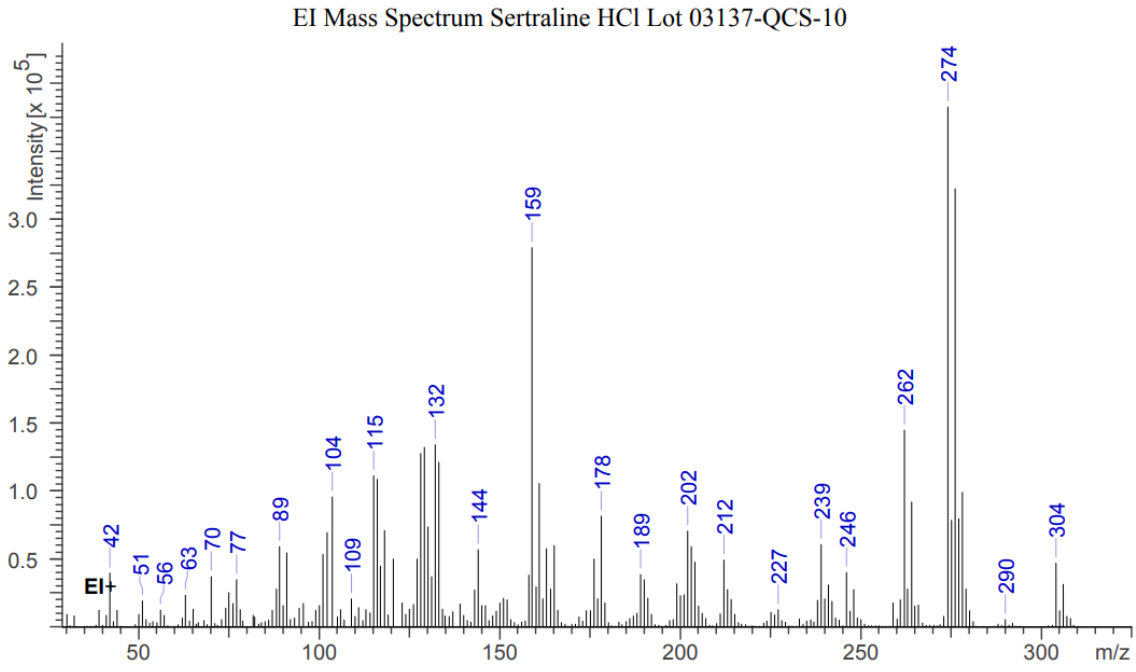


Figure 2.77: MS spectrum of sertraline taken from SWGDRUG (2014)

The sample was also analysed by LC-MS and compared to samples within the Agilent Forensic Toxicology library, resulting in a 90% match to sertraline. This information was relayed back to staff at the West Midlands Prison Group to notify that although this was not a complete confirmatory analysis, as the sample was only based on library results and not compared to a chemical standard, there was a potential that it could have been

sertraline. Liaison with staff at West Midlands Prison Group suggested the sample could have been prescribed medication that had been stockpiled to be sold or taken in greater quantities and they were satisfied with the intelligence gained (Sherwin, 2022).

In terms of the other miscellaneous samples submitted to the University, they were all analysed *via* FTIR to give an indication of the substance present but were not a priority for full confirmatory analysis *via* GC-MS, LC-MS and NMR as most were not considered likely to be synthetic cannabinoid containing samples. Furthermore, FTIR was favoured for these substances as the sample types were very varied and sample preparation for GC-MS, LC-MS and NMR could be cumbersome and difficult to determine compared to FTIR, where no sample preparation was necessary.

MJA50 was the only other sample that was submitted due to a suspected presence of synthetic cannabinoids after screening with an Itemiser 3E® within a prison, with indication of 5F-PB-22 and a peak between 8-10 ms. The lip plumper had been seized from a member of staff and analysed on site before being submitted to the University for confirmatory analysis. Due to the packaging not detailing the list of chemicals to inform sample preparation, it was decided that the best process would be to analyse the sample using FTIR. Upon comparison to the Thermo Scientific libraries, the top match was polyvinyl stearate, often used in the plastics industry (Gooch, 2011), with 86.67% match. The spectrum was also compared to a 5F-PB-22 spectrum, where there are similar peaks within the 3000-2840 cm^{-1} region which could be due to C-H stretching of the alkanes present (Merck, 2023), and some peaks within the fingerprint region (1466 and 721 cm^{-1}) as shown in Figure 2.78. The majority of the peaks did not have the same peak number, peak shape or intensity, therefore ruling out 5F-PB-22 as being present and determining the identification on the Itemiser 3E® to be a false positive. It was not possible at the time of analysis to obtain a control sample for comparison.

All samples that were not deemed to have a synthetic cannabinoid presence were submitted either upon intelligence of a drug being present or due to general suspicion surrounding the sample. Given the focus of the research, these samples were not seen as a priority and therefore any unidentified samples after FTIR analysis were not analysed further but information for each was still communicated back to staff at the West Midlands Prison Group to help towards their intelligence investigations. The results for these samples have been summarised in Table 2.16.

Table 2.16: FTIR analysis results for miscellaneous samples

Evidence number	Visual observation	FTIR analysis summary
MJA39	Colourless solution with light blue floating lumps. Blue/green lump at top of squeeze top bottle, so likely topped up with colourless liquid. Alcohol-like smell from both.	Liquid and gel tested separately. Liquid 66.84% and gel 61.43% match percentage to denatured ethyl alcohol on Thermo Fisher library. Both samples were compared to Purell hand sanitiser where liquid had 98.37% and gel 86.43% match percentage.
MJA48	Prison issued deodorant - Faintly blue liquid inside and fragranced like deodorant.	No sign of tampering with the roll-on deodorant. Sample rolled onto diamond window and allowed to evaporate for 5 minutes. Analysed alongside a Sure Cotton Dry antiperspirant roll-on for comparison resulting in 56% match, however major similarity seen with overlay of spectra as seen in Figure 2.79.
MJA49	Two Sure roll-on deodorants. Yellow oil freely dripped from roll on. The two were sampled separately and labelled according to product codes 03:03 and 03:34	Suspicion of tampering due to yellow liquid dripping from the roll-on deodorant. MJA49 03:03 had 88.88% match to castor oil and MJA49 03:34 had a 77.79% match to ethyl undecanoate, a flavouring agent (PubChem, 2022k). Focus turned to the sample potentially being a CBD and THC oil, however traces were not seen using the deconvolution software. Sample compared to a CBD oil standard with 80.83% match for MJA49 03:03 and 77.30% match for MJA49 03:34, however deconvolution software could not detect the CBD in the CBD oil standard, therefore CBD could have been present in the MJA49 samples but at too low concentrations for FTIR to detect.
MJA53	Purple/blue liquid in sample bottle from a prison cell kettle. Light lavender smell.	Evaporated quickly when placed on FTIR window. Top library match seen was seen to be ultra-thick bleach with a match score of 94.22%
MJA54	Two thank you cards glued together to allow for a void between the two fronts of the cards. One small envelope containing one white cigarette paper wrap. White cigarette paper wrap containing brown powder	Brown powder sampled on FTIR resulting in 55.50% match to heroin saved to the Georgia State Crime Laboratory library utilised by Thermo Scientific. Major similarities in fingerprint region compared to 4000-2000 cm^{-1} region, however not prioritised for further testing
MJA57	Drumstick bath crystals pot containing a 2nd class stamp and some crystals. Solution	Sample split into liquid and powder samples and analysed separately, however could not achieve more than 50% match score to any standard in

	tested pH 5, colourless with white powder settling through.	any of the libraries available, ruling out presence of amphetamine as seen in Itemiser 3E® results.
MJA59	Jeyes Odour neutraliser bottle with lid made out of gloves and tape.	No presence of heroin detected despite Itemiser 3E® result indication, with the top library hit on the liquid being trimethyl bromide at 78.17%, which was not included on the Jeyes material safety data sheet (Jeyes Professional, 2020)
MJA60	Supreme Imports branded Vitamin D3 pot including a slight orange tinted (very faint) gel consistency. Fruity sweet smell, similar to shampoo or soap.	Due to soap like consistency and smell, the sample was compared to some liquid hand soap available in the laboratory, resulting in a 66.12% match score.

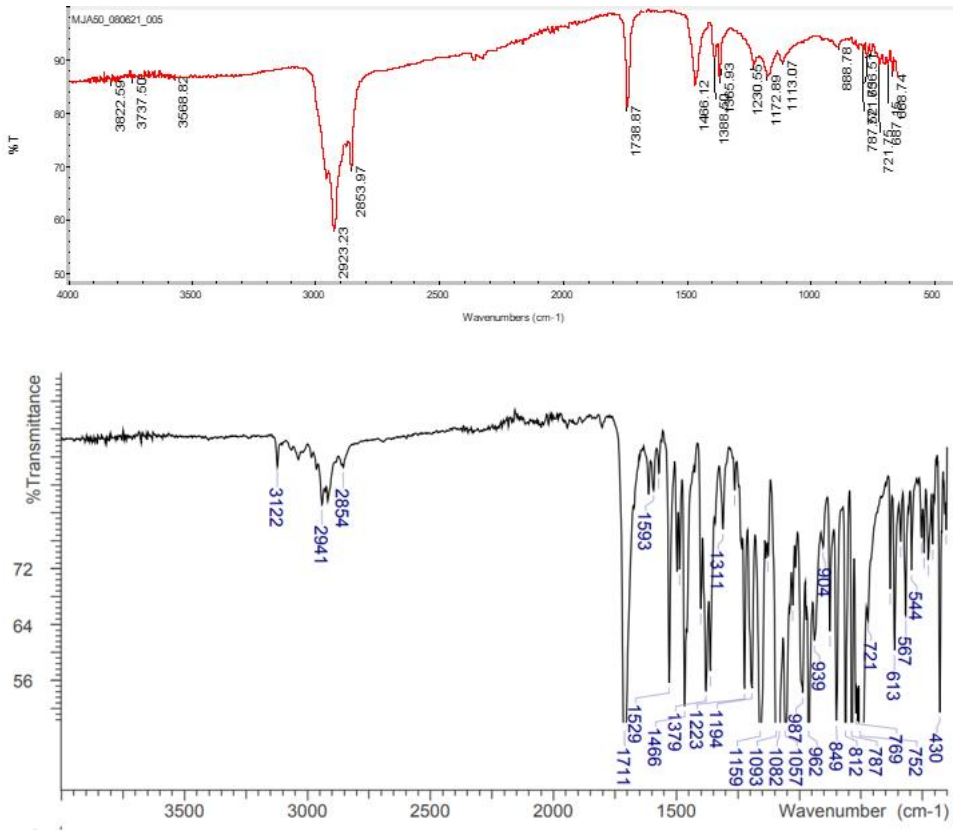


Figure 2.78: FTIR spectra comparison between MJA50 (red) and 5F-PB-22 (black) from SWGDRUG (2013b)

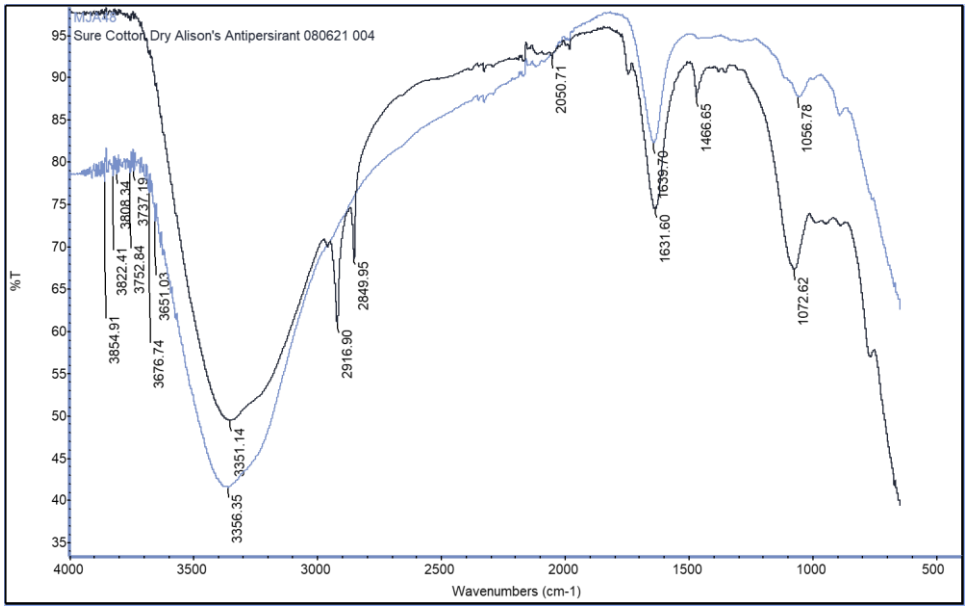


Figure 2.79: FTIR comparison between MJA48 (blue) and Sure Cotton Dry antiperspirant roll-on (black)

2.4 Summary

Ion-Trap Mobility Spectrometry (ITMS™) was used alongside analytical techniques to analyse and identify the presence of synthetic cannabinoids in prison samples. The results for the nine paper samples and the associated detected synthetic cannabinoids can be seen in the summary table below (Table 2.17).

Table 2.17: Summary table for the identification of synthetic cannabinoids from the associated paper samples

Sample	Detected synthetic cannabinoids
MJA3	MMB-022 and 5F-MDMB-PICA
MJA5 and MJA6	5F-MDMB-PICA
MJA7 and MJA8	4F-MDMB-BUTINACA
MJA14 and MJA17	5F-MDMB-PICA and MDMB-4en-PINACA
MJA38	MMB-FUBINACA
MJA40	MDMB-4en-PINACA

The confirmatory analysis utilised GC-MS, LC-MS, NMR and FTIR. GC-MS was the most useful technique overall as it sometimes acted as an effective screening technique as well as confirmatory when analysis had not been undertaken using an Itemiser 3E®. The MS also offered the opportunity to compare to libraries and reference spectra in the absence of certified reference standards, plus the fragmentation patterns could be used for structural elucidation. LC-MS was often used to confirm the relative molecular mass of a substance, especially when clarifying the identification of an unknown, and offered the opportunity to compare to extensive online reference spectra collections and libraries. NMR was an extremely helpful technique for structural elucidation and identification; however, it was often not needed throughout the research due to identifications being able to be produced using only the GC-MS and the LC-MS. The FTIR was used at the end to highlight similarities in functional groups but was not a primary identification technique. This technique was used primarily for the non-synthetic cannabinoid containing miscellaneous samples due to the quick analysis time and flexibility of sample state (liquid or solid), but was often not needed for the synthetic cannabinoids, and did not provide as much structural information as some of the other techniques.

The results for all samples, regardless of the outcome, were fed back to the prison directly or to the West Midlands Prison Group to notify them of what was present within each sample. Positive synthetic cannabinoid identifications were discussed with Rapiscan Systems Limited and made a significant contribution to updating the Itemiser 3E® libraries, whether it was for a new substance or checking the existing time-of-flight

definitions. This screening, confirmation and feedback cycle for eight of the nine positive paper samples has been able to inform the implementation or update of three synthetic cannabinoid library compounds on the Itemiser 3E® library and confirmed that seized samples can be provisionally identified using the Itemiser 3E®. Although only nine samples of the 47 paper samples were identified to contain synthetic cannabinoids, the samples represent approximately 25 A4 sheets of paper (or 15,593 individual 1cm^2 doses, if the whole pieces of paper were soaked) which could have entered prisons for prisoners to sell and smoke, ultimately resulting in adverse health effects and influence bullying and organised crime. Furthermore, with the seizure and identification of two paste samples, it halted the opportunity to produce even more synthetic cannabinoid-soaked paper within the prison.

The study undertaken by Norman *et al.,* (2021) showed 79.8% of paper samples analysed contained synthetic cannabinoids in Scotland and 27.4% in Wales, whereas this analysis found synthetic cannabinoids in 17.02% of paper samples. This could be due to method design, where samples were only sent to the University for analysis if there was potential need to verify the presence of a compound or to analyse an unknown within the synthetic cannabinoid window. Norman *et al.,* (2021) outlines how, although many of the samples had been screened by ITMS™ in Scotland, the samples were all sent for analysis, and in Wales, all the seizures were sent for analysis by the WEDINOS group, therefore influencing the percentage of positive substances seen their work. Another potential is that the screening may not be as controlled, with differences in screening applications, however, with the introduction of the Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework (Ministry of Justice, 2021) and the Use of Drug Trace Detection Equipment in Prisons guidance (Ministry of Justice, 2023a), it is hoped that screening will be more standardised.

This screening, confirmation and feedback cycle, undertaken to meet Objective 1, has been proven to work in this study and in larger scale studies such as those outlined by Norman *et al*., (2021) to reduce the amount of synthetic cannabinoids entering prisons, increase intelligence surrounding which synthetic cannabinoids are attempting to enter prisons and ultimately disrupting the knock on effect of organised crime groups sending these substances into prisons. However, there is currently no national system for this level of identification within England or information on the scale of demand it would have.

Further research should investigate what chemicals are causing the false positives that were raised. The focus of this research was to identify synthetic cannabinoid presence

and therefore if there was no detection, then further investigation was not a priority. However, there is scope for future analysis to aid the determination of what was causing the false positives to be able to inform Itemiser 3E® users and Rapiscan Systems Limited, plus increase confidence in use.

The method and results for the positive synthetic cannabinoid detections from this chapter were published in Forensic Science International in February 2023 and the article is included in Appendix 8 – Abbott, Dunnett, Wheeler and Davidson (2023). The production, publication and dissemination of this research has provided new knowledge to the drug analysis field.

Chapter 3 Analysis of Itemiser 3E® Detection Data from an operational instrument

3.1 Introduction

The use of trace detection equipment for the screening of drugs is not a new phenomenon in security and aviation settings. Prisons followed this model in the United Kingdom from 2016 when custodial institutions bought or loaned instruments to aid detection of synthetic cannabinoids (Chandler, 2022b). The implementation of such equipment in prisons for the identification of synthetic cannabinoids increased in popularity around 2017-2019 after the '10 Prison Project' was launched. The project was announced in August 2018 and aimed to reduce the amount of violence within ten particularly problematic prisons *via* increased security standards for drugs and disruptive behaviour (Ministry of Justice, 2018). The '10 Prison Project' was officially branded a success in 2019, with an average 50% reduction in drug use within the ten prisons (Ministry of Justice, 2019), and further inspired the prevalence of detection equipment to increase from 2018 onwards, resulting in 40 of the most challenging prisons having equipment such as drug trace detection instrumentation and metal detecting devices by 2022 (Ministry of Justice, 2022).

HMP Featherstone trialled an Itemiser 3E® from Rapiscan Systems Limited in January 2018 on a short-term contract in conjunction with undergraduate research conducted by the author, which led to the purchase of an instrument by the prison in July 2018. Furthermore, the West Midlands Prison Group purchased six instruments soon after to use throughout the region. The analysis of the Itemiser 3E® data described in this chapter provided an opportunity to investigate the impact of the analytical support outlined in Chapter 2 over an established timeframe, as well as the determination of which synthetic cannabinoids were being encountered in prisons and which were previously undetected prior to library updates.

3.2 Method

Data from the Itemiser 3E® situated at HMP Featherstone were extracted at the end of the research period to investigate trends and the effect of definition changes in disrupting synthetic cannabinoids entering prisons. The data, spanning 40 months from June 2018 – September 2021, consisted of three different file types. Calibration (CAL) files were recorded after each calibration trap use. This should have been conducted daily and after any routine maintenance work. Alarm (ALM) files were recorded from when the instrument would recognise a sample drift time which had sufficient similarity to the drift times listed for substances in the library above the designated threshold value to trigger an alarm, stating "Drugs Detected" on the Itemiser 3E® screen. Alarm

files are generated with all peaks included in the case of a mixture, which for the purpose of this chapter, will be referred to as sub-alarms. Sub-alarms account for each time-of-flight detected, with at least one surpassing the library defined thresholds to generate an alarm file, however not all of the sub-alarms will have triggered an alarm if their time-of-flights have not met the conditions of the library definition. These data are still retained and have been utilised in the analysis. Signal (SIG) files were also recorded, where the time-of-flights are recorded, but either the time-of-flight did not have sufficient similarity to a library substance, or the time-of-flight did not reach the threshold value. Similarly, one signal file can hold the data for multiple peaks, or sub-signals, however none of the time-of-flights for each sub-signal have met the conditions of the library definition to trigger alarm. The signal files were only available on this instrument from June 2018 to July 2019 as the setting on the instrument to ensure the data were saved had been disengaged from July 2019 onwards.

All data were extracted using the desktop Itemiser 8.34 software, and, with the use of the drift time ranges supplied by Rapiscan Systems Limited (shown in Table 3.1), the data were processed with Microsoft Excel 365 to identify, for each of the drugs in question, any sample which had been screened but had not alarmed and, following changes in definition, any sample where these drugs did then produce an alarm. The former was only able to be investigated for June 2018 to July 2019 due to the lack of signal files after this time, however the alarm information was still available to be processed. Comparison was also undertaken to traditional drugs which were grouped by drug type, for example “opiates and substitutes”, although some substances were added to a broader group, such as LSD, which was added to “stimulants and others”. A full list of the drug groups is included in Appendix 9 – Traditional drug groups Itemiser 3E® alarm list.

It should be noted that there are no records of the size of the samples tested (e.g., paper size), therefore no measure of the dosage accumulation can be made. There was also no record of whether multiple tests were undertaken on one sample, although this was not common practice. Furthermore, there is an example of multiple tests being taken on multiple pages within one sample, e.g., five pages tested from a total of 19 (MJA40), and this may have happened on other occasions, although again, not common practice.

Table 3.1: Minimum and maximum time-of-flight times on the Itemiser 3E® for various synthetic cannabinoids

Synthetic cannabinoid	Time-of-flight (ms)	Time-of-flight (ms) Minimum	Time-of-flight (ms) Maximum
5F-ADB	9.255	9.215	9.275
MMB-FUBINACA	9.290	9.270	9.330
MDMB-CHMICA	9.815	9.755	9.875
5F-MDMB-PICA	9.400	9.370	9.485
4F-MDMB-BUTINACA/ MDMB-4en-PINACA	9.120	9.060	9.160
ADB-4en-PINACA	8.789	8.729	8.849
ADB-BUTINACA	8.599	8.539	8.659

3.3 Results and Discussion

The extracted dataset had 72,040 rows, with Figure 3.1 showing the first 37 rows of the .csv spreadsheet to show how the data were structured. The extracted raw data included 1015 calibration files, 3444 alarm files and 11665 signal files for the 40 months. Figure 3.1 also highlights how one alarm file, for example ALM00887 (row 228) could have multiple sub-alarms (rows 229-234). These were later labelled with a numbered suffix, such as ALM00887-1, ALM00887-2, to ensure each row was accounted for during processing, and the recorded time-of-flight data were associated with the correct sub-alarm. The columns used primarily for the data extraction (and highlighted in yellow in Figure 3.1) focused on “Pos at Max Slope”, which was the recorded time-of-flight, and the “Substance”, which was the drug in the library that the unknown substance in the test sample had alarmed for, per sub-alarm. Figure 3.1 shows examples of alarm and calibration files, and how there were incidents where the “Substance” column would have “none”, when the time-of-flight has not been sufficiently similar to any drug listed in the library, or an instrument related code, such as “Pos-VER” or “Pos-CAL”.

The data extracted from the HMP Featherstone Itemiser 3E® enabled a retrospective investigation of the trends seen for each of the drugs and an assessment of the effect of the implementation of the time-of-flight definitions. In terms of the insights the file types can provide, the graph shown in Figure 3.2 shows the alarm files, signal files and calibration file counts per month over the 40-month period alongside the total amount of sub-alarms, and Figure 3.3 reflects these data without the signal files.

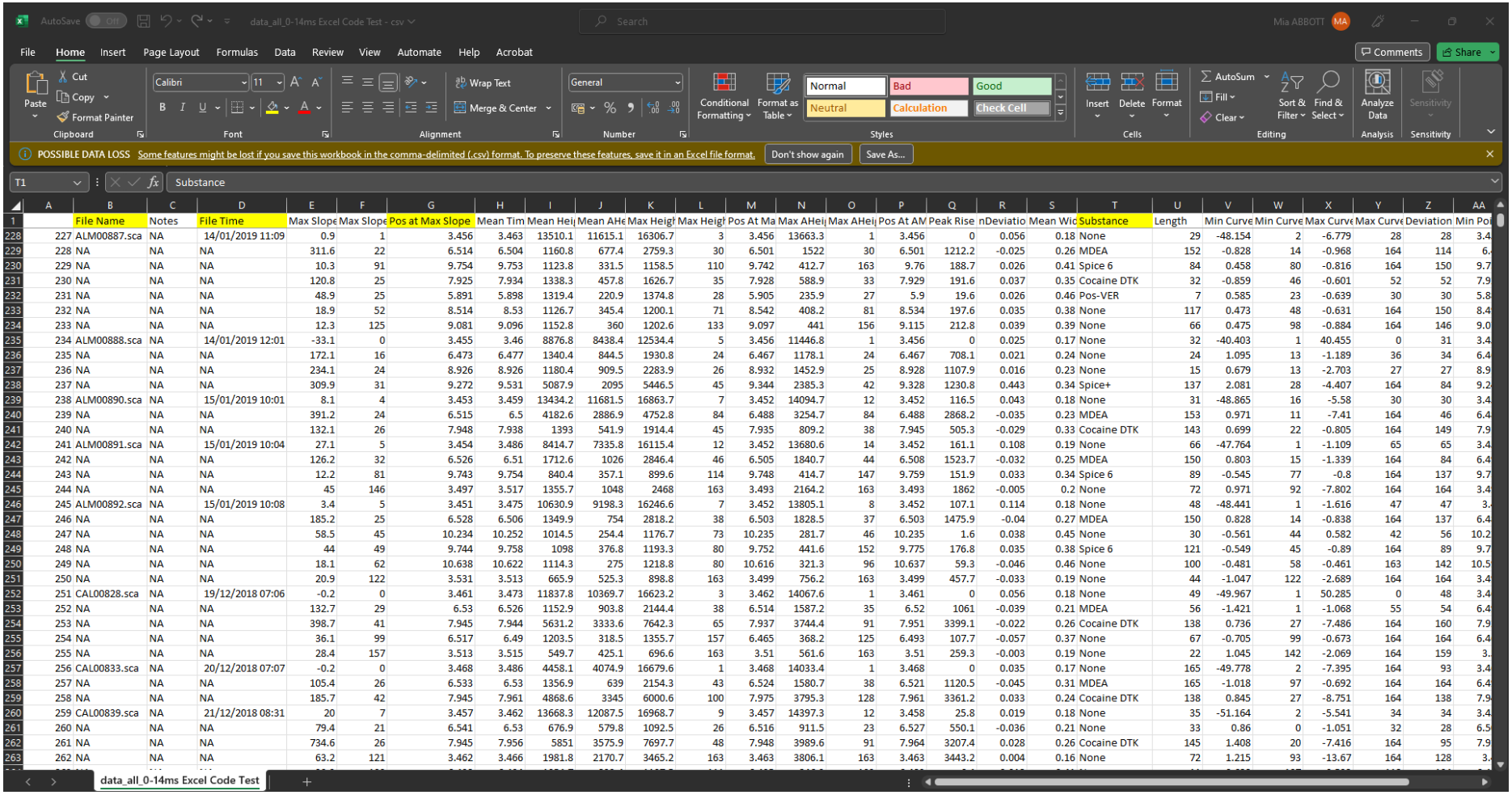


Figure 3.1: Example screenshot of raw extracted dataset including ALM and CAL files, with the important columns for the data analysis highlighted in yellow

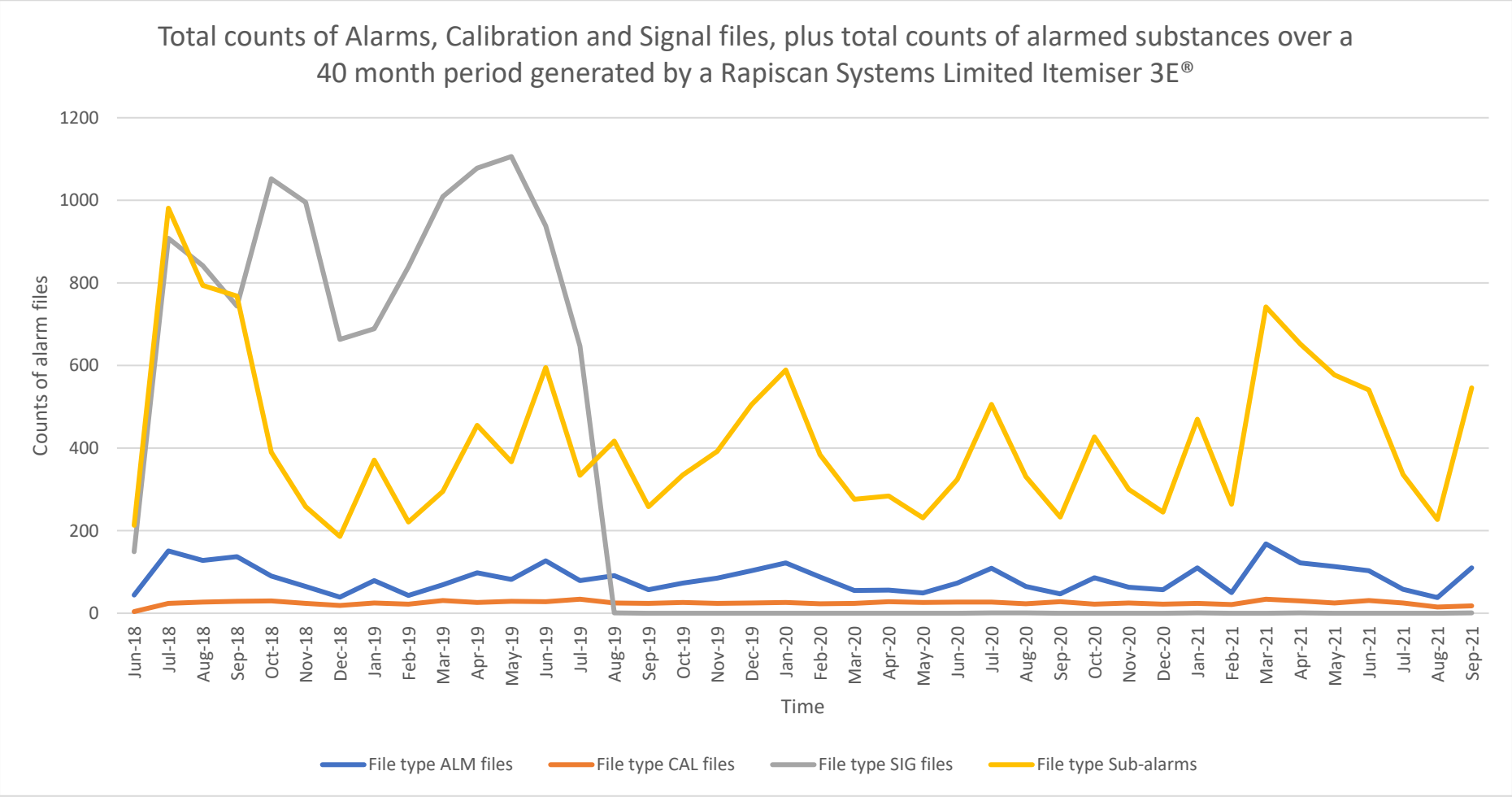


Figure 3.2: Counts for alarm, calibration and signal file types over 40-month period from Itemiser 3E®

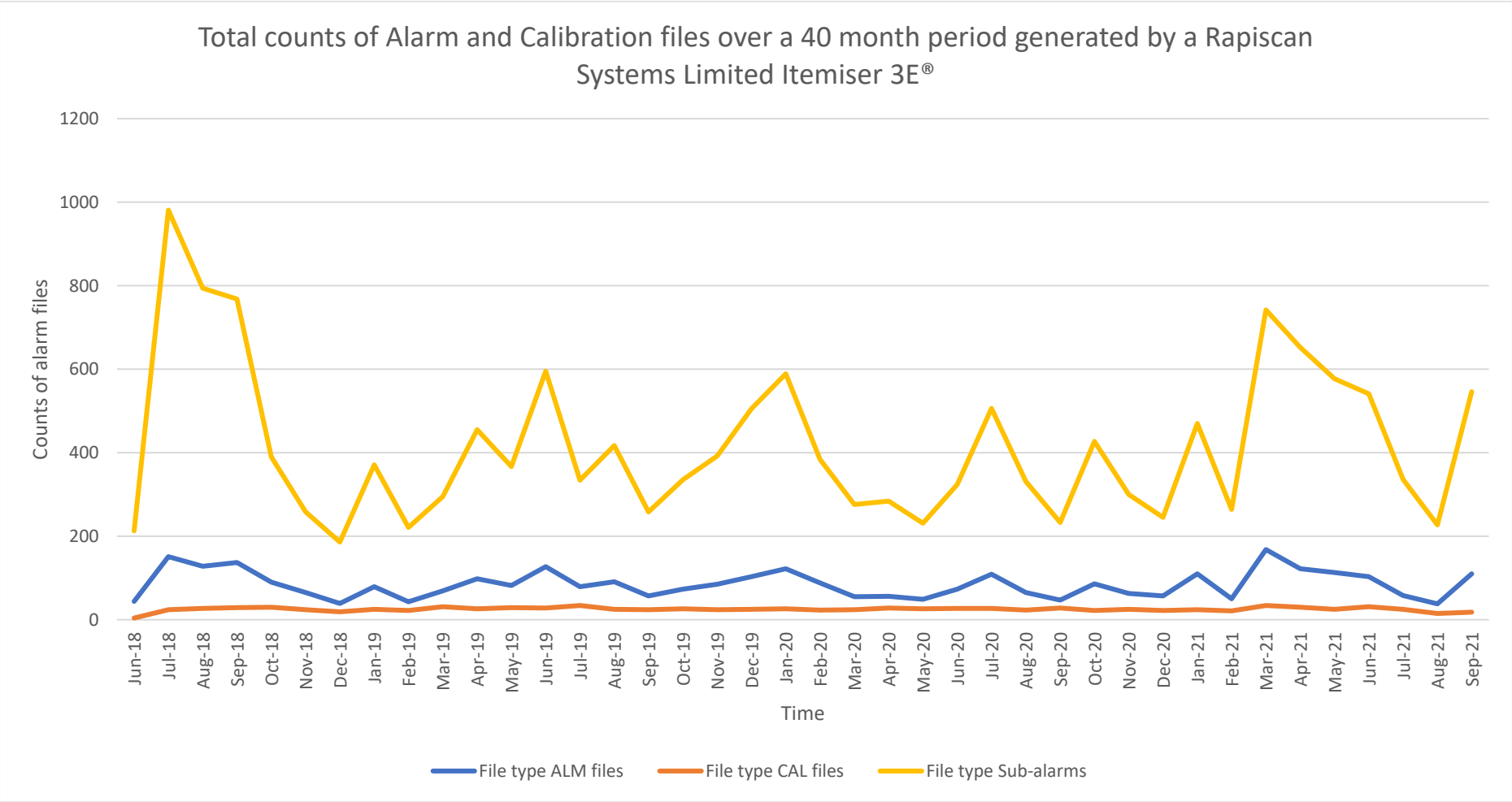


Figure 3.3: Counts for alarm and calibration file types over 40-month period from Itemiser 3E®

On average, calibration was conducted approximately 25 times a month, which can give a rough estimation of the amount of days the Itemiser 3E® was being used within the month, as it should be conducted daily. There would have been incidents when the instrument was calibrated more than once in a day, such as if the instrument had been overloaded from being exposed to a bulk sample or if it had any routine maintenance conducted, such as a membrane change. The variation in the number of calibrations was five times per month, so it was not consistent every month, however it must be noted the instrument was only running for four days in the first month as the instrument was installed late in the month, plus, although it was hoped that all received post would be analysed with the Itemiser 3E®, in busy or understaffed periods, the screening was not a priority.

Figure 3.2 shows the signal files were only available between June 2018 and July 2019, restricting the deeper analysis of the data to this period, however the alarm data was available throughout the research period. The fluctuation seen per month in alarm file data may have been influenced by the amount of post being analysed or the number of drugs being present. Ideally the ratio of signal files to alarm files would have provided a realistic measure of whether the amount of drugs entering the prison was showing any trend over time, accounting for the amount of post being screened, however this is only present for the first year. As multiple alarms for different drugs could occur per alarm file, the lines in yellow in Figure 3.2 and Figure 3.3 are included to show the amount of sub-alarms, and highlight the number of mixtures that would have been present for each alarm file. The general trends in the counts for the alarm files and sub-alarms are very similar, just at a greater number for the sub-alarms due to the large amount of mixtures.

There are potential external factors which may have impacted the results, such as seasonal events, with the dip in screening reflected in both the alarms and signals shown in Figure 3.2 and Figure 3.3 surrounding Christmas in December 2018, and a dip in the alarms for February 2018 around Valentine’s Day, where there may have been too much of an influx in post and therefore analysis would not have been as much of a priority due to staffing capabilities, however this does not seem to be the case for the other Christmas or Valentine’s Day periods throughout the rest of the study. Furthermore, although the prisons were under strict rules regarding social distancing during the COVID-19 lockdown periods, testing continued, and alarms were still being seen. With prison visits suspended between March – July 2020, January – March 2021 and localised suspensions to reflect the tier system between November 2020 – January 2021, plus the reduced contact and social distancing measures (Ministry of

Justice, 2023b), the opportunity to exchange contraband items would have been minimal, therefore there would have been a need to adapt to other smuggling routes. The suspension of visitors, along with the reduced transport in and out of the prison, was noted by the EMCDDA (2021a) to be key factors in the reduced drug availability in many European countries, and therefore more efforts to throw substances over the walls were reported. Prison post would have been another option to take advantage of, however there was a noticeable dip, shown by Figure 3.3 from January - March 2020 in alarms which continued until the June, suggesting there were fewer drugs being seen at that time or potentially less post overall due to the disruptions to the postal service during the pandemic.

The sub-alarms were further investigated to determine trends over the 40-month period. Firstly, the sub-alarms which had a “substance” associated were investigated. Figure 3.4 shows these data over the 40-month period for each of the synthetic cannabinoids and includes key dates for the library updates discussed in Chapter 2. The application of library additions and updates for 5F-MDMB-PICA and 4F-MDMB-BUTINACA/MDMB-4en-PINACA highlight the popularity of the drugs, as from the point at which each definition was added, alarms for that substance occurred in almost every month, resulting in 258 alarms for 5F-MDMB-PICA and 647 alarms for 4F-MDMB-BUTINACA/MDMB-4en-PINACA over the 40-month period. The abundance of 4F-MDMB-BUTINACA/MDMB-4en-PINACA alarms in Figure 3.4 demonstrates that one or both of these drugs were very prevalent. Alarms for 5F-MDMB-PICA were the second most common after the January 2019 library update, showing that for all three drugs, there was continued attempts to send them into the prison after their definitions had been added to the instrument. Information regarding prevalence internationally has been discussed in Chapter 2 for all three of these drugs.

Figure 3.3 also highlights the continued popularity of MDMB-CHMICA throughout the analysis period, with a greater abundance in 2018-2019 than from 2020 onwards. MDMB-CHMICA was first reported to the EMCDDA early warning system in September 2014 and risk assessed in 2016 (EMCDDA, 2017). When compared to the data represented by Norman *et al.,* (2021), this substance was not identified in screened post from Scottish prisons or in urine samples from prisoners in Germany between the third quarter of 2018 and the third quarter of 2020, however it was seen in 0-10% of detections in the third quarter of 2019 from seized samples from Welsh prisons. The prevalence in the HMP Featherstone dataset suggests that MDMB-CHMICA could have been a more popular substance in the West Midlands region compared to other

areas, although no samples which had alarmed for MDMB-CHMICA were submitted for confirmatory testing.

5F-ADB and MMB-FUBINACA each had a definition on the Itemiser 3E®, but to capture any crossover between the two, due to their similarity in drift times (as shown in Table 3.1), there was an extra combined definition for the two named Spice + developed by Rapiscan Systems Limited that was installed on instruments. As shown in Figure 3.4, the abundance of the combined definition (pink) is much greater than the abundance seen for each definition. Using Excel 365, each alarm for Spice + was investigated to determine if 5F-ADB and MMB-FUBINACA could be differentiated from each other using the drift time definitions and variation allowance (± 0.040 ms) for each. When the drift times for each synthetic cannabinoid were applied, these were labelled as the “identities”, compared to the Itemiser 3E® library defined “substance”. This process was applied to the Spice + data to produce the graph in Figure 3.5. Only 4% of the Spice + alarms could not be differentiated to determine exactly which of the two synthetic cannabinoids they were, with 42% attributed to 5F-ADB and 54% attributed to MMB-FUBINACA. Figure 3.5, in combination with Figure 3.4, highlights the prevalence of both substances over the time period. In comparison, Norman *et al.,* (2021) describes how 5F-ADB was seen in both urine samples from prisoners in Germany and seized samples from prisons in Scotland from 2018 to 2020 (the start and end of the study), whereas prevalence in seized samples from prisons in Wales dropped from the end of 2019. In terms of MMB-FUBINACA, this was not identified in urine from prisoners in Germany from 2018-2020, but it was seen in seized samples from prisons in Scotland and Wales during 2019 (Norman *et al.,* 2021). Figure 3.4 and Figure 3.5, demonstrate that for both drugs, there seemed to be more prevalence into 2021 compared to the other timeframes, but due to the existence of the definitions in the library, these synthetic cannabinoids would not have entered the prison *via* the mail screened by prison staff (however, mail containing the drug that was not screened would have entered the prisons).

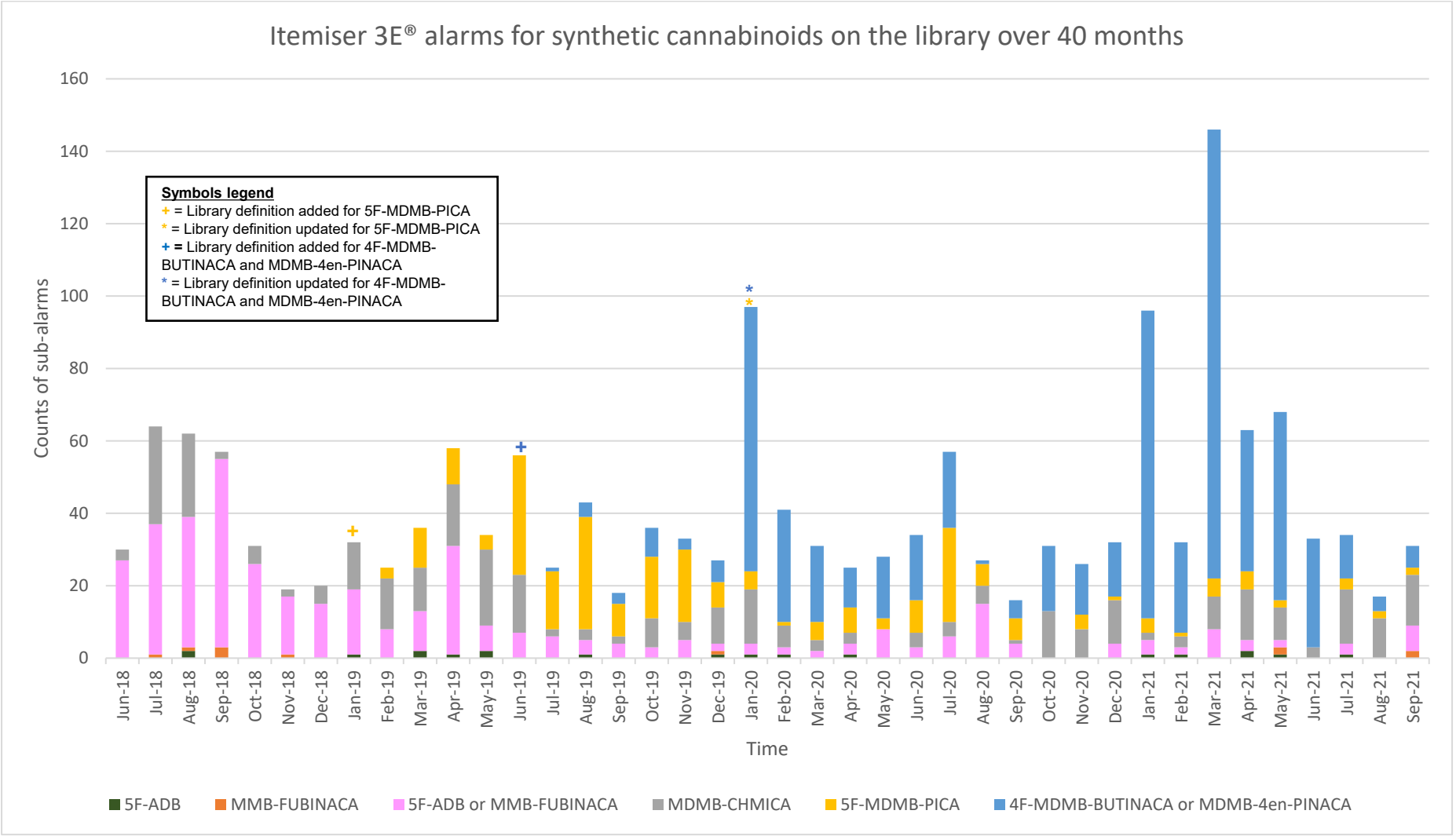


Figure 3.4: Stacked bar chart for synthetic cannabinoid sub-alarms from Itemiser 3E® over 40-month period

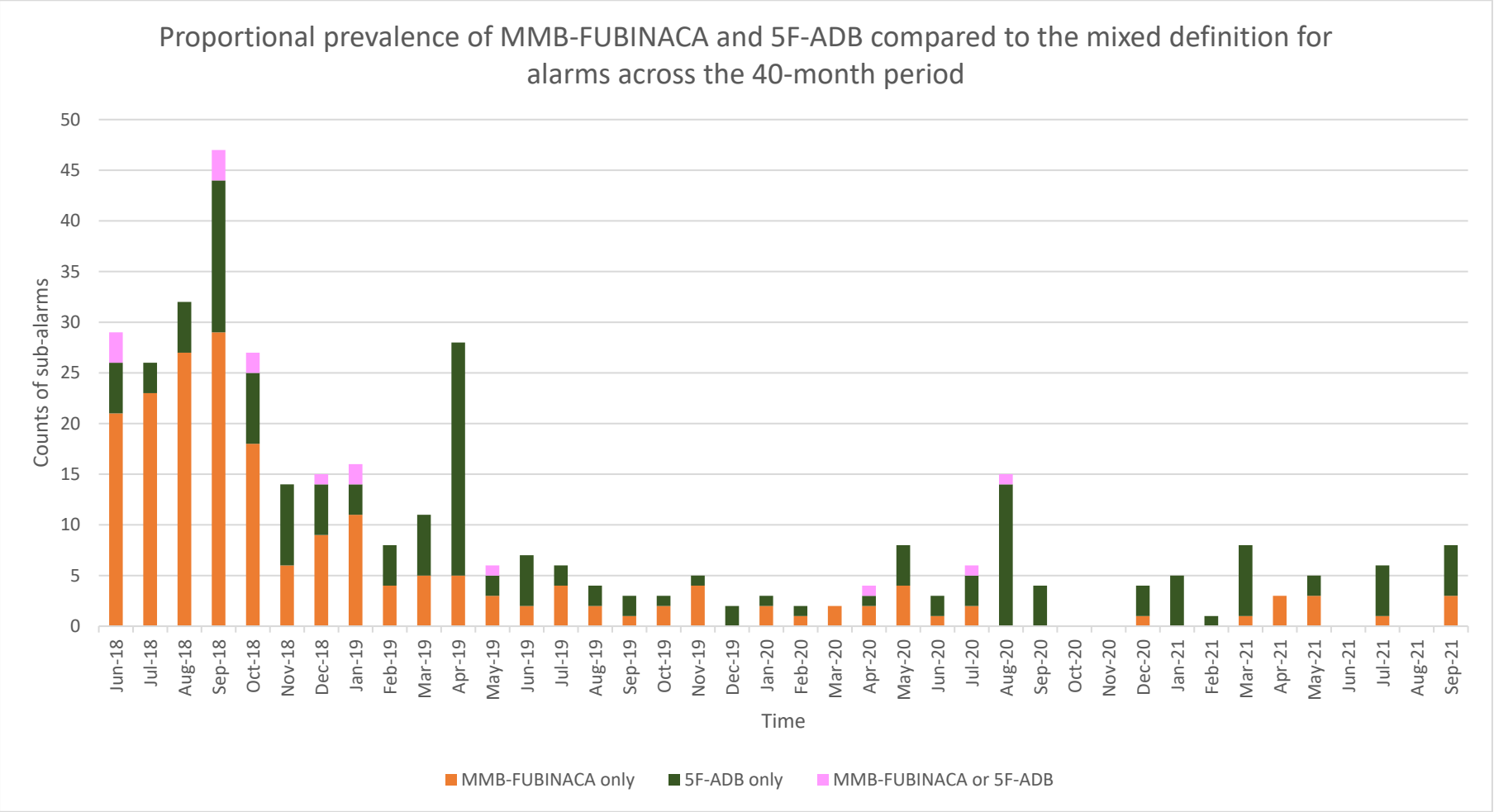


Figure 3.5: Stacked bar chart to aid differentiation between MMB-FUBINACA and 5F-ADB alarms from Itemiser 3E® over 40-month period

The investigation of the sub-alarms for each of the synthetic cannabinoids did pose the question of how long were the drugs potentially entering the prison prior to the addition of the library definitions, as although the analysis of synthetic cannabinoid soaked paper from the prisons was conducted throughout the 2018 – 2021 period, the samples that were submitted for analysis (discussed in Chapter 2) were likely not the first of their kind, and therefore 5F-MDMB-PICA, 4F-MDMB-BUTINACA and MDMB-4en-PINACA could have been entering the prison prior to confirmatory analysis.

Focus was firstly on identifying the prevalence of each synthetic cannabinoid within the sub-alarms by applying the drift time data provided by Rapiscan Systems Limited in the same manner as outlined above for the differentiation of the Spice + alarms. An "identity" column was produced using the time-of-flight information included in Table 3.1 for each synthetic cannabinoid, including those synthetic cannabinoids that would not have had a definition at the time of analysis. This allowed a retrospective insight into the possible detection of synthetic cannabinoids prior to their definitions being added onto the instrument. For some definitions, it should be noted that they may have been slightly different to those expected from library results at the time of analysis which could have been a product of extracting the data through the desktop Itemiser 8.34 software: the version used to extract the data in 2022 would have been the most up-to-date version of the library at the time, whereas the instrument itself at the time of each analysis would not have been updated until the next relevant opportunity. Therefore, it cannot be guaranteed that the results shown there will directly reflect what the instrument would have recorded at the time.

Figure 3.7 shows the prevalence of each synthetic cannabinoid over the 40-month period after the application of drift times to the alarm data, and Figure 3.7 represents these data as a percentage of the sub-alarms each month. In a similar manner, Figure 3.8 shows the sum of the synthetic cannabinoid sub-alarms for each month in comparison to groups of traditional drugs, and Figure 3.9 represents these data as a percentage of the total sub-alarm each month. It should be noted that as alarm files which contain multiple sub-alarms may alarm for multiple substances, the total number of alarms per month exceeds 100% for Figure 3.9.

Comparison between Figure 3.6 and Figure 3.7 highlights the contribution of synthetic cannabinoids to the monthly alarms. Data from June 2018 did not represent a full month due to the implementation of the instrument occurring at the end of the month, and therefore the counts shown in Figure 3.6 account for a high percentage of the alarms for the month of June in Figure 3.7. December 2018, February 2019, May 2020,

June 2020 and September 2020 all feature low counts for the month (as shown in Figure 3.6), but account for a larger percentage of the total number of alarms (as shown in Figure 3.7) compared with other low count months such as September 2019 and November 2020. On the other hand, although March 2021 had the second greatest total number of alarms for synthetic cannabinoids (Figure 3.6), these only accounted for 11.92% of the total number alarms in that month (as shown in Figure 3.7).

In terms of the traditional drugs to synthetic cannabinoid comparison, Figure 3.8 and Figure 3.9 show that almost all drug groups alarmed in every month across the 40 month period, with the only exception being “opiates and substitutes” in December 2018 and December 2020. The prevalence of “opiates and substitutes” does vary greatly over the 40 months, and the group accounted for the least number of alarms overall. The “stimulants and others” drug group accounted for the greatest total number of alarms across the timeframe, with Figure 3.8 highlighting the prevalence compared to other groups, although, 1620 of the total 1782 “stimulants and others” alarms originate from cocaine DTK alarms (other totals can be seen in Appendix 9 – Traditional drug groups Itemiser 3E® alarm list). The DTK definitions are present on the library for multiple traditional drugs to allow for the drift time to change when using the water-based kits for bulk sample preparation. This process involves diluting a sample by mixing a small amount of powder into a dropper bottle of water to produce a trace sample for analysis and reduce overloading the instrument. The presence of DTK alarms is surprising given that HMP Featherstone did not use the kits, and therefore it is a topic of further investigation. There is a chance that accidental cross contamination occurred from the cocaine-laced calibration traps, however it is expected that this would have been seen as cocaine alarms on the instrument and not as cocaine DTK alarms. The discrepancy may also have been caused when extracting the data using the Itemiser 8.34 software: there is a crossover between the cocaine and cocaine DTK library definitions, so those seen for cocaine DTK may have all been for cocaine. Another explanation could be contamination or surface-level presence of cocaine on the samples, because as discussed in Chapter 2, there were indications of cocaine on some of the samples analysed by the Itemiser 3E® but not detected during confirmatory analysis, therefore they were expected to be surface-level compared to impregnated into the paper. It should be noted that Itemiser 3E® operators at Scottish prisons deselect the DTK alarms from their libraries as they do not use the kits (Norman, 2023).

Synthetic cannabinoids were the second most prevalent substance across the 40-month period, with alarms present every month. The median number of alarms per

month for the synthetic cannabinoid data included in Figure 3.8 was 32.5 with a range of 14 – 94 alarms, showing there was a large variation per month. This variation could be due to detection capabilities, for example before and after library updates (as shown in Figure 3.6 and Figure 3.7), and drug trends. “Amphetamines and cathinones” were the third most prevalent drug group that alarmed as shown in Figure 3.8, but the least as shown in Figure 3.9, with the majority identified as MDEA (see Appendix 9 – Traditional drug groups Itemiser 3E® alarm list for total alarms per compound). MDEA was indicated as being present due to an alarm on the Itemiser 3E® on MJA44, a sample discussed in Chapter 2, however the drug was confirmed not to be present upon confirmatory analysis. MDEA can be present in ecstasy tablets (EMCDDA, 2021b) and is known to have been used by prisoners within custody, however the occurrence is much less than opiates and cannabis (Norman, 2022), inferring that the 707 alarms may have been due to false positives.

For the sub-alarm data, the use of the “identities” versus “substance” data resulted in some synthetic cannabinoids being shown to be present before there was a definition to cause an alarm. An example for this is ADB-BUTINACA, which did not have a definition assigned until April 2022 on the HMP Featherstone instrument, based on information and detection definitions provided to Rapiscan Systems Limited by the Leverhulme Research Centre for Forensic Science at the University of Dundee, but there is information to indicate that this compound might have been present in test samples from June 2018, as shown in Figure 3.6. In this instance, the sub-alarms recorded when the “identity” was ADB-BUTINACA all had “none” as the corresponding listed “substance” because there was no definition for ADB-BUTINACA at the time, meaning that the actual alarm file was produced for another sub-alarm meeting the parameters of another substance in the library. ADB-BUTINACA was recorded for the first time in the UK between April 2019 and March 2020 through Border Force seizure identifications (Advisory Council for the Misuse of Drugs, 2020), in Sweden in the form of a powder during a seizure in July 2019 (Kronstrand *et al.,* 2021), and it was identified for the first time in Scottish prison post in January 2021 (Kronstrand *et al.,* 2021). Although it is plausible for ADB-BUTINACA to have been present in HMP Featherstone from June 2018, this would have been before any recorded detections elsewhere in Europe.

For months such as July and August 2018, seen in Figure 3.7, the potential alarms for ADB-BUTINACA account for 3.98% and 2.77% respectively, indicating popularity early in the data collection period if it was ADB-BUTINACA present, however there is potential that it may have been due to a false positive. The analysis of paper samples

from prisons, as outlined in Chapter 2, was undertaken from September 2018, and at the time, focused on samples which had an indication of a synthetic cannabinoid from a peak present on the plasmogram between 9 – 10 ms. The time-of-flight definition for ADB-BUTINACA was 8.599 ms, which may have been missed by prison staff at HMP Featherstone as it was outside of the typical synthetic cannabinoid window they were trained to focus on.

If a version of this process was able to be implemented on a regular basis, there would be more scope to identify new synthetic cannabinoids trying to enter prisons that do not have a library definition. This could be in the form of highlighting reoccurring drift times at any time-of-flight or applied after library updates to determine the scale of the issue regarding popularity. If the information gathered regarding ADB-BUTINACA was highlighted between 2018-2021, this would have been able to indicate the prevalence in prisons and aid in developing an accurate definition sooner to implement a library update, however 143 “none” alarms were produced for the corresponding definition and therefore potentially 143 samples containing ADB-BUTINACA may have entered the prison in this timeframe.

ADB-4en-PINACA was not included as a synthetic cannabinoid definition as part of Figure 3.6 and Figure 3.7 as although there was indication of prevalence within the timeframe, the drift time definition was indistinguishable from those already established for gabapentin and heroin (similarity in drift times seen in Table 3.1). As the definition for ADB-4en-PINACA was only added in April 2022, there were no alarms for this drug during the data timeframe, however, data analysis was conducted to attempt to differentiate between which sub-alarms may have been gabapentin only, heroin only, heroin or ADB-4en-PINACA, gabapentin or ADB-4en-PINACA, and finally which may have been any of the three. The data included in Figure 3.8 and Figure 3.9 utilised the alarm data without any analysis, and therefore may have featured some alarms due to the presence of ADB-4en-PINACA in both the “opiates and substitutes” category and the “benzodiazepines and similar” category compared to Figure 3.10 which attempts to differentiate the alarms between the drugs by accounting for the drift time definitions.

All three drugs can be seen within prison drugs markets, although with varied levels of popularity shown in Figure 3.8, with synthetic cannabinoids being the second most popular across the 40 months, followed by “benzodiazepines and similar” and then “opiates and substitutes”. This popularity is reflected by Figure 3.10, with the “ADB-4en-PINACA or heroin” portion of alarms being the largest overall and the largest contribution for 11 of the 40 months. The popularity is also present across the period,

with alarms of this type featured in 31 months of the study. ADB-4en-PINACA was documented in a National Medical Services Laboratories (NMS Labs) and Center for Forensic Science Research and Excellence monograph as being present in a seized herbal sample in the United States in January 2021, with the report published in March 2021 (Krotulski *et al.,* 2021). Furthermore, Kronstrand *et al.,* (2021) outlined how a paper sample from a Scottish prison was found to be soaked in ADB-4en-PINACA in December 2020. The potential presence of ADB-4en-PINACA is reflected from February 2021 onwards when comparing to the American and Scottish appearances, but also as potentially far back as June 2018 at the start of the data collection. The data seen in those categories though could be a result of heroin or gabapentin.

Heroin is known to be used by people who use drugs before they enter prison and within prisons, therefore continued priority by users and organised crime groups is to ensure heroin is entering establishments (Norman, 2022; Wakeling and Lynch, 2020). Although the method for soaking drugs into paper for concealment purpose predominantly used for synthetic cannabinoids (Norman, 2022), it is also possible to soak opiates into paper (Garratt, 2019; Giorgetti, *et al.,* 2022), and therefore could have been present on some of the post. In terms of the analysis undertaken in Chapter 2, heroin was only encountered as a powder in MJA54, and the only paper sample with an indication of heroin from the Itemiser 3E® was MJA32, which after investigation *via* confirmatory analysis, did not result in a heroin identification. Heroin may have been present, such as with MJA54, on multiple occasions from people trying to conceal the powder within cards and tested on the Itemiser 3E® to result in the alarms present. With the “heroin only” alarms shown in Figure 3.10 resulting in the third most abundant total alarms shown within the graph, there is a chance that many of the alarms seen by the “ADB-4en-PINACA or heroin” definition were in fact heroin.

Gabapentin, a prescription anti-convulsant and pain management medicine, is also popular within prison settings, as although there have been warnings not to prescribe gabapentin and pregabalin as the first course of treatment (Public Health England, 2013), there has been an over prescription of gabapentin within prisons which has emphasised issues surrounding dependence and potential for misuse (Iverson, 2016; Public Health England, 2014). Gabapentinoids were reclassified in 2019 to Schedule II medications and Class C drugs due to their potential for abuse and have been seen in prescribed and illicit forms by the National Programme on Substance Abuse Deaths between 2004 – 2020 alongside opiates (Kalk *et al.,* 2022). Therefore, the suggested presence of gabapentin in the Itemiser 3E® data could be valid as it is abused in a prison setting and could therefore influence the amount that is smuggled into the

prison, however, to date, there is no literature to suggest gabapentin is actively being impregnated into letters for use. Similar to the heroin data, there could be incidents where powders, tablets or surfaces have been swabbed and analysed using the Itemiser 3E® in the post-room, however this was not routine. The “gabapentin only” data accounts for the lowest total overall in Figure 3.10, suggesting the ADB-4en-PINACA within the mixed definitions may have been the cause of the alarms, which may have increased the popularity of the “benzodiazepine and similar” category in Figure 3.8, overall ranking fourth most prevalent substance compared to “opiates and substitutes”, which was fifth. For Figure 3.9, the percentage contribution of “benzodiazepine and similar” was the third most prevalent, followed by “opiates and substitutes”, which was fourth. The “ADB-4en-PINACA or gabapentin” group was very prevalent in Figure 3.10 at the beginning of the sampling period and consistently seen across 36 of the 40 months, however this could have been drift time differences of the gabapentin resulting in more falling within the same range as ADB-4en-PINACA compared to the drift time window where only gabapentin could reside. Furthermore, ADB-4en-PINACA prevalence in 2018 would be years prior to documentation by Krotulski *et al.,* (2021) and Kronstrand *et al.,* (2021). Similar to ADB-BUTINACA, the drift time for ADB-4en-PINACA falls within the 8 – 9 ms window and therefore staff at HMP Featherstone may not have acknowledged these peaks if they were present on the plasmograms as this was outside of the 9 – 10 ms synthetic cannabinoid window. ADB-4en-PINACA was not present on any paper samples analysed as part of the work outlined in Chapter 2, and it is unlikely that any samples from 2018 would be retained at the prison to analyse to confirm the presence of the drug from that time, however the data does suggest potential presence.

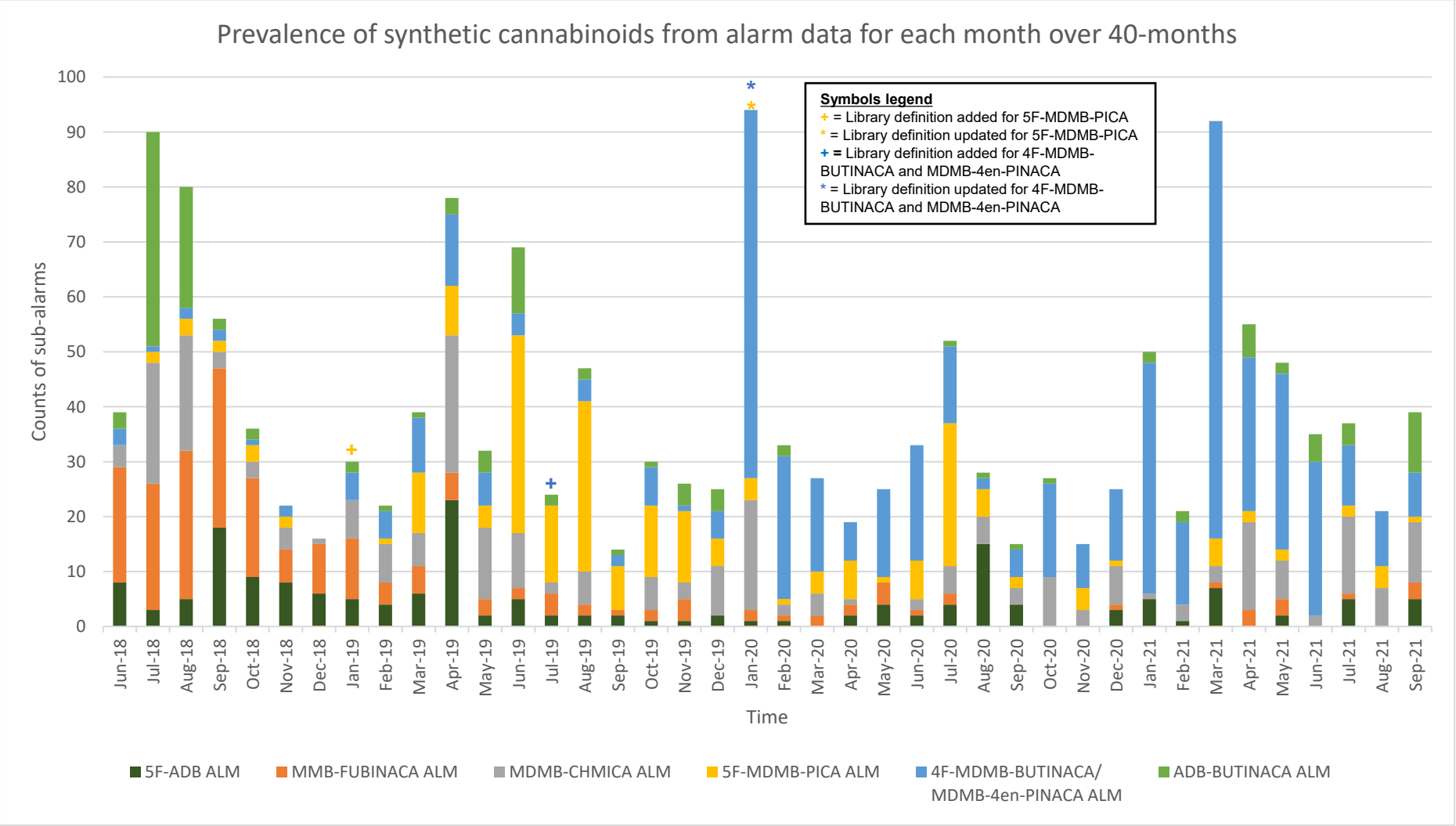


Figure 3.6: Stacked bar chart depicting Itemiser 3E® alarms per month from each synthetic cannabinoid after retrospective time-of-flight definitions applied

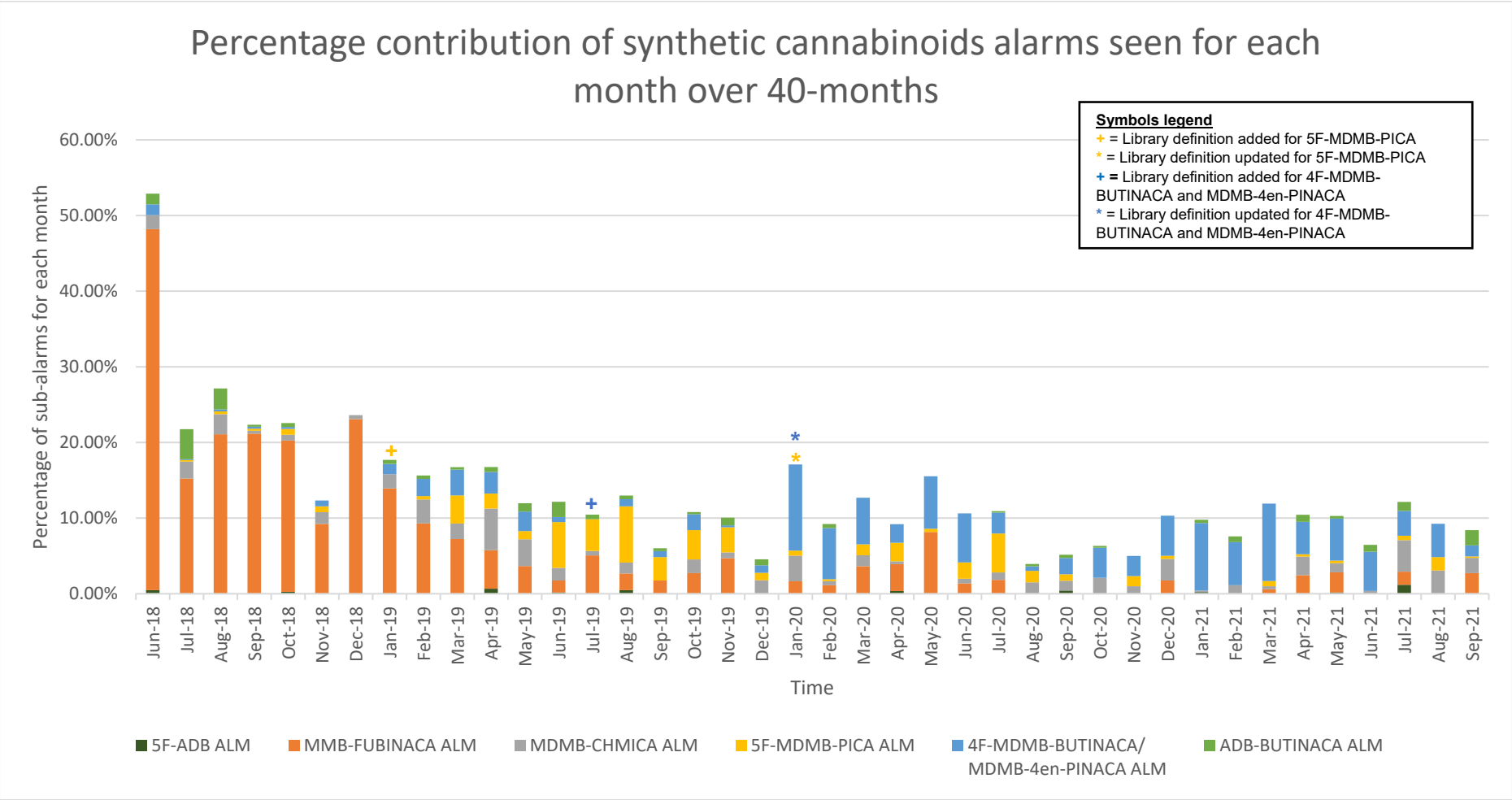


Figure 3.7: Stacked bar chart depicting Itemiser 3E® alarms as a percentage per month from each synthetic cannabinoid after retrospective time-of-flight definitions applied

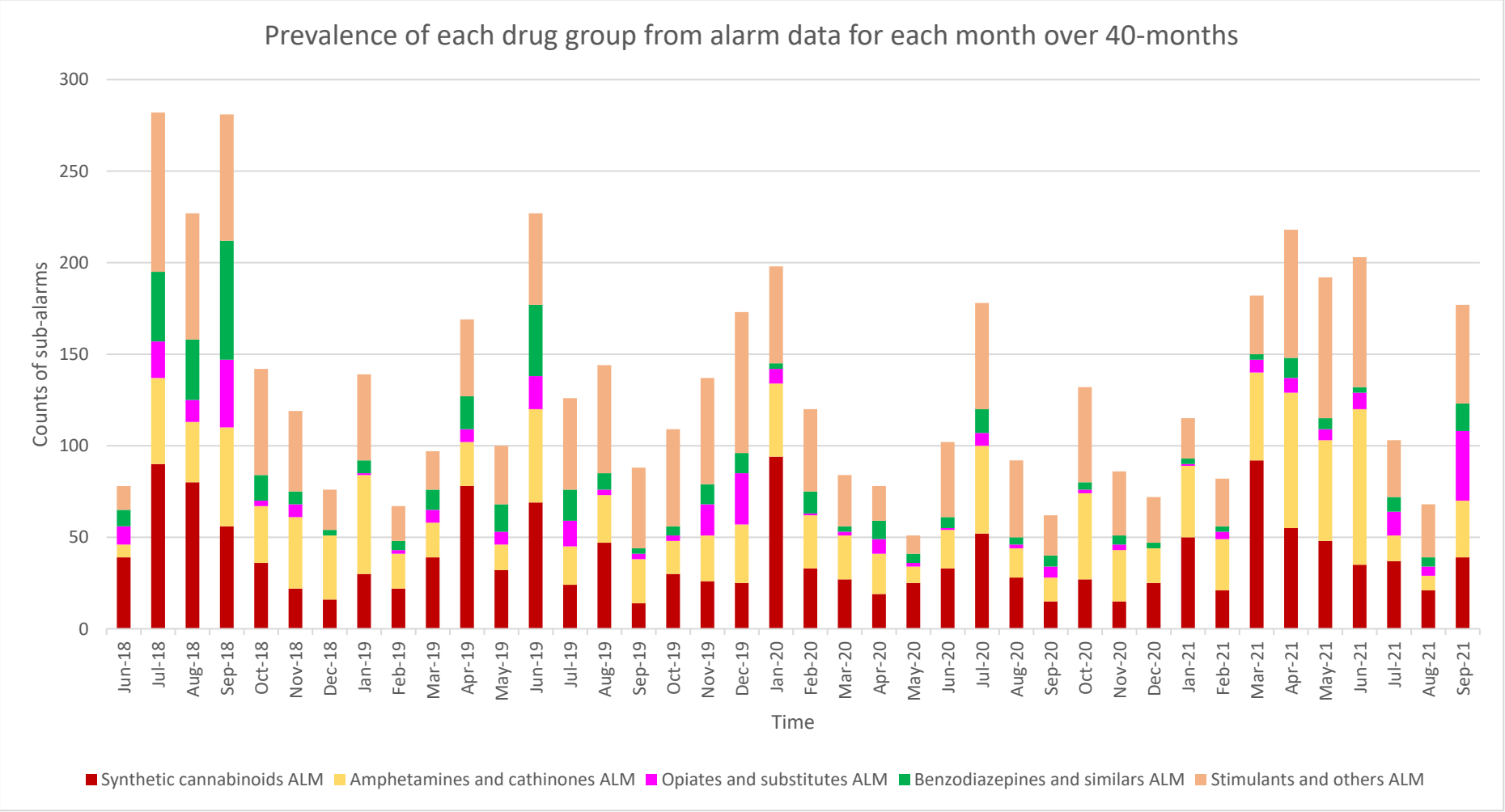


Figure 3.8: Stacked bar chart depicting the Itemiser 3E® alarms per month from each drug group after retrospective time-of-flight definitions applied

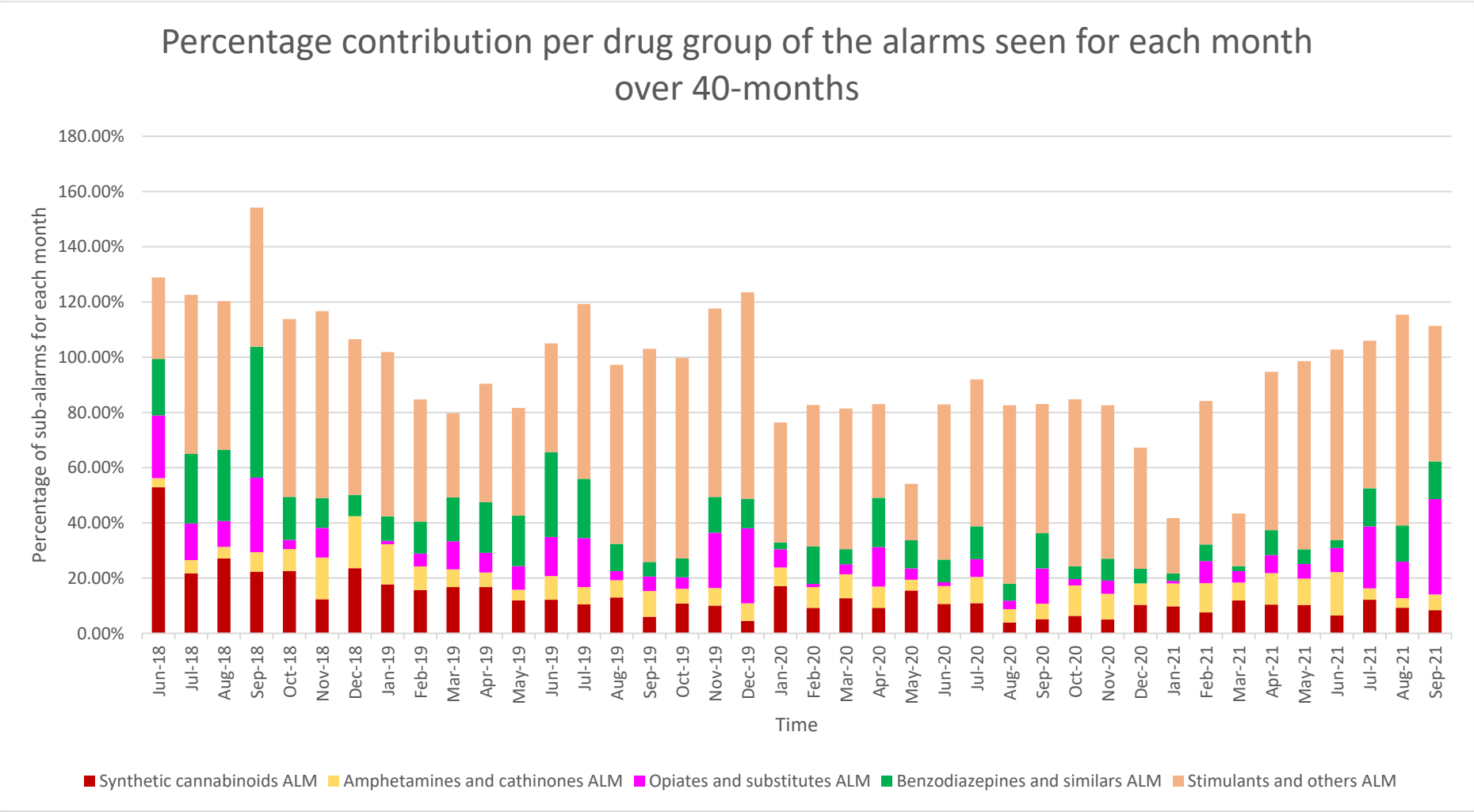


Figure 3.9: Stacked bar chart depicting the Itemiser 3E® alarms as a percentage per month from each drug group after retrospective time-of-flight definitions applied

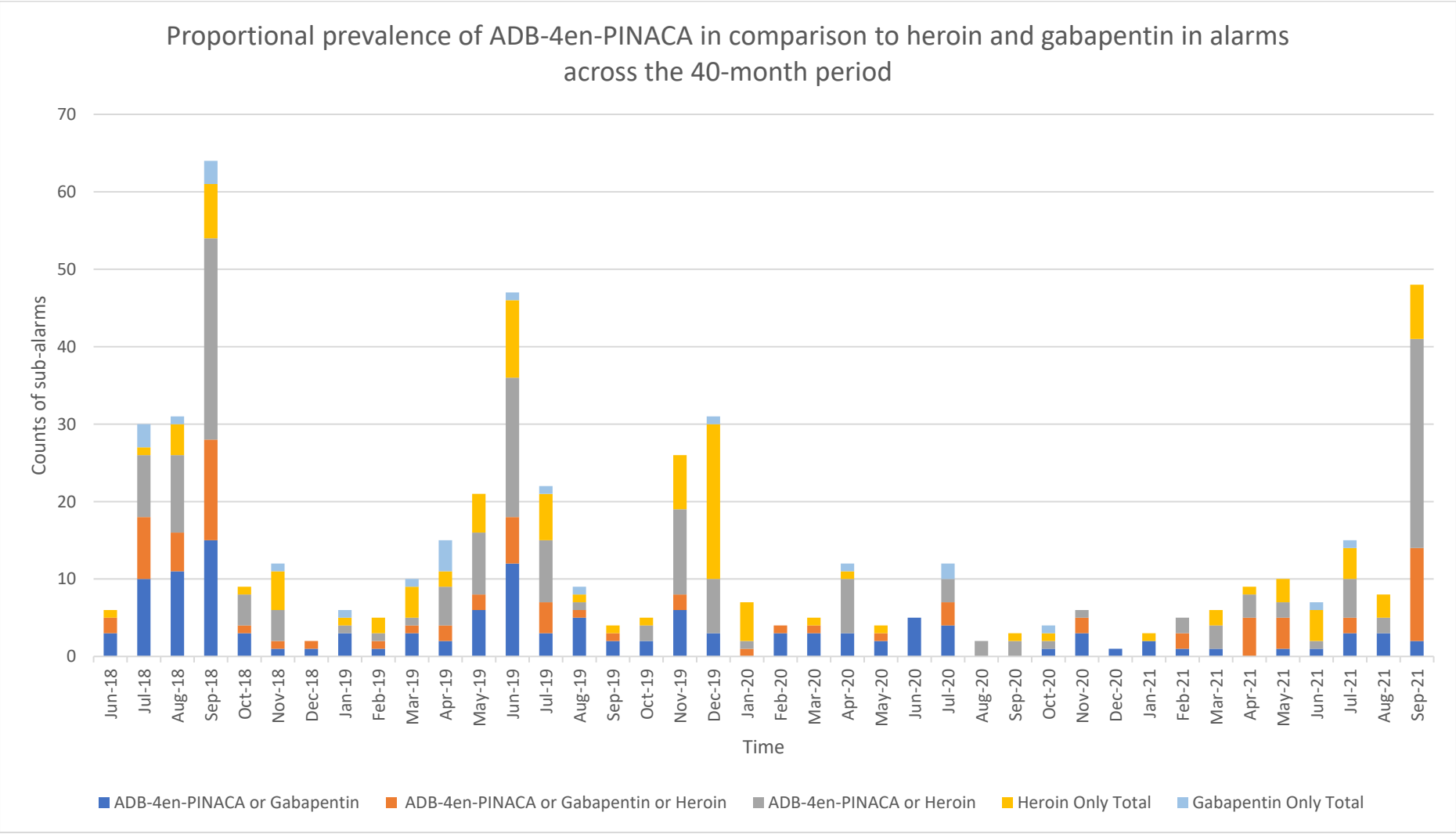


Figure 3.10: Stacked bar chart to aid differentiation between ADB-4en-PINACA, heroin and gabapentin alarms from Itemiser 3E® over 40-month period

To highlight the impact that the library definitions have had, Figure 3.11 was produced with both the alarm and signal data using the drift time definitions. Figure 3.11 shows the presence of 5F-MDMB-PICA in prison post from June 2018, when the study commenced, with an increased prevalence in Autumn 2018, when several samples were submitted (see Chapter 2 regarding MJA3, MJA5 and MJA6). The implementation of the first library definition for 5F-MDMB-PICA in January 2019 appears to have been very timely as there was a surge in the prevalence of this drug in May to September 2019. Figure 3.11 highlights that a substantial number of samples containing 5F-MDMB-PICA would have entered the prison and caused significant harm and disruption had the definition not been added. Although the majority of the 5F-MDMB-PICA samples were identified by the first iteration of the definition, the investigation of the sample in November 2019 (discussed in Chapter 2 regarding MJA14 and MJA17) highlighted that some samples were not triggering alarms, leading to an update of the definition in January 2020 (see Figure 3.11). It should be noted that as the “no alarms” includes signal file data for Figure 3.11, the major decrease after July 2019 was influenced by the lack of signal files from August 2019 onwards (as shown in Figure 3.2), whereas the “no alarm” data from July 2019 onwards only originated from the alarm files. Figure 3.8 and Figure 3.9 do not include the signal file data.

5F-MDMB-PICA was first registered by early warning systems in 2016 (WHO, 2019) and Norman *et al*. (2021) noted its popularity in Scottish and German prisons until the end of 2020 (the end of the study). The drug was included in Schedule II of the 1971 Convention on Psychotropic Substances from November 2020, however it still featured in United States of America prevalence data in 2022 (NPS Discovery, 2022). This shows that the popularity of 5F-MDMB-PICA allowed it to prevail in the wider environment over multiple years despite being controlled internationally. After the implementation of the library update in January 2020, Figure 3.11 shows there was a clear reduction in alarms for 5F-MDMB-PICA, with most months seeing a maximum of seven alarms apart from July 2020 where 25 alarms were produced for 5F-MDMB-PICA. This suggests that, although internationally there was still popularity for the drug, there was a reduction in organised crime groups attempting to send 5F-MDMB-PICA into prisons from September 2019 onwards. Furthermore, the influence of the update to the library in January 2020 is shown in Figure 3.11, with a significant lack of 5F-MDMB-PICA samples present without an alarm, indicating that the instrument was working effectively and reducing this synthetic cannabinoid entering prisons.

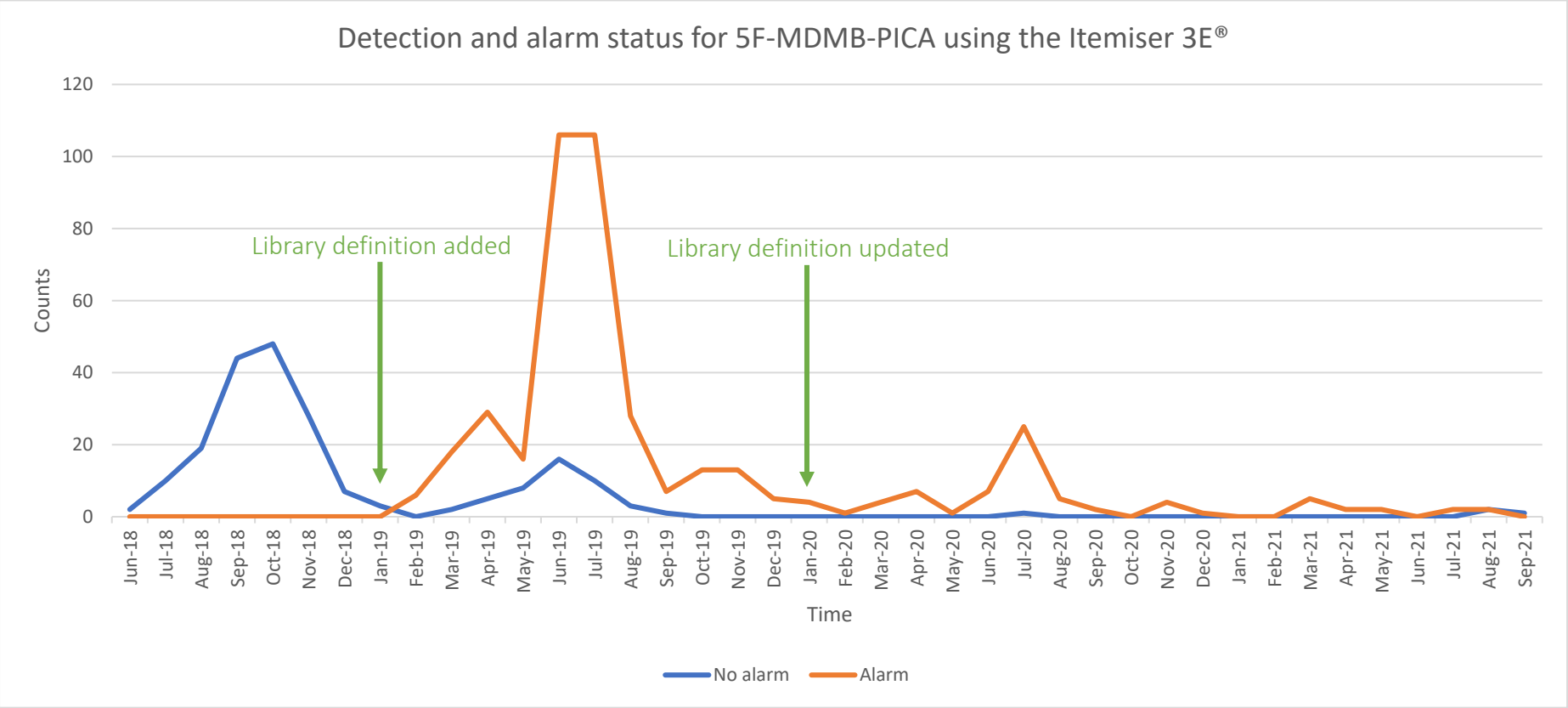


Figure 3.11: Line graph for Itemiser 3E® data depicting 5F-MDMB-PICA detection and alarm trends

The first samples containing 4F-MDMB-BUTINACA and MDMB-4en-PINACA were received in May 2019 (discussed in Chapter 2 regarding MJA7 and MJA8) and the graph in

Figure 3.12 shows that samples had been entering the prison undetected since at least June 2018 (when the Itemiser 3E® was installed) and showed a dramatic increase in the prevalence of this drug in the first half of 2019. The implementation of the library definition was not the sole reason for the apparent sudden decline of popularity of these drugs in terms of the “no alarms”, due to the data until July 2019 including the signal data which was not included from August 2019 onwards. Figure 3.8 and Figure 3.9 highlight the prevalence in 4F-MDMB-BUTINACA and MDMB-4en-PINACA prior to the library update, as the updated library definition was applied to the updated Itemiser 8.34 software when extracting the data. After the library definition update, as discussed in Chapter 2 following the investigation of MJA40, the Itemiser 3E® definition for 4F-MDMB-BUTINACA was expanded to include drift times for MDMB-4en-PINACA, resulting in a peak in alarms in January 2020 shown by

Figure 3.12. Furthermore,

Figure 3.12 highlights the alarms for 4F-MDMB-BUTINACA and MDMB-4en-PINACA reaching a high of 71 alarms in March 2021, showing that more than a year after the library updates, 4F-MDMB-BUTINACA and MDMB-4en-PINACA were still attempted to be sent into the prison by organised crime groups. The number of alarms for 4F-MDMB-BUTINACA and MDMB-4en-PINACA dwindled after March 2021 until the end of the data capture period (

Figure 3.12). However, at the time of writing, both drugs are still being reported as being seen in seizures in the United States but 4F-MDMB-BUTINACA has reduced in popularity since summer 2022 (NPS Discovery, 2023).

For all of the samples, there is the possibility of carryover indicating false positives, as particularly large amounts of synthetic cannabinoids introduced to the instrument could become overloaded on the instrument membrane and therefore test positive until the membrane was cleaned or replaced. Nevertheless, this information gives insight into the use of the Itemiser 3E® and capabilities of analytical support to update and amend time-of-flight definitions.

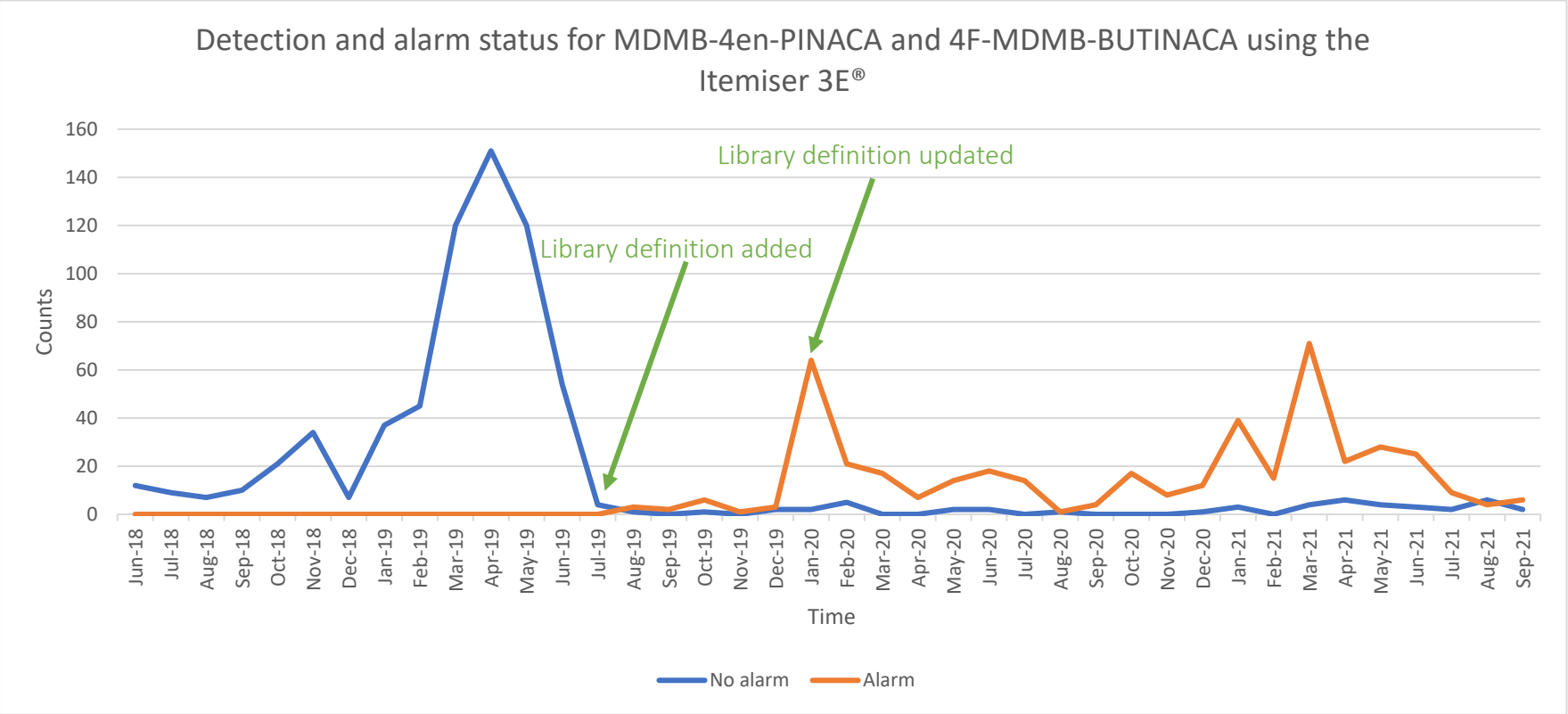


Figure 3.12: Line graph for Itemiser 3E® data depicting MDMB-4en-PINACA and 4F-MDMB-BUTINACA detection and alarm trends

3.4 Summary

The data from the HMP Featherstone Rapiscan Systems Limited Itemiser 3E® were extracted and analysed to identify trends and investigate the influence of library updates on the screening and detection of drugs between July 2018 and September 2021 to meet Objective 2 of this project. The opportunity to retrospectively analyse the data has highlighted the possible prevalence of synthetic cannabinoids in prisons throughout the timeframe in relation to traditional drugs, as well as showcased the impact of updating the library to detect new synthetic cannabinoids. The analysis has also shown the value of the data, and the necessity to ensure signal and alarm files are retained for future processing, overall adding new knowledge to the area, whilst producing recommendations for future operations. The process undertaken for this research has been sufficient to determine trends and prevalence of a selection of synthetic cannabinoids, however if the process was to be implemented in a more timely manner, there is an opportunity to use it as an early warning system for the emergence of new substances. Efforts could also be dedicated to applying automated processes to make the process more streamlined.

Chapter 4 Monograph and Recommendations

4.1 Introduction

Samples from English and Welsh prisons identified as needing confirmatory analysis to determine the presence of drugs for criminal investigations are submitted to a contracted private forensic provider as per The Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework (Ministry of Justice, 2021) and the Use of Drug Trace Detection Equipment in Prisons guidelines (Ministry of Justice, 2023a). The sample is passed onto the local police constabulary through the police liaison and used as evidence to inform which crime had been undertaken and determine related sentencing. For non-judicial samples, there has been less opportunity for investigation into which drugs, if any, are present because they are not being applied to a criminal case and therefore there is limited reason for the police to pay for the analysis to be conducted. This reduces the chance of building an overall intelligence picture surrounding the drug in relation to the prison drug market, how prevalent it may be and how the trends may vary surrounding use. In terms of analysis, this also lessens the chance of detecting a drug through screening techniques which has not been previously encountered.

To address this issue, various research groups are conducting research into the detection and identification of drugs from prisons. These groups include researchers associated with universities, hospitals, governments, and non-profit organisations as discussed below. Large-scale companies are often used by these groups as they provide tools such as certified reference standards, monographs for spectral comparison and searchable libraries, plus provide insight into general trends of use and seizures, early warning information and methods for analysis. For drug analysts, the outputs associated with these research groups allow for the detection of drugs efficiently and effectively, reducing misidentification and increasing the chance of detecting newly encountered compounds. These compounds may be seen for the first time in prisons before being associated with a criminal proceeding, however, this requires effective dissemination of the related information to those who need access.

In England, there is currently no national initiative focused on the confirmatory identification of drugs from screened prison samples purely for intelligence purposes at this time. To meet Objective 3, this chapter discusses the work of independent research groups that have increasingly taken on this role in England, Scotland, Wales, across Europe and in the United States of America, and the cooperations and foundations providing tools for identification.

4.2 Large-scale companies and organisations with international impact

There are multiple companies which research the analysis of drugs or produce tools to aid others in achieving this goal. Tools such as certified reference standards, monographs for spectral comparison and searchable libraries are a necessity for those working in drug analysis to aid in identification and are often produced by large-scale drug manufacturers with research agendas. The National Institute of Standards and Technology (NIST) is a government agency that sits within the United States Department of Commerce, and their widely renowned EI-mass spectral library is periodically updated to include relevant substances as chemical development evolves. The most current version at the time of writing is NIST20, which includes spectral information and associated names for over 300,000 compounds (NIST, 2020).

Chiron AS and the Cayman Chemical Company are reference standard providers. Chiron AS produce reference materials and have dedicated projects regarding the exploration and production of synthetic cannabinoid certified reference standards such as the EU funded NPS Reform and EUFORIaR projects (Chiron AS, 2023). The Cayman Chemical Company collaborate with the NPS Discovery programme at the Center of Forensic Science Research and Excellence to produce certified reference standards for emerging drugs in the United States (Center for Forensic Research and Excellence, 2023). Additionally, a GC-MS EI spectral library is continually updated and openly available on the Cayman Chemical Company website for most of the drugs that they produce and sell. The Cayman Chemical Company GC-MS Drug Identification Tool allows searching *via* structural characteristics such as base peak, second base peak and relative molecular mass for many of the drugs included on their website, allowing drug analysts to compare sample spectra to reference spectra (Cayman Chemical Company, 2022a). Cayman Chemical Company also produce the Cayman Spectral Library which is compatible with the NIST library and Agilent software for GC-MS to aid in the identification of substances through mass spectral comparison, and guides are produced surrounding nomenclature for emerging synthetic cannabinoids. Finally, both Cayman Chemical and Chiron AS also offer analytical consultancy services including synthesis and analysis of novel substances and metabolites to aid with identification, which is especially useful for NPS compounds. In terms of their impact, they are predominantly benefitting drug analysts with their identification resources, however this has a wider impact on the availability of information and intelligence for all related and interested parties, as the tools that are provided by these companies rely on open access policies for anyone interested to be able to access this information.

The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) are a collective group of forensic scientists in the drug analysis field that aim to produce minimum standards for the identification of drugs and implement best practice, such as the sharing of methods and results using monographs. Some of their aims are to produce tools and resources and provide an opportunity for knowledge exchange, which they achieve through sharing information surrounding topics such as drug solubility in various solvents to help choose appropriate extraction conditions, method parameters for instrumentation and MS results for comparison. Furthermore, they also produce MS and infrared spectral libraries from collated certified reference standard identification data which are compatible with a variety of instrument software formats to increase the potential of drug identification when using GC-MS and FTIR. The availability of this information, alongside guidelines for practitioners, increases the quality and confidence of the identifications made, therefore allowing researchers outside of private forensic providers to produce reliable identifications and intelligence.

Another United States of America-based organisation with international impact is the Center for Forensic Science Research and Excellence (CFSRE), which is part of the Fredric Rieders Family Foundation. The CFSRE was founded in 2010 by Dr Barry Logan, and the NPS Discovery programme was launched in 2018 to provide an evidence based early warning system for NPS. Sample information originates from drug seizures, clinical toxicology data from hospitalisations and criminal justice agency investigations to identify novel, emerging substances and produce trend reports quarterly to determine prevalence and popularity yearly. Similar to the Cayman Chemical Company and SWGDRUG, NPS Discovery provide monographs to aid identification of newly emerged substances, often in collaboration with National Medical Services Laboratories (NMS Labs). Furthermore, to increase harm reduction opportunities, they offer drug checking services in collaboration with public health initiatives and disseminate this analysis *via* public health alerts, drug supply assessments and drug checking reports. Although these alerts are not readily accessed by the public, they are available to those in drug analysis, intervention and intelligence areas to help provide insight into what substances are being encountered in the United States of America, when they are being seen and how popular they are. The scope of CFSRE is also very broad, as alongside their analyses, the team regularly disseminate information *via* social media channels and mailing lists, increasing the opportunity for those in the area to access the information. The outputs generated by the research team are paving the way in the drug analysis area in terms of producing resources, collating data and result sharing.

Finally, early warning systems such as the European Union Early Warning System (EU EWS) run by the EMCDDA also offer an opportunity for the sharing of information from hospitalisations and test seizures to indicate the current drugs being encountered, which is especially helpful with regards to NPS with their ever-evolving nature. However, following Brexit, those outside the EU cannot formally contribute to the dataset. Additionally, the Forensic Early Warning System (FEWS), produced by the UK Government Defence Science and Technology Laboratory, does provide insight into the seizures in borders and prisons (DSTL, 2022), although, until recently, yearly updates regarding seizures were not released as regularly as from other sources.

4.3 Private Forensic Providers

Commercial laboratories, such as Eurofins Forensic Services, Abbott Limited, LGC Group and Socotec, are examples of the type of organisation who will routinely purchase certified reference standards and library updates as they are a necessity to adhere to ISO/IEC 17025 accreditation and ensure accurate identifications are produced for contracted drug analysis work in criminal proceedings. However, due to the nature of the business, the identifications are produced for the customer (police constabulary) and are often not shared outside of the investigation or criminal justice system. Yearly and quarterly reports can be produced by these companies; however, they are shared with customers only.

In terms of prisons, confirmatory testing of a sample can be undertaken by the forensic provider affiliated with the local police constabulary after an indication of a positive substance from screening techniques alongside associated intelligence (Ministry of Justice, 2021; Ministry of Justice, 2023a). When the indication of a drug by a screening technique is the only supporting information and there is no accompanying intelligence and the sample is not deemed to look suspicious, the only option is to hand a suspect item to the prisoner and assume a false positive. Although this ensures that prisoners still have access to correspondence with their families and friends, as per the Prison Rules 1999, at the time of writing, these options could result in drug-soaked paper not having any confirmatory analysis undertaken due to missing intelligence or screening technique information (which could be the result of the library not being regularly updated), missing the opportunity for the analysis and identification of previously unencountered drugs entering the prison on the “front-line”, and opening the opportunity for harm, with prisoners accessing their post without major intervention. The analysis of prison samples, including intelligence-based samples, was previously routinely undertaken by private forensic providers, however due to the nature of the complex samples often requiring extensive sample preparation, and the amount of

samples being submitted, focus needed to be primarily on meeting turn-around times for criminal justice system samples, and therefore intelligence-based analysis stopped in the West Midlands region around 2017-2018 (Butler, 2018), even with synthetic cannabinoids still prevalent within the UK prisons at that time, as shown in Chapter Chapter 2 (Grace, Lloyd and Perry, 2019; Norman, McKirdy, Walker, *et al.*, 2020).

4.4 UK-based Drug Analysis Services

In addition to the large-scale organisations, there are smaller organisations who work to produce outputs for others to use as resources. TICTAC Communications Limited is a company based at St. George's University of London which focuses on drug identification *via* contractual analysis, FTIR and Raman spectral libraries, drug imaging and visual identifiers. Due to the time and effort dedicated to the libraries, they are popular amongst drug analysts, with their FTIR and Raman libraries being the largest and most current libraries in Europe for NPS (TICTAC Communications Limited, 2023). However, for those in the area to benefit, they need to purchase the library and the updates, which happen approximately once a year. TICTAC have also undertaken research to identify drugs soaked in paper from prisons in England between 2018 – 2020, in collaboration with HMPPS and Queen Mary University of London. This work helped to build their FTIR spectral library and detect the substances being seen in prisons, plus give indications into the prevalence of certain drugs amongst prisoners depending on sex, prison category and geographical region (Akca, 2022). Their research has highlighted the extent of drug prevalence in paper samples in twelve English prisons and the necessity for confirmatory analysis to identify the drugs present, plus increased the opportunity for others to be able to detect drugs in paper through FTIR analysis.

Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS), on the other hand, are a drug checking organisation for traditional substances, illicit pharmaceutical substances and NPS in collaboration with Public Health Wales and Cardiff Toxicology Laboratories. Their work allows for a variety of people within the UK, including people who use drugs, law enforcement and public services, health care providers, educators and those from housing teams to submit samples for analysis to determine the major and minor constituent components (although the information and samples should not be from criminal proceedings or forensic cases). Anonymity is maintained throughout *via* the use of submission forms and unique web generated reference numbers. Information is also gathered from user experiences through the forms and is published with the purchase-intended drug identity alongside the identification. This harm reduction approach allows users and associated support

providers to access their results online on the WEDINOS website to understand what drugs are present in the substances submitted. WEDINOS also publish any updates and public health alerts through social media, widening the opportunity for people to access this information. Collated data has also allowed trend information to be gathered which can be accessed through monthly, quarterly, and yearly reports (WEDINOS, 2023a). In terms of prisons, WEDINOS has been able to offer drug identification for non-judicial samples from the six prisons in Wales, providing much needed intelligence for regional intelligence analysts, increasing awareness of the substances attempting to and entering prisons and opportunity for comparison to prisons in other areas (Norman *et al.,* 2021). This information can then be utilised by other researchers to determine potential prevalence of drugs of interest in local areas and on a national scale to build an intelligence picture for the UK.

4.5 Research Groups

Research groups are also key to facilitate drug identification of NPS through effective dissemination of research outputs and the development of shared resources. HighRes NPS, NPS DataHub and the Response 2 Project are all examples of these types of groups. HighRes NPS, founded by the University of Copenhagen, Denmark, provides crowd-sourced high resolution mass spectral information in the form of a database and widely compatible downloadable spectral libraries. The database is regularly updated and currently includes 2317 compounds, with 1624 of those including high resolution mass spectral fragment data, plus an online closed-group database contains more than 5600 entries. Furthermore, predicted LC retention times can be generated upon entry of method parameters, overall helping drug analysts identify unknown or previously unencountered substances more readily. To join the closed-group, information regarding purpose of application is needed but the application process allows interested parties from the field to access the information. The group encourages the submission of multiple spectra for the same drug to help with the ‘self-validation’ process. This is not as stringent as other groups, but HighRes NPS do reiterate that their data should be used for screening purposes rather than absolute identification (HighRes NPS, 2023).

NPS DataHub was developed by NIST, the German Federal Criminal Police Office (the Bundeskriminalamt, or BKA) and the U.S. Drug Enforcement Agency. NPS DataHub aim to verify all of their data entries to increase value and confidence in the identifications through comparison and use of their reference data. The closed group allows opportunities for membership through their website, as long as the applicant provides verification that they work within or in partnership with a law enforcement

agency to justify accessing the information available. NPS DataHub provides monographs including formula, CAS numbers, material safety data sheets, relative molecular mass, structure diagrams and molecular names, plus NMR spectra, FTIR spectra and MS spectra, however all three spectra are not available for each compound in the database. The data are often derived from certified reference material, but there are some spectra included that are from seized samples in cases where it could be a novel occurrence. In these incidents, the data would be checked to ensure the spectra produced is of high enough quality for others to use and comments need to be associated to define it as a seized sample. In cases where seized samples may include mixtures or adulterants, NPS DataHub encourage users to purify the sample or label the spectra to highlight the other compounds present.

NPS DataHub also work closely with the ADEBAR Plus project in association with the BKA, the seven German State Bureaus of Criminal Investigation, the University of Freiburg and the University of Mainz to share analytical results they encounter through test purchases and law enforcement seizures of NPS. They do this *via* published journal articles and updating the database (Pulver, Fischmann, *et al.,* 2022b). To promote accessibility and verification, NPS DataHub suggest certain datafile types, for example NMR data is suggested to be JCAMP files so that the CSEARCH automated consistency checker can verify ^{13}C and ^{1}H peak assignments compared to predicted assignments (Urbas et al, 2018).

Finally, the Response to Challenges in Forensic Drugs Analyses project, known as the Response or Response 2 project, was funded by the EU between January 2015 and June 2017 to provide reliable spectral data in the form of monographs and databases to support identification when there may be a lack of certified reference material available. Although the project funding ended in 2017, the online database managed by the Slovenian National Forensic Laboratory (NFL) continues to grow, with new entries included throughout 2023. The database is open access and includes information such as substance class, common, systematic and other names, structures, formula, relative molecular mass, top three most abundant MS peaks labelled as base peak 1, 2, and 3, corresponding information regarding the sample, such as whether it was a test purchase or certified reference material, date of entry and contributor, plus the MS and FTIR spectra (Response, 2022). This dissemination method offers the opportunity for other researchers to easily access spectral information to aid in the screening and identification of novel substances prior to certified reference materials being obtained. For NPS, this is particularly pertinent as novel compounds may be imported and experienced in one country first before being seen by others, therefore increasing the

chance of time effective identification and readiness when substances are encountered in other areas, such as if samples identified first through test purchases in mainland Europe prior to detection in prisons in the UK.

The role of drug analysis for non-judicial samples has increasingly been taken on by research groups in the UK and Europe and there have been a few research groups in Germany who have focused their work on the detection and analysis drugs within prisons. Researchers at the University of Freiburg have conducted analysis regarding sample preparation of drug-soaked paper, more specifically investigating the homogeneity across the paper, the visible differences seen depending on the concentration of synthetic cannabinoid solution and the amount of solvent that can be absorbed by the paper. This information has been able to give an insight into the preparation methods that organised crime groups undertake to produce the sheets of paper, the approximate dosages that might be exhibited and intelligence information for future detection for those working in prisons (Angerer, Möller and Auwärter, 2018). There has also been screening, confirmation and feedback undertaken with the use of Smiths Detection IonScan600 instruments in some German prisons. The work published by Metternich, *et al.,* (2019) discusses the use of screening instruments in prisons and the development of synthetic cannabinoid libraries for future detection, with analytical support using GC-MS, NMR and ultra-performance liquid chromatography (UPLC) from associated forensic laboratories at State Office of Criminal Investigation, Rhineland-Palatinate.

One of the most impactful country-wide initiatives has been introduced in Scotland, which focuses on the confirmatory identification of synthetic cannabinoids from screened prison samples purely for intelligence purposes *via* collaboration between the Scottish Prison Service and the University of Dundee's Leverhulme Research Centre for Forensic Science (LRCFS). Regular prison post in Scotland is photocopied to reduce the chance of drugs entering the prisons from soaked paper, however Rule 39 legal post should still be sent directly to the prisoner and therefore allows opportunity for imitation letters to be produced by organised crime groups (Blakey, 2008; Norman, McKirdy, Walker, *et al.,* 2020). Researchers at LRCFS routinely analyse seized prison post and other samples (including vaporising devices, associated solutions and other seized products) from Scottish prisons to provide analytical support alongside screening using the Rapiscan Systems Limited Itemiser 3E® and 4DN® instruments based at the prisons. Due to the partnership with the Scottish Prison System, Rapiscan Systems Limited has continued to provide support since 2018 and has grown to service all public Scottish prisons, develop the Rapiscan Systems Limited libraries to include

novel substances (e.g., ADB-BUTINACA, ADB-4en-PINACA and etizolam) and to provide an effective screening, confirmation, and feedback cycle (Norman, McKirdy, Walker, *et al.,* 2020). Furthermore, they have been able to uphold the network between the users of the Rapiscan Systems Limited product to create regular user group meetings for sharing analytical results, which has produced a space for representatives from each Scottish prison to report their experiences surrounding drug prevalence and detection, plus troubleshoot any issues with the instruments (Nic Daéid, 2023). In addition, the research team have a closed group email distribution list to share information with official bodies and collaborators, and have published regularly to summarise analysis methods, qualitative and quantitative identifications, trends and prevalence of the substances identified (Nic Daéid, 2023; Norman, McKirdy, Walker, *et al.,* 2020; Norman, Walker, McKirdy, *et al.,* 2020; Norman *et al.*, 2021). Although the system that has been implemented in Scotland has been able to service that country well, currently there is no national initiative for all of the UK, considering there are 142 prisons in total: 116 prisons in England, six in Wales, 17 in Scotland and three in Northern Ireland. For England, there has been a move towards research groups aiding their local area.

In terms of the research undertaken at Staffordshire University, research began with a 12-week MSci project focusing on the implication of Itemiser 3E® equipment within a prison setting for the analysis of synthetic cannabinoids in paper. At the time, HMP Featherstone had the equipment on loan and the research undertaken highlighted the opportunity for screening to be coupled with confirmatory analysis by a university to identify the substances present on samples, but also relay information to Rapiscan Systems Limited of the synthetic cannabinoids present within prisons for intelligence purposes. The screening, confirmation and feedback cycle has been undertaken since, with continued collaboration with HMP Featherstone from 2018, expansion to other West Midlands prisons through the West Midlands Prisons Group from 2020 (as detailed in Chapter Chapter 2 and Chapter 3), and recent expansion to providing this service to HMP Stocken, Rutland, from February 2022. This move towards encompassing East Midlands prisons is ongoing, and efforts will be dedicated to reestablishing routine testing for the West and East Midlands prisons upon the completion of the PhD. Discussions have also been undertaken with representatives from the Substance Misuse Group, HMPPS, regarding the screening, confirmation and feedback cycle, and intelligence analysts at the Substance Misuse, Illicit Economy, Escape and Abscond department, HMPPS, surrounding the opportunity for retrospective data analysis. Information regarding the work undertaken has been

disseminated *via* posters and oral presentations at conferences and meetings (Abbott, 2019; Abbott, 2022; Abbott, 2023) and publication (see Appendix 8 – Abbott, Dunnett, Wheeler and Davidson (2023)). One of the most impactful aspects of the research is the network that has been produced, and the opportunities for expansion that have been made available, with discussion surrounding the work undertaken between HMPPS dog handler teams, Rapiscan Systems Limited and through the HMPPS security teams, ensuring staff understand the benefits the opportunity for screening and confirmatory analysis holds. Therefore, plans are currently being developed to present at the HMPPS Insights23 conference and to organise a special interest user group for security and search teams from prisons in the local area, as well as representatives from Rapiscan Systems Limited and the HMPPS Substance Misuse Group to determine what needs to be improved and what expansion could look like to maintain and grow the screening, confirmation and feedback cycle.

MANchester DRug Analysis and Knowledge Exchange (MANDRAKE) is a publicly funded drug testing and harm reduction research group based at Manchester Metropolitan University, in collaboration with Greater Manchester Police, which provides analysis support for the city and local region. The partnership has resulted in MANDRAKE analysing samples from local seizures to gain qualitative and quantitative insight for the drugs encountered by the local police in a format similar to that of WEDINOS with deposit forms (GM Trends, 2021). Unlike WEDINOS, the results are not openly shared unless in the form of a public health and harm reduction alert or publication to highlight novel samples or current research, such as their recent publication Gilbert *et al.,* (2021). In terms of prison analysis, the MANDRAKE team announced *via* Twitter in February 2022 that they were providing real-time drug testing for HMPPS for non-judicial samples to support harm reduction (MANDRAKE, 2022), primarily servicing the North-West of England *via* analytical support, however no results have yet been publicly shared to show the information on the sample types, drugs encountered, or any trends associated from the prisons. Although this information would be helpful for other researchers to ascertain intelligence surrounding the drugs, the primary beneficiaries are the prisons associated and the corresponding police forces to aid their intelligence gathering. Furthermore, research groups like MANDRAKE help to justify others as it shows the impact research groups can have and what they provide for their local communities and prisons. Such projects also provide a model to show what could be provided to stakeholders in a different region.

For other research groups, the focus has been on the application of various technologies to try and tackle the issue of screening within prisons. Vaccaro *et al.,*

(2019) and colleagues at the University of Hertfordshire have trialled the use of handheld Raman spectrometers, specifically the Progeny™ system from Rigaku, using caffeine and paracetamol with various matrices, including Kinder Eggs, cloth, paper, glass vials enclosing e-cigarette liquid and polythene bags enclosing paper envelopes to simulate concealment methods. The requirement for further work was noted by the author to more fully investigate the detection of drugs in paper, cloth, and liquid detection matrices.

Another example of exploratory drug detection work in prisons is the research undertaken by Paul, Smith, Gent and Sutherill (2021) at Bournemouth University, who focused on air monitoring within prisons. This analysis aimed to determine if drug fumes, generated by smoking or vaping synthetic cannabinoids, could lead to an identification of the substance, with the research having staff safety at the forefront. Using fixed sequential samplers and personal air sampling units worn by prison officers, collected air was analysed using GCxGC-TOF-MS *via* transfer onto thermal desorption tubes. Paul, Smith, Gent and Sutherill (2021) reported that no synthetic cannabinoids were identified in the prison air samples, however, it was surmised by the researchers that this could have been hampered by the logistics of the study, as at the time, less prisoners were outside of their cells due to COVID-19 risks and less visits were being conducted, reducing opportunity for prisoners to access synthetic cannabinoids. Furthermore, Paul, Smith, Gent and Sutherill (2021) did note that no synthetic cannabinoids may have been smoked during the study duration or the substance level was very low and unable to detect. Laboratory-based trials were effective, and therefore there is promise that this would work for future use if the further work was tailored to be more targeted or allow a longer, more varied period of time for sample capture. This work enables an opportunity to see what could be put in place to not only indicate which synthetic cannabinoids are being actively consumed, but also protect those who could be affected by the second-hand smoke or fumes, i.e., prison officers and health care workers based in the prisons.

May *et al.,* (2019) and Andrews *et al.,* (2023), both in association with the University of Bath, demonstrate the potential of fluorescence and photochemical spectral fingerprinting for point-of-care detection of synthetic cannabinoids. May *et al.,* (2019) outlines the successful detection of synthetic cannabinoids before (≥ 1 µg/mL) and after combustion, plus identification of synthetic cannabinoids in saliva samples. Although fluorescence spectroscopy is listed as a Category C (SWGDRUG, 2019) technique, the fluorescent spectral fingerprints were found to be unique when differentiated using applied mathematics processes, therefore increasing specificity capability. However,

the researchers stress it was more useful at the time to be used as a small, portable instrument to differentiate between structural groups of synthetic cannabinoids. May *et al.,* (2019) also noted that there may be issues with mixtures in complex matrices, therefore further work needs to be established before being used as a point-of-care unit. The work undertaken by Andrews *et. al.,* (2023) has focused on expanding from fluorescent spectral fingerprints to include photochemical fingerprinting for discrimination between specific synthetic cannabinoids in saliva from herbal matrices. This work has led to a prototype instrument being produced to determine opportunity for point-of-care, with the promise of analysing saliva samples to prove use of synthetic cannabinoids, an extremely valuable opportunity for homeless community workers and prisons alike.

In terms of biological sample analysis, the Newcastle University-led Identification Of Novel psychoActive substances (IONA) study collates data from toxicity-based clinical samples across England, Wales and Scotland. Some of these data have been published and encompass identifications of the substances used, whether it has been used alongside other drugs, associated mental and physical health effects presented and pharmacological data (Hill *et al.,* 2016; White *et al.,* 2018; Haden *et al.,* 2021; Pucci, Hudon, Hill and Thomas, 2021; Potts, Thomas and Hill, 2022). Their data also give an insight into the differences in toxicity-related hospitalisations before and after the Psychoactive Substances Act 2016 (Craft *et al.,* 2022). Furthermore, due to the scope of the research and participating collaborators, research can be conducted into geographical studies to determine substance use across England, Wales and Scotland, and develop a timeline of hospitalisation incidents from non-medical substances. The confirmatory analysis was undertaken by LGC Limited once the sample, often in the form of plasma, serum, whole blood or urine, has been collected and consent given by the adult in question. There are exclusions to the study, such as there has to be clinical suspicion of drug misuse, samples cannot be used if consent is not granted, if the person providing the sample is known to be HIV positive, if they are a child or young person, or if the sample collected was for investigation into suspected non-accidental injury (IONA, 2021). Sample collection information, data collection sheets and training material are easily accessible on their website for hospitals to be involved with the data collection project, further opening the opportunity to build a more representative picture for England, Wales and Scotland (IONA, 2023). The research being conducted by the team is extremely impactful to the discipline, as they can provide accurate depictions of what people are being hospitalised from, where and when, as seizures of substances can only indicate a potential substance that could likely be consumed, compared to this

analysis where data can be gathered regarding what substances have actually been consumed. Therefore, there is opportunity and scope for collaborators to couple this information with research surrounding seizures to compare the substances being used in specific regions, any potential quantitative analysis opportunities, and the opportunity to explore if particular substances are more likely to be used in a poly-drug format.

4.6 Recommendations for a model for England

If the private forensic provider role is to continue with the current system outlined in the Use of Narcotics Trace Detection Equipment on Correspondence Policy (Ministry of Justice, 2021) and the Use of Drug Trace Detection Equipment in Prisons (Ministry of Justice, 2023a), and only offer confirmatory analysis for judicial samples, then there is a continued opportunity and significant benefit for drug research groups to provide intelligence-based testing. There are 116 prisons and young offender institutions in England and Wales, and 17 in Scotland. The University of Dundee's Leverhulme Research Centre for Forensic Science (LRCFS) has been able to provide analytical support to the Scottish Prison Service, and the WEDINOS group have provided analytical support to Welsh establishments in collaboration with HMPPS, however, it would be beneficial to have a system implemented to service England.

One approach would be to utilise existing drug research groups associated with universities across England to provide consultancy work for their local area and feed all intelligence back to HMPPS as a central hub. Staffordshire University could continue to provide analytical support for the West Midlands region and expand to include the East Midlands prisons, and the MANDRAKE group, based at Manchester Metropolitan University, could continue to service the North-West region, with Queen Mary University of London and/or St. George's University of London, in association with researchers at TICTAC Communications Limited, could provide analytical support for institutions in the London area. Furthermore, there could be the opportunity for Newcastle University's IONA study to expand to analyse seized paper samples from their local prisons, and compare to the information they gather from hospitalisations, and Bournemouth University could explore the analysis of synthetic cannabinoid-soaked paper alongside air samples in prisons to investigate if similar substances are seen within local establishments. This testing should be in collaboration with the screening provisions that are already in place within the prisons, whether that be the Rapiscan Systems Limited Itemiser 3E® and/or Smiths Detection IonScan600, to prioritise samples that have been unable to be identified and therefore understand what substances could be entering the prisons until libraries can be updated. This system

would also give the opportunity to expand to implement new technology, such as if the University of Bath were to provide consultancy analysis for their local area and conduct research to compare their instrument alongside those that are already in use. If all of the universities discussed, plus potentially the University of Hertfordshire, were to be involved in delivering intelligence-based analytical support for prison samples, then this could ensure that each prison would have access to analytical support in their region, i.e., the North West, North East, Midlands, South East, South West and London.

Some of the considerations highlighted by the University of Dundee's LRCFS and Staffordshire University would be the cost of this analysis, and that research groups would need to have funding support from HMPPS, however non-profit funding models could be implemented to create a desirable option compared to paying a private forensic provider. This would look to cover consumable prices, the time dedicated by the analysts and the instrument running costs. Service level agreements would need to be accounted for, outlining parameters regarding turnaround times, number of samples, instrument availability and level of analysis, i.e., qualitative analysis versus quantitative analysis. A fixed cost would likely be difficult to set if the sample was outside of either being a paper sample or powder due to extra time needed for sample preparation and instrument method development, so negotiation on sample type would also be needed to outline and justify the types of samples that would feasibly be able to be analysed through this system.

In the event of a change in the current process and a private forensic provider being able to conduct the confirmatory analysis for intelligence purposes as well as judicial, then drug research groups will likely still be required to undertake research in areas where the private forensic provider cannot dedicate extra time and resources, or into areas outside of their remit, but are still influential to the screening, confirmation, and feedback cycle. One example of an area for research focus by drug research groups would be exploratory research into novel compounds. With access to techniques such as LC-MS and NMR, universities will often have the opportunity to conduct this investigative research. Structural elucidation is not out of the remit for private forensic providers, especially when needing to identify a substance that has not been previously encountered, however it is not routine, so this work may be able to be undertaken by a research group to provide valuable information regarding the identification of novel substances, similar to the research conducted by the ADEBAR Plus project in Germany (Pulver, Fischmann, *et al.,* 2022b).

Secondly, independent evaluations of trace detection equipment could be conducted by research groups to investigate accuracy and precision of the instrument and therefore it's efficiency when applied to the prison system. This work is pertinent to increase confidence in the trace detection equipment being used, plus understand how different trace detection equipment, like the Rapiscan Systems Limited Itemiser 3E® and the Smiths Detection IonScan600, can be used alongside each other within a prison for screening practices. Key investigation opportunities would include reviewing how successfully both instruments are used alongside each other in airports for drug screening, determine likely false positives and limits of detection which may influence one or both instruments, and conduct side-by-side analysis for quality assurance of detection capabilities. If the instruments do not give a synonymous response, this can cause major confusion for the operator, investigating prison officer and security teams, as they will struggle to determine which substances are trying to enter or have entered the prison. Furthermore, this reduces confidence in the instrument capabilities, as questions are raised regarding which presumptive identification is correct, or if in fact neither are correct. Therefore, continued efforts would be needed to establish instrument libraries, but also ensure similarity in terms of output to ensure staff are receiving reliable information from the instruments.

Research groups may also be able to provide a data analysis service to assist with the interpretation and application of information from the trace detection equipment that would not be undertaken by any forensic provider. Intelligence information from prisons is researched and mapped already, however the interpretation and analysis of the information from the trace equipment is not currently undertaken by HMPPS or the instrument providers (McGough, 2023). Chapter Chapter 3 shows how the analysis of one Itemiser 3E® instrument's data can highlight how an emerging substance can be investigated to determine how long a substance has been detected but not alarmed for, the extent of prevalence of a substance in the prison system and the effect of instrument library updates. This analysis could be expanded when applied to more than one Itemiser 3E®, enabling the opportunity for geographical profiling to investigate any localised issues, determine if some prisons may be targeted and see a particular substance first, and compare associated practice with Itemiser 3E® results. Furthermore, this could be coupled with the trace detection equipment evaluation, for example, investigating the following:

- how each prison uses their Itemiser 3E® and associated data
- if the prison routinely photocopy their letters
- how often they use trace detection equipment

- if there is a routine operator and if only authorised personnel use the instrument
- if they compare information between the two instruments in situations where they have more than one brand of trace detection equipment
- if they encounter regular false positives and how they tend to use the instrument, i.e. sole focus on screening all letters or sporadically analyse suspicious substances.

This data collection, alongside structural elucidation, trace detection evaluation and confirmatory analysis conducted by private forensic providers could hold great significance for HMPPS and individual prisons across the estate to enhance the intelligence picture surrounding drugs in prisons.

Whether intelligence based analytical testing is conducted by research groups or private forensic providers, there is an opportunity to build a large-scale intelligence network further down the line. This opportunity could combine the data gathered from prison seizures and trace detection with toxicology results from the rMDT process and hospitalisations. This collection of data could show which drugs:

- are at risk of entering prisons
- are found within prisons
- have been taken by the prison population
- have caused adverse health issues to a user.

If this analysis and information sharing was conducted in a timely manner, and if a process was applied to the prison estate across England, and the UK as a whole, this could generate a process to highlight particularly problematic substances and specifically targeted prisons to allow for swift intervention to reduce the opportunity for escalation. Furthermore, this could generate an efficient network to share information regarding these substances and prepare other prisons for imminent emerging substances. This opportunity would need to be supported by HMPPS to facilitate the network, plus those conducting the analytical support, trace detection equipment providers, the private forensic providers who analyse the rMDT results, and the NHS hospitals in the local area providing healthcare for those affected, but this scale of intelligence would be greatly beneficial to the prison sector. Additionally, with some people in homeless communities, Community Rehabilitation Companies and Approved Premises using synthetic cannabinoids (Grace, Lloyd and Perry, 2019), the information gathered through this network could be shared with support schemes to help provide harm reduction and education. Although this approach would still originate from reactive processes, it would allow for more proactive interventions across the country.

The following recommendations and considerations have been listed to suggest a model for applying a screening, confirmation, and feedback cycle across England for the analysis of drugs from prisons:

a) Build and establish networks for partnerships with local prison security teams, search teams and regional hubs to investigate current processes for the identification of drugs in prisons. The opportunity to discuss the drug strategies with the security and search teams directly will establish what support should be provided and measure the success of current processes. The needs of the prison may tailor the approach needed, for example, more effort may be needed for the analysis of throw-over samples rather than letters if that is their most common seizure type, so the research group may need to dedicate time to developing new sample extraction methods.
b) Organise logistics surrounding the transportation of samples under United Kingdom Controlled Drug Licence, Misuse of Drugs Act 1971 and Misuse of Drugs Regulations 2001 (Regulations 5). This system would ideally utilise local police forces and dog handler vehicles due to the vehicles having appropriate safes for the transportation of drugs for training purposes.
c) Produce a plan for quantities of samples and selection criteria for analysis. This needs to be established to determine whether all post from the collaborating prisons will be analysed per research group or whether analysis will be on an intelligence-based approach utilising the screening equipment results. If analysis is undertaken *via* screening instruments, efforts could be dedicated to training staff in the prisons and in the research group for the appropriate screening technique to be prepared for substances that are not included in the library. An example of this is outlined in Chapter Chapter 2, where training was undertaken on the Itemiser 3E® to identify substances within the 9 – 10 ms region which may not produce an alarm. Rapiscan Systems Limited Itemiser 3E® or Smiths Detection IonScan600 are the primary two screening instruments available in prisons at the time of writing.
d) Establish a collaboration or partnership with the relevant screening instrument manufacturer(s) to ensure opportunities for analytical results to inform library updates upon the identification of a previous unencountered substances. This is particularly pertinent for NPS due to their ever-evolving nature. The prospect of building the libraries with definitions for each previously unencountered substance, allows for the opportunity for the instrument to alarm for the substance when encountered after the fact, and therefore reduces the chance

of the substances entering the prison. Examples of this process have been discussed in Chapters Chapter 2 and Chapter 3.

e) Measure the impact of library updates by systematically gathering and processing screening data from instruments across multiple sites. The opportunity to investigate the data collected by each screening instrument allows for a retrospective analysis of the signal and alarm data, which can determine the prevalence of a substance prior to library updates. The data analysis will also be able to highlight the impact of the intervention by showing any relationship or trends in alarms and signals after library updates (both alarm and signal data should be recorded for the purpose of this analysis). Examples of this analysis has been conducted in Chapter Chapter 3 using an Itemiser 3E®.

f) Plan opportunities for resource, information and intelligence sharing throughout research groups. This should include HMPPS as a centralised unit to allow for the information gathered to be disseminated to prison intelligence units across the country. This system should be as timely as possible to try make any reactive responses for substances at one institution proactive for other institutions. These responses would be in the form of library updates and intelligence surrounding notification of sample types or substances to be aware of. Certified reference standards could also be shared between research groups if needed.

g) Funding would need to be considered depending on the level and scale of service provided. Pricing would need to be reasonable to enable prisons to factor the costs into budgets, therefore there may need to be a scale depending on the level of service that is able to be provided, i.e., use of certified reference standards for quantification would need to be charged at a higher rate than qualitative identifications using GC-MS with MS libraries and online reference spectra. Discussions surrounding method development time for the identification of samples and drugs outside of the routine type would need to be discussed. These funding opportunities may be able to be accounted for by the governing body at some point in the future, such as the work of Norman, Walker, and Mckirdy (2020) at the University of Dundee’s Leverhulme Research Centre for Forensic Science (LRCFS) being funded through the Scottish Prison Service, however, in the meantime, this may need to draw from regionalised HMPPS budgets.

In terms of stakeholder benefit, recommendation (a) would provide the structure within HMPPS for the network to build upon, and recommendations (c), (e) and (f) could aid HMPPS intelligence teams when utilising the information gathered, plus add strength and integrity when sharing with drug early warning networks. In terms of the instrument provider, they would benefit from recommendations (d) and (e) for product and service development, which in turn would benefit HMPPS as a primary customer.

Finally, if research groups already investigating drugs in prisons across the country (especially those discussed within section 4.5) were to consider and adopt these recommendations into their practice, then there would be an opportunity to offer a screening, confirmation and feedback cycle for the identification of drugs, specifically synthetic cannabinoids, across English prisons.

4.7 Future threats and challenges

The focus of this research has been on synthetic cannabinoids, however, as the drug markets change over time, there may be new threats in the near future. Some examples of substances which may prove to be popular within UK prisons in the coming years are hexahydrocannabinol, nitazenes and xylazines.

Hexahydrocannabinol (HHC) is a semi-synthetic cannabinoid produced from cannabidiol (CBD) and exhibits similar effects to THC on the user. It has grown popular as a legal replacement for cannabis and THC across the United States of America (due to legislation changes) and Europe, and is often branded as undetectable *via* drug testing. It is not currently scheduled under the 1961 and 1971 United Nations drug conventions but would be controlled under the Psychoactive Substances Act 2016 in the UK (EMCDDA, 2023). At the time of writing, there is very little information regarding the use of HHC within UK prisons, however, it could potentially act as an alternative to synthetic cannabinoids and therefore may become popular within prisons, as users may prefer a substance that has more similar potency and effects to THC (EMCDDA, 2023). In response to this potential rise in popularity, security teams within prisons may wish to ensure their trace detection equipment will include definitions to be able to identify HHC presence, plus ensure it will be detected on rMDT when screening for consumption.

Outside of cannabinoids, the use of nitazenes may pose an emerging threat and cause challenges within UK prisons. Nitazenes are new synthetic opiates (NSO) and are significantly more potent than fentanyl. The use of nitazenes has been raised as a concern to public health by the Advisory Council for the Misuse of Drugs due to the significant potencies they exhibit (Advisory Council for the Misuse of Drugs, 2022). As

a result, 11 synthetic opiates were added to the Misuse of Drugs Act 1971 list of Class A scheduled substances and classified as Schedule 1 substances for the Misuse of Drugs regulations 2001 in February 2023, to try to control the use of these drugs and limit associated deaths (Home Office, 2023). This movement was partly because of 27 fatalities involving nitazene presence in post-mortem samples (alongside other drugs) being recorded in 2021 (Advisory Council for the Misuse of Drugs, 2022), plus nitazenes being present within 36 screened public samples analysed by WEDINOS between April 2022 and March 2023. Of these samples, none were recorded to have nitazene as the substance intended to be purchased (WEDINOS, 2023b) and therefore highlighting that users were not aware that nitazenes were present. Furthermore, fatalities have continued to occur into 2023, with the National Crime Agency reporting 54 deaths where nitazenes were identified to be present between July and December 2023 (Holland *et al.,* 2024).

The presence of nitazenes has also been documented within prisons within the UK, specifically Scotland, in the form of pills and soaked paper alongside synthetic cannabinoids and benzodiazepines (Public Health Scotland, 2023). One major concern surrounding use within prisons is that users are not aware of the substances that they are administering, especially if they are using in a poly-drug format. Furthermore, if nitazenes enter the prisons and are used by those who may use drugs sporadically or only when they are available, they may be more susceptible to overdoses due to such high potencies (Holland *et al.,* 2024). In terms of detection, care will need to be taken to ensure intelligence is gathered to allow for competent identification *via* screening and confirmatory tests for the current and potential future nitazenes that may enter prisons. The Advisory Council for the Misuse of Drugs list 31 nitazene compounds which have been investigated (Advisory Council for the Misuse of Drugs, 2023a), and therefore a selection of these need to be included in screening instrument libraries to increase the chance of detection and prevent them entering prisons, plus included on rMDT libraries to track use. In addition, prisons may need to be prepared for increased opioid overdoses, and therefore increase awareness of the risks associated, signs, symptoms and intervention protocols, such as increasing naloxone availability and ensure staff are trained on how to administer it (Public Health Scotland, 2023).

Finally, in the near future, xylazine may also pose as a threat to public health, and therefore raise concerns within prisons. Xylazine is a non-opioid sedative often used in veterinary settings and not registered for human consumption. It has been found in samples sent to the WEDINOS project between April 2022 to March 2023 by those intending to purchase a benzodiazepine, heroin, or THC (WEDINOS, 2023b) and

contributed to a fatality in the UK in December 2022 after the user had administered a mixture of xylazine, heroin, fentanyl, and cocaine (Rock *et al.,* 2023), leading to the Advisory Council for the Misuse of Drugs contacting the Home Office to offer advice on amending the Misuse of Drugs Act 1971 in June 2023 (Advisory Council for the Misuse of Drugs, 2023b). Xylazine has since been found alongside nitazenes in post-mortem samples, which is a cause for concern considering both are potent central nervous system depressants and they are being taken in conjunction with one another. Furthermore, as xylazine is not an opiate, administration of naloxone will not prove effective, therefore, prisons need to expend effort on ensuring screening techniques include xylazine to reduce the chance of it entering prisons. In the event it does enter prisons, and is used by a prisoner, staff need to be aware that if a user exhibits signs and symptoms associated with opiate overdose, but naloxone administration does not seem effective, it may be due to xylazine presence, and will require intervention by emergency services as soon as possible as there is no effective antidote for xylazine overdose at this time (Nahar, Andrews and Paterson, 2023).

In conclusion, to prepare for these future threats, time needs to be dedicated to ensuring instrument libraries include these substances and staff involved with analysis at every level (screening, confirmation by analytical techniques and urine screening through rMDT) are aware of these upcoming substances, with updates and queries communicated between these groups *via* security and central HMPPS teams.

4.8 Summary

The current work being undertaken by research groups in the UK, with the support of international organisations, including private instrument manufacturers and reference material providers, has highlighted that seizures of synthetic cannabinoids from prisons can be analysed to gain intelligence on the most prevalent and emerging substances. This work has successfully provided intelligence to HMPPS for Welsh prisons and the Scottish Prison Service through WEDINOS and the LRCFS respectively, however, the current situation does not provide an accessible route for all English prisons to have intelligence-based samples analysed by a research group or a private forensic provider. A model has been synthesised and proposed to provide a potential pathway, focusing on the expansion of current processes being implemented at various research groups based at universities across England to eventually provide the screening, confirmation, and feedback cycle service for the country. The work undertaken by the author and other research groups in England so far has been able to provide confirmatory analysis to the respective prisons in their local vicinities, however with

support from HMPPS and consideration for the recommendations provided, there is potential for growth. In the event of a private forensic provider supplying this information for prisons in England, there is still opportunity for research groups to provide investigative research surrounding screening technologies, exploratory data analysis for trend identification, and structural elucidation for substance identification.

In late 2023, the Ministry of Justice and HMPPS provided new guidance surrounding the use of detection equipment for the testing of drugs, superseding the Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework (Ministry of Justice, 2021), however, there was no outline for intelligence-based confirmatory analysis of prison post samples (Ministry of Justice, 2023a). Although this may be considered in the future, this process is not currently accounted for, and therefore, independent research groups could continue to provide this research for their local prisons, and look to expand if there is an opportunity to help serve their local communities. Without a continued process to provide a screening, confirmation, and feedback cycle for the analysis of synthetic cannabinoids from prisons for intelligence based samples, there may be a greater opportunity for synthetic cannabinoids to enter prisons, which will have adverse effects for prisoner safety and security, therefore research groups could play an important role in case this process will not be provided through contracted work.

Chapter 5 Conclusion and Further Work

The aims of this research were to apply screening and confirmatory techniques to produce an effective method to identify synthetic cannabinoids that have entered prisons, and to investigate methods surrounding feedback and dissemination of results to benefit the criminal justice system and provide more effective harm reduction to people using drugs in prisons. These aims were met through the following objectives:

Objective 1 – Work in conjunction with prison staff using the Rapiscan Systems Limited Itemiser 3E® to undertake sampling of seized prison post to identify previously unencountered synthetic cannabinoids, with the results and information disseminated to the prison and Rapiscan Systems Limited. Collected samples will be identified through structural elucidation using relevant confirmatory techniques (GC-MS, LC-MS, FTIR & NMR) to undertake the screening, confirmation and feedback cycle, which will be ongoing throughout the research.

The research undertaken to meet Objective 1 has demonstrated the opportunities, benefits and limitations that come with each step of the screening, confirmation, and feedback cycle. The analysis of 62 prison samples, including 47 prison post or similar samples, highlighted the potential to use Rapiscan Systems Limited Itemiser 3E® instruments as screening tools within local prisons to give an indication of a drug presence. Furthermore, the analytical support provided has enabled intelligence to be gathered regarding the synthetic cannabinoids that are being attempted to be smuggled into the prisons and has been used to inform library updates to the Itemiser 3E® to increase detection opportunities, therefore reduce the chance of the substances entering the prisons. The nine paper samples containing synthetic cannabinoids included approximately 25 A4 sheets of paper of paper in total. If the whole pieces of paper were soaked with synthetic cannabinoids, this would be the equivalent of 15,593 $1cm^2$ doses. Without a screening, confirmation and feedback cycle being implemented across the eleven prisons, these pieces of paper would have entered the prison for prisoners to potentially deal, sell and smoke, ultimately resulting in adverse health effects, influence bullying and fuel organised crime.

Objective 2 - Collect data from Itemiser 3E® instrument records to determine trends of synthetic cannabinoid detection across the West Midlands region and provide representative information on the impact of Itemiser 3E®, and this project, on synthetic cannabinoid prevalence in West Midlands prisons.

To meet Objective 2, analysis was conducted on 40-months' worth of data extracted from the HMP Featherstone Itemiser 3E®. The extracted data included calibration, alarm and signal files to provide insight regarding the general use of the instrument, the prevalence of synthetic cannabinoid alarms in relation to traditional drugs, prevalence comparisons of synthetic cannabinoids over the 40-month period and the impact of library additions and updates. From the confirmatory analysis conducted to meet Objective 1, library additions and updates were produced by Rapiscan Systems Limited for 5F-MDMB-PICA and 4F-MDMB-BUTINACA/MDMB-4en-PINACA, resulting in 258 alarms for 5F-MDMB-PICA and 647 alarms for 4F-MDMB-BUTINACA/MDMB-4en-PINACA after the additions and updates to the library. Furthermore, retrospective analysis through the application of drift time data to alarm and signal data was able to highlight potential 5F-MDMB-PICA, 4F-MDMB-BUTINACA/MDMB-4en-PINACA, ADB-BUTINACA and ADB-4en-PINACA presence months prior to the library amendments. This application of retrospective analysis has shown the opportunity that could be implemented for routine data collection and analysis from Itemiser 3E® instruments to determine emerging synthetic cannabinoids for more proactive approaches to library updates.

Objective 3 - Review the impact of major contributors within the area and their approaches to disseminating information on synthetic cannabinoids to determine the potential avenues for the longevity of intelligence-based analysis of synthetic cannabinoids from prisons in England.

Objective 3 surrounded the intelligence gathering of those working in the field to gain insight on best practice and inform a strategy for the analysis of intelligence-based samples from English prisons. This objective was met by researching the various university-based research groups who are undertaking research surrounding the analysis of synthetic cannabinoids in prisons, and the organisations who provide tools to aid in the analysis of drugs. In terms of the outputs of the research groups, each are producing invaluable research, however these groups are all working towards their own aims with their local prisons. In terms of researching opportunities for country-wide initiatives, focus was predominantly on the research groups within the United Kingdom that are providing confirmatory analysis services to their local prisons and private forensic companies that are conducting research across the UK, however they are not providing an ongoing opportunity for the analysis of intelligence-based prison samples. Recommendations for research groups to consider have been produced to describe how each could expand to analyse intelligence-based samples for their local prisons, and how a country-wide system could be implemented to provide the analysis of

intelligence-based samples for all of England's 116 prisons, as without the process highlighted by this research, prisons will continue to be vulnerable to the next emerging drug threat.

The aims of this research were met through the analysis conducted to meet each objective. The research has proved the importance of a screening, confirmation and feedback cycle for providing analytical support to reduce the opportunity for synthetic cannabinoids to enter prisons, and the application of data analysis has shown the impact that screening instrument updates can have. Finally, recommendations have been produced to highlight changes that should be implemented to ensure intelligence-based analysis of prison samples can occur, therefore benefitting HMPPS and those in its care.

There are various avenues for potential further work that could be undertaken following the research findings. The primary suggestion would be the continuation of the analytical support for prisons, with focus to include research surrounding the screening information gathered by the Smiths Detection IonScan600. The Smiths Detection instruments are used alongside Rapiscan Systems Limited Itemiser 3E® instruments in England, therefore research into how the Smiths Detection IonScan600s could be implemented within the screening, confirmation and feedback cycle would allow prisons to be more prepared for emerging drugs.

Although the prioritised sample type for this research has been paper, there is scope to analyse more sample types which could also have synthetic cannabinoids soaked into them, including clothing and other items that may be included in prisoner transfer possessions or in parcel deliveries to prisoners. However, research will need to be dedicated to sampling and extraction methods, which may be applied to large paper sample seizures too.

Expansion of the research, in collaboration with HMPPS, would include recruitment of more prisons in the Midlands region. Funding opportunities would need to be explored to be able to recruit additional researchers, purchase certified reference standards for confirmation of identifications and potential quantification opportunities, as well as to cover the price of consumables and instrument use.

In terms of further work applications for the methods used, more time and research needs to be dedicated to the LC-MS method to understand the retention time shifts seen. This investigation should focus on different sample injection parameters, such as mixing some of the eluent solvents with the sample prior to injection, and also analysing certified reference standards alongside the samples.

To gain more intelligence surrounding the pharmacological effect of the synthetic cannabinoids encountered in prison samples, further work could be dedicated to applying biological receptor assay testing to determine the affinity of the substances to the CB_1 and CB_2 receptors, similar to the work undertaken by Kronstrand *et al.,* (2021) for prison paper samples or Pulver, Riedel *et al.,* (2022) for test purchases and seizures. This analysis can give an insight into potency, and therefore could be helpful information for health services within the prison system to increase awareness of potentially problematic substances. Furthermore, further work could be dedicated to collaborating with certified reference material manufacturers and researchers focusing on prophetic drug discovery, such as Banister *et al.*, (2016), to build awareness of the potential next emerging drugs and therefore aim to apply proactive approaches to confirmatory analysis.

Research should also be dedicated into identifying the cause of false positives on the Itemiser 3E® instrument. Many of the substances analysed and discussed in Section 2.3.5 were submitted as a result of a false positive alarm indication by the Itemiser 3E® instrument. Although the analysis of these substances identified some chemicals and potential narratives surrounding why they may have been present, they were not the synthetic cannabinoids suggested during screening. In addition, there were samples that were clearly odorous and heavily stained, however no synthetic cannabinoid was detected. There is more research that is needed to discover if the presence of a cleaning product or commonly occurring chemicals seen in the GC-MS results may be the reason for the false positive for some of the synthetic cannabinoids, and if so, why it may be present on paper samples. Although there is a benefit in being cautious and withholding the post when there have been false positives, unnecessarily withholding post from prisoners is not the intention, and therefore there should be more confidence in the indications provided by the Itemiser 3E® instrument to reduce the chance of this occurring.

Chapter 6 References

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Appendices

Appendix 1 – Sample preparation method tables

Table 1: Sample table depicting which samples were analysed on GC-MS and LC-MS and the corresponding solvent used (blue for acetone, green for methanol)

Sample preparation method	Samples analysed by GC-MS	Samples analysed by LC-MS
Method 1	Acetone: MJA1, MJA2, RANBY1, RANBY2	
Method 2	Acetone: MJA3, MJA4, MJA5, MJA6, MJA7, MJA9, MJA11, MJA12, MJA13, MJA14, MJA15, MJA16, MJA17 and MJA18	Methanol: MJA3, MJA5, MJA11, MJA12, MJA13, MJA14, MJA15, MJA16, MJA17, MJA18
Method 3	Methanol: MJA3, MJA5, MJA6	
Method 4	Methanol: MJA8, MJA20, MJA21, MJA22, MJA23, MJA24, MJA25, MJA26, MJA27, MJA28, MJA29, MJA30, MJA31, MJA40, MJA41, MJA42, MJA43, MJA44, MJA45, MJA46, MJA47, MJA56, MJA58 Acetone: MJA32, MJA33, MJA34, MJA35, MJA36, MJA37, MJA38	Methanol: MJA8, MJA19, MJA20, MJA21, MJA22, MJA23, MJA24, MJA25, MJA26, MJA27, MJA28, MJA29, MJA30, MJA31, MJA40, MJA41, MJA42, MJA43, MJA44, MJA45, MJA46, MJA47, MJA56, MJA58 Acetone: MJA32, MJA33, MJA34, MJA35, MJA36, MJA37, MJA38
Method 5	Methanol: MJA19, MJA52, MJA55	Methanol: MJA19, MJA52, MJA55
Method 6	Methanol: MJA10	

Table 2: Sample preparation methods for samples analysed by NMR

Sample preparation method	Samples
NMR Method 1	MJA11
NMR Method 2	MJA3, MJA5, MJA6

Table 3: Sample preparation methods for the samples analysed by FTIR and the corresponding instruments

Sample preparation method	Samples
Sample direct onto ATR window (Thermo Fisher iS10)	MJA20, MJA21, MJA22, MJA23, MJA24, MJA25, MJA26, MJA39, MJA48, MJA49, MJA50, MJA53, MJA54, MJA57, MJA59, MJA60
Reconstitution in acetone (Spectrum 2)	MJA3, MJA5, MJA7, MJA14, MJA38
Sample in methanol (Spectrum 2)	MJA40a

Appendix 2 – In-house synthetic cannabinoid Excel spreadsheet for PCDL

Name	Synonyms &/or CAS	Formula	RMM	Base Peak	Exact Mass	SMILES
5F-ADB-PINACA	1863065-90-0	C19H27FN4O2	362.5	233	362.211792	O=C(NC(C(N)=O)C(C)(C)C)C1=NN(CCCCCF)C2=C1C=CC=C2
ADB-PINACA	1633766-73-0	C19H28N4O2	344.5	215.1	344.221222	O=C(NC(C(N)=O)C(C)(C)C)C1=NN(CCCCC)C2=C1C=CC=C2
5F-AMB	(S)-5F-AMB/5-fluoro AMP/5-fluoro MMB-PINACA/5F-AMP/1801552-03-3	C19H26FN3O3	363.4	233	363.19582	O=C(N[C@H](C(OC)=O)C(C)C)C1=NN(CCCCCF)C2=C1C=CC=C2
MMB-FUBINACA	AMB-FUBINACA/ FUB-AMB/1971007-92-7	C21H22FN3O3	383.4	109/253	383.16452	FC(C=C1)=CC=C1CN2N=C(C(N[C@H](C(OC)=O)C(C)C)=O)C3=CC=CC=C32
MAB-CHMINACA	ADB-CHMINACA/1863065-92-2	C21H30N4O2	370.5	241	370.23688	O=C(NC(C(N)=O)C(C)(C)C)C1=NN(CC2CCCCC2)C3=C1C=CC=C3
MDMB-CHMICA	1971007-95-0	C23H32N2O3	384.5	240.1	384.24129	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CC2CCCCC2)C3=C1C=CC=C3
AB-CHMINACA	1185887-21-1	C20H28N4O2	356.5	241	356.22123	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CC2CCCCC2)C3=C1C=CC=C3
5F-ADB	(R)-5F-MDMB-PINACA/1838134-16-9	C20H28FN3O3	377.5	233	377.21147	O=C(N[C@@H](C(OC)=O)C(C)(C)C)C1=NN(CCCCCF)C2=C1C=CC=C2
4-cyano CUMYL-BUTINACA	4-CN-BINACA-ADB/ 4-CN CUMYL-BINACA/ CUMYL-4CN-BINACA/ CUMYL-CB-PINACA/ CUMYL-CYBINACA/ SGT-78/1631074-54-8	C22H24N4O	360.5	226	360.19501	O=C(NC(C)(C)C1=CC=CC=C1)C2=NN(CCCCC#N)C3=C2C=CC=C3
5F-AKB48	AKB48 N-(5-fluoropentyl) analog/5-fluoro APINACA/ APINACA 5-fluoropentyl analog/1400742-13-3	C23H30FN3O	383.5	233	383.23729	O=C(NC1(C[C@@H]2C3)C[C@H](C2)C[C@H]3C1)C4=NN(CCCCCF)C5=CC=CC=C54
5F-PB22	5-fluoro QUPIC/1400742-41-7	C23H21FN2O2	376.4	232	376.15871	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=CN(CCCCCF)C4=C3C=CC=C4

MMB-2201	5-fluoro AMB-PICA/I-AMB/5-fluoro MMB-PICA/1971007-87-0	C20H27FN2O3	362.5	232	362.20057	O=C(N[C@H](C(OC)=O)C(C)C)C1=CN(CCCCCF)C2=C1C=CC=C2
5F-MDMB-PICA	MDMB-2201/1971007-88-1	C21H29FN2O3	376.5	232	376.21622	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CCCCCF)C2=C1C=CC=C2
MMB-CHMICA	AMB-CHMICA/1971007-94-9	C22H30N2O3	370.5	240.1	370.22564	O=C(N[C@H](C(OC)=O)C(C)C)C1=CN(CC2CCCCC2)C3=C1C=CC=C3
THJ-2201	AM2201 indazole analog/5-fluoropentyl JWH 018 indazole analog/5-fluoro THJ 018/1801552-01-1	C23H21FN2O	360.4	127	360.16379	O=C(C1=CC=CC2=C1C=CC=C2)C3=NN(CCCCCF)C4=C3C=CC=C4
AB-FUBINACA	1185282-01-2	C20H21FN4O2	368.4	109	368.16485	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CC2=CC=C(F)C=C2)C3=C1C=CC=C3
UR-144	KM-X1/1199943-44-6	C21H29NO	311.5	214	311.22491	CCCCCN1C2=CC=CC=C2C(C(C3C(C)(C)C3(C)C)=O)=C1
FUBIMINA	BIM-2201/BZ-2201/FTHJ/1984789-90-3	C23H21FN2O	360.4	127/271	360.16379	O=C(C1=NC2=C(C=CC=C2)N1CCCCCF)C3=CC=CC4=CC=CC=C43
AKB48	APINACA/1345973-53-6	C23H31N3O	365.5	215	365.24671	O=C(NC1(C[C@@H]2C3)C[C@H](C2)C[C@H]3C1)C4=NN(CCCCC)C5=CC=CC=C54
MDMB-CHMCZCA	EGMB-CHMINACA/NO CAS	C27H34N2O3	434.6	290.1	434.25694	O=C(N[C@@H](C(C)(C)C)C(OC)=O)C1=CC2=C(C=C1)N(CC3CCCCC3)C4=C2C=CC=C4
ADB-FUBINACA	1445583-51-6	C21H23FN4O2	382.4	109	382.1805	O=C(NC(C(N)=O)C(C)(C)C)C1=NN(CC2=CC=C(F)C=C2)C3=C1C=CC=C3
STS-135	5-fluoro APICA/N-adamantyl-1-fluoropentylindole-3-Carboxamide/1354631-26-7	C24H31FN2O	382.5	232	382.24204	FCCCCCN1C=C(C(NC2(C[C@@H]3C4)C[C@H](C3)C[C@H]4C2)=O)C5=CC=CC=C51
FAB-144	CHEMSPIDER=32055552	C20H27FN2O	330.4	233	330.21074	FCCCCCN1N=C(C(C2C(C)(C)C2(C)C)=O)C3=C1C=CC=C3
THJ-018	JWH 018 indazole analog/1364933-55-0	C23H22N2O	342.4	127	342.17321	O=C(C1=NN(CCCCC)C2=C1C=CC=C2)C3=C4C(C=CC=C4)=CC=C3
AB-PINACA	1445752-09-9	C18H26N4O2	330.4	215	330.20558	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CCCCC)C2=C1C=CC=C2
BB-22	QUCHIC/1400742-42-8	C25H24N2O2	384.5	240	384.18378	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=CN(CC4CCCCC4)C5=C3C=CC=C5
MDMB-FUBINACA	FUB-MDMB/MDMB-Bz-F/1971007-93-8	C22H24FN3O3	397.4	109	397.18017	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=NN(CC2=CC=C(F)C=C2)C3=C1C=CC=C3

SDB-005	NO CAS OR SYNONYM	C23H22N2O2	358.4	215	358.16813	O=C(OC1=C(C=CC=C2)C2=CC=C1)C3=NN(CCCCC)C4=CC=CC=C43
SDB-006	695213-59-3	C21H24N2O	320.4	214	320.18886	CCCCCN1C=C(C(NCC2=CC=CC=C2)=O)C3=C1C=CC=C3
5F-PCN	5-fluoro MN-21	C23H22FN3O	375.4	233.1	375.17469	O=C(NC1=C(C=CC=C2)C2=CC=C1)C3=CN(CCCCCF)C4=C3C=NC=C4
NM-2201	CBL-2201/CHEMSPIDER=30922478	C24H22FNO2	375.4	232.1	375.16346	FCCCCCN1C=C(C(OC2=C(C=CC=C3)C3=CC=C2)=O)C4=CC=CC=C41
5-fluoro CUMYL-PINACA (CRM)	SGT-25/1400742-16-6	C22H26FN3O	367.5	233.1	367.20599	O=C(NC(C)(C)C1=CC=CC=C1)C2=NN(CCCCCF)C3=C2C=CC=C3
AKB48 N-(4-fluorobenzyl) analog	AFB-48/AFUBINACA/FUB-AKB-48/FUB-APINACA/CHEMSPIDER=30922497	C25H26FN3O	403.5	109	403.20599	O=C(NC1(C[C@H]2C3)C[C@H]3C[C@H](C2)C1)C4=NN(CC5=CC=C(F)C=C5)C6=C4C=CC=C6
IPO-33	CHEMSPIDER=52085250	C20H22N2O	306.4	?	306.17321	CCCCCn1c2ccccc2c(n1)C(=O)Cc3ccccc3
FDU-PB-22	1883284-94-3	C26H18FNO2	395.4	109	395.13216	O=C(OC1=C(C=CC=C2)C2=CC=C1)C3=CN(CC4=CC=C(F)C=C4)C5=C3C=CC=C5
5F-NPB-22	1445579-79-2	C22H20FN3O2	377.4	233	377.15396	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=NN(CCCCCF)C4=C3C=CC=C4
PX 2	FU-PX/5F-APP-PINACA/CHEMSPIDER=58190367	C22H25FN4O2	396.5	232.9	396.19615	O=C(N[C@H](C(N)=O)CC1=CC=CC=C1)C2=NN(CCCCCF)C3=C2C=CC=C3
EG-2201		C28H24FNO	409.5	334.1	409.18419	O=C(C1=CC=CC2=C1C=CC=C2)C3=CC(C(C=CC=C4)=C4N5CCCCCF)=C5C=C3
MEP-FUBINACA	MMB-FUBINACA isomer 1	C21H22FN3O3	383.4	109	383.16452	FC(C=C1)=CC=C1CN2N=C(C(N[C@H](C(OC)=O)CCC)=O)C3=CC=CC=C32
5C-AB-PINACA	5-chloro ABP/1801552-02-2	C18H25ClN4O2	364.9	249	364.1666	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CCCCCCl)C2=C1C=CC=C2
APP-CHMINACA	PX 3/1185887-14-2	C24H28N4O2	404.5	241.1	404.22123	O=C(N[C@H](C(N)=O)CC1=CC=CC=C1)C2=NN(CC3CCCCC3)C4=C2C=CC=C4
5F-phenyl-PICA	LTI-701/1776086-01-1	C20H21FN2O	324.4	232	324.16379	FCCCCCN1C=C(C(NC2=CC=CC=C2)=O)C3=CC=CC=C31
JTE-907	282089-49-0	C24H26N2O6	438.5	?	438.17909	O=C1NC2=C(OCCCCC)C(OC)=CC=C2C=C1C(NCC3=CC=C(OCO4)C4=C3)=O

URB-597	546141-08-6	C20H22N2O3	338.4	213	338.16304	O=C(NC1CCCCC1)Oc1cccc(c1)c1cccc(c1)C(=O)N
AM-2201	335161-24-5	C24H22FNO	359.4	359	359.16854	O=C(C1=CC=CC2=C1C=CC=C2)C3=CN(CCCCCF)C4=CC=CC=C43
AM-1248	335160-66-2	C26H34N2O	390.6	98	390.26711	O=C(C1(C2)C[C@@H]3C[C@H](C1)C[C@H]2C3)C4=CN(CC5N(C)CCCC5)C6=C4C=CC=C6
AM-906	180989-26-8/ CHEMSPIDER= 8265345	C23H34O3	358.5	?	358.25079	CCCCC/C=C\C1=CC(=C2[C@@H]3C[C@@H](CC[C@H]3C(OC2=C1)(C)C)CO)O
EG-018	CHEMSPIDER=30922490	C28H25NO	391.5	334	391.19361	O=C(C1=CC=CC2=C1C=CC=C2)C3=CC(C(C=CC=C4)=C4N5CCCCC)=C5C=C3
3-CAF	CHEMSPIDER=32055555	C24H15FN2O2	382.4	238.9	382.11176	O=C(OC1=CC(C=CC=C2)=C2C=C1)C3=NN(C4=CC=CC=C4F)C5=C3C=CC=C5
5C-AKB-48	5-chloro APINACA/2160555-52-0	C23H30ClN3O	400	249	399.20774	ClCCCCCN1N=C(C(NC23C[C@H]4C[C@H](C[C@@H](C3)C4)C2)=O)C5=CC=CC=C51
5-fluoro-3,5-AB-PFUPPYCA	AB-FUPPYCA/5-fluoro AB-FUPPYCA/ 5-fluoro AB-FUPYCA/ AZ-037	C20H26F2N4O2	392.4	249	392.20238	FC1=CC=C(C2=NN(CCCCCF)C(C(N[C@@H](C(C)C)C(N)=O)=O)=C2)C=C1
5F-SDB-005	CHEMSPIDER=30646766	C23H21FN2O2	376.4	233	376.15871	O=C(OC1=C(C=CC=C2)C2=CC=C1)C3=NN(CCCCCF)C4=CC=CC=C43
FUB-PB-22	1800098-36-5	C25H17FN2O2	396.4	109	396.12741	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=CN(CC4=CC=C(F)C=C4)C5=C3C=CC=C5
Cumyl-PeGaClone	SGT-151/2160555-55-3	C25H28N2O	372.5	254	372.22016	CC(C1=CC=CC=C1)(C)N2C=CC(N(CCCCC)C3=C4C=CC=C3)=C4C2=O
5-fluoro Cumyl-PeGaClone	5F-SGT-151	C25H27FN2O	390.5	272	390.21074	CC(C1=CC=CC=C1)(C)N2C=CC(N(CCCCCF)C3=C4C=CC=C3)=C4C2=O
AM-2233	444912-75-8	C22H23IN2O	458.3	98	458.08551	O=C(C1=C(I)C=CC=C1)C2=CN(CC3N(C)CCCC3)C4=CC=CC=C42
5F-AB-PINACA	AB-PINACA 5-fluoro analog/ 1800101-60-3	C18H25FN4O2	348.4	233	348.19615	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CCCCCF)C2=C1C=CC=C2
5F-AMBICA	5F-AB-144/MBA-2201/5F-ABICA/5F-AB-PICA/1801338-26-0	C19H26FN3O2	347.4	232	347.20091	NC(C(C(C)C)NC(=O)C1=CN(C2=CC=CC=C12)CCCCCF)=O
ADSB-FUB-187	CHEMSPIDER= 65322246	C26H31ClFN5O4S	564.1		563.17693	FC1=CC=C(C=C1)CN2C3=C(C(C(NC(C(C)(C)C)C)C(NCCNS(C4CC4)(=O)=O)=O)=O)=N2)C=CC=C3Cl
AB-001	JWH 018 adamantyl analog/1345973-49-0	C24H31NO	349.5	214	349.24056	CCCCCN1C2=CC=CC=C2C(C([C@@]3(C4)CC5CC4CC(C5)C3)=O)=C1
5-chloro AB-PINACA	5-chloro ABP/1801552-02-2	C18H25ClN4O2	364.9	249	364.1666	O=C(N[C@H](C(N)=O)C(C)C)C1=NN(CCCCCCl)C2=C1C=CC=C2

4F-ADB	4F-MDMB-PINACA	C20H28FN3O3	377.5	233	377.21147	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=NN(CCCC(F)C)C2=C1C=CC=C2
MMB022	MMB-4en-PICA	C20H26N2O3	342.4	212	342.19434	O=C(N[C@H](C(OC)=O)C(C)C)C1=CN(CCCC=C)C2=C1C=CC=C2
5,3-AB-CHMFUPPYCA	AB-CHFUPYCA/ AZ-037	C22H29FN4O2	400.5	285.1	400.22745	FC(C=C1)=CC=C1C2=CC(C(N[C@H](C(N)=O)C(C)C)=O)=NN2CC3CCCCC3
5-fluoro MPP-PICA	MPHP-2201	C24H27FN2O3	410.48	232	410.20057	O=C(N[C@H](C(OC)=O)CC1=CC=CC=C1)C2=CN(CCCCCF)C3=C2C=CC=C3
5-fluoro CUMYL-PICA	SGT-67	C23H27FN2O	366.5	232	366.21074	O=C(NC(C)(C)C1=CC=CC=C1)C2=CN(CCCCCF)C3=C2C=CC=C3
EMB-FUBINACA	AEB-FUBINACA/ FUB-EMB/ FU-AEB	C22H24FN3O3	397.5	109	397.18017	FC(C=C1)=CC=C1CN2N=C(C(N[C@H](C(OCC)=O)C(C)C)=O)C3=CC=CC=C32
AM-679	335160-91-3	C20H20INO	417.3	214	417.05896	CCCCCN1C2=CC=CC=C2C(C(C3=CC=CC=C3I)=O)=C1
5-fluoro CUMYL-P7AICA	CUMYL-5-fluoro P7AICA/5-fluoro CUMYL-7-PAICA/SGT-263	C22H26FN3O	367.5	233	367.20599	O=C(NC(C)(C)C1=CC=CC=C1)C2=CN(CCCCCF)C3=C2C=CC=N3
EAM2201	JWH 210 N-(5-fluoropentyl) analog/1364933-60-7	C26H26FNO	387.5	232	387.19984	CCC1=CC=C(C(C2=CN(CCCCCF)C3=C2C=CC=C3)=O)C4=C1C=CC=C4
JWH-018	AM678/209414-07-3	C24H23NO	341.5	127	341.17796	CCCCCn1cc(C(=O)c2cccc3ccccc23)c2ccccc12
JWH-122	619294-47-2	C25H25NO	355.5	355	355.19361	CCCCCN1C2=C(C=CC=C2)C(C(C3=CC=C(C)C4=C3C=CC=C4)=O)=C1
PB-22	QUPIC/1400742-17-7	C23H22N2O2	358.4	214	358.16813	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=CN(CCCCC)C4=C3C=CC=C4
4F-MDMB-BUTINACA	4F-MDMB-BINACA	C19H26FN3O3	363.4	219	363.1958	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=NN(CCCCF)C2=C1C=CC=C2
MDMB-4en-PINACA	5CL-ADB-A/MDMB-PENINACA/MDMB-PINACA N1-pentyl-4-en isomer	C20H27N3O3	357.5	213	357.20524	O=C(N[C@@H](C(C)(C)C)C(OC)=O)C1=NN(CCCC=C)C2=C1C=CC=C2
5Br-AKB48	5Br-APINACA/2160555-51-9	C23H30BrN3O	444.41	294	443.15723	BrCCCCCN1N=C(C(NC23C[C@H]4C[C@H](C[C@@H](C3)C4)C2)=O)C5=CC=CC=C51

ACHMINACA	Adamantyl-CHMINACA/ 1400742-33-7	C25H33N3O	391.6	241	391.26236	O=C(NC12C[C@@H]3C[C@@H](C[C@@H](C3)C2)C1)C4=NN(CC5CCCCC5)C6=C4C=CC=C6
MMB-FUBICA	AMB-FUBICA/ 1971007-90-5	C22H23FN2O3	382.43	109	382.16927	FC(C=C1)=CC=C1CN2C=C(C(N[C@H](C(OC)=O)C(C)C)=O)C3=CC=CC=C32
MDMB-FUBICA	1971007-91-6	C23H25FN2O3	396.5	109	396.18492	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CC2=CC=C(F)C=C2)C3=C1C=CC=C3
APP-BUTINACA	APP-BINACA	C21H24N4O2	364.4	201	364.18993	O=C(N[C@H](C(N)=O)CC1=CC=CC=C1)C2=NN(CCCC)C3=C2C=CC=C3
CP 55,490	83002-04-4/ CHEMSPIDER=21467436	C24H40O3	376.6	147	376.29776	CCCCCCC(C)(C)c1ccc(c(O)c1)[C@@H]1C[C@H](O)CCC1CCCO
AMB-CHMINACA	MA-CHMINACA/AMB N-methylcyclohexyl analog/MAB-AB-CHMINACA/MMB-CHMINACA/ 1971007-96-1/CHEMSPIDER=32055578	C21H29N3O3	371.5	241.1	371.22089	O=C(N[C@@H](C(C)C)C(OC)=O)C1=NN(CC2CCCCC2)C3=C1C=CC=C3
MDMB-CHMINACA	(S)-MDMB-CHMINACA/1185888-32-7/CHEMSPIDER=32055574	C22H31N3O3	385.5	241.1	385.23654	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=NN(CC2CCCCC2)C3=C1C=CC=C3
AMB-PINACA	AMB/AMP MMB-PINACA/1890250-13-1/CHEMSPIDER=30646782	C19H27N3O3	345.4	215	345.20524	O=C(N[C@H](C(OC)=O)C(C)C)C1=NN(CCCCC)C2=C1C=CC=C2
5F-PY-PICA	CHEMSPIDER=68028037	C18H23FN2O	302.4	232.1	302.17944	O=C(N1CCCC1)C2=CN(CCCCCF)C3=C2C=CC=C3
5F-PY-PINACA	CHEMSPIDER=68028052	C17H22FN3O	303.4	?	303.17469	O=C(N1CCCC1)C2=NN(CCCCCF)C3=C2C=CC=C3
MEPIRAPIM	CHEMSPIDER=52085735	C19H27N3O•HCl	349.9	214	349.19209	CCCCCN1C=C(C(N2CCN(C)CC2)=O)C3=CC=CC=C31.Cl
5F-EMB-PICA	EMB-2201/CHEMSPIDER = 84400588	C21H29FN2O3	376.5	232	376.21622	O=C(N[C@H](C(OCC)=O)C(C)C)C1=CN(CCCCCF)C2=C1C=CC=C2

NPB-22	CAS=1445579-61-2/ CHEMSPIDER= 30922491	C22H21N3O 2	359.4	215	359.163 391	O=C(OC1=C(N=CC=C2)C2=CC=C1)C3=NN(CCCCC)C4=C3C=CC=C4
MN-18	CAS=1391484-80-2/ CHEMSPIDER=29763729	C23H23N3O	357.5	215	357.184 113	O=C(NC1=C(C=CC=C2)C2=CC=C1)C3=NN(CCCCC)C4=C3C=CC=C4
JWH-081	CAS=210179-46-7/ CHEMSPIDER = 8722599	C25H25NO2	371.5	371	371.188 538	O=C(C1=CN(CCCCC)C2=C1C=CC=C2)C3=CC=C(OC)C4=CC=CC=C4 3
XLR-11	5-fluoro UR-144/5-FUR-144/ CAS=1364933-54-9/ CHEMSPIDER=28537382	C21H28FNO	329.5	232	329.215 485	FCCCCCN1C=C(C(C2C(C)(C)C2(C)C)=O)C3=C1C=CC=C3
JWH-073	CAS=208987-48-8/ CHEMSPIDER=8647081	C23H21NO	327.4	327	327.162 323	CCCCn1cc(C(=O)c2cccc3ccccc23)c2ccccc12
MAM-2201	AM2201 4-methylnaphthyl analog/ JWH 122 N-(5-fluoropentyl) analog/ CAS=1354631-24-5/ CHEMSPIDER=28289977	C25H24FNO	373.5	373	373.184 204	FCCCCCN1C2=CC=CC=C2C(C(C3=CC=C(C)C4=C3C=CC=C4)=O)=C1
APICA	JWH 018 adamantyl carboxamide/ 2NE1/ SDB-001/CAS = 1345973-50-3/ CHEMSPIDER = 29341717	C24H32N2O	364.5	214	364.251 46	O=C(NC12C[C@H]3C[C@H](C[C@@H](C2)C3)C1)C4=CN(CCCCC)C5 =C4C=CC=C5
5F-AB-P7AICA	5-fluoro AB-P7AICA/ CHEMSPIDER = 84400526	C18H25FN4 O2	348.4	233	348.196 15	O=C(N[C@H](C(N)=O)C(C)C)C1=CN(CCCCCF)C2=C1C=CC=N2
5F-MDMB-P7AICA	7'N-5-fluoro ADB/ 5-fluoro MDMB-P7AICA/ CHEMSPIDER=71117165	C20H28FN3 O3	377.5	233	377.211 47	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CCCCCF)C2=C1C=CC=N2
5F-EDMB-PICA	5-fluoro EDMB-2201/ CHEMSPIDER = 84400586	C22H31FN2 O3	390.5	232	390.231 87	O=C(N[C@H](C(OCC)=O)C(C)(C)C)C1=CN(CCCCCF)C2=C1C=CC=C2
Cumyl-CBMICA	CHEMSPIDER=84400460	C23H26N2O	346.5	212	346.204 51	O=C(NC(C)(C)C1=CC=CC=C1)C2=CN(CC3CCC3)C4=C2C=CC=C4
XLR11 N-(4-pentenyl) analog	UR-144 N-(4-pentenyl) analog/1445578-20-0/ CHEMSPIDER = 29341447	C21H27NO	309.5	212	309.209 26	O=C(C1C(C)(C)C1(C)C)C2=CN(CCCC=C)C3=C2C=CC=C3

ADB-BINACA	Cayman Chemical - ADB-BUTINACA (NMS Labs ADB-BINACA)/ CHEMSPIDER = 81407832	C18H26N4O2	330.4	201	330.20558	O=C(N[C@H](C(N)=O)C(C)(C)C)C1=NN(CCCC)C2=C1C=CC=C2
4F-MDMB-BICA	4-fluoro MDMB-BUTICA/ CHEMSPIDER=90606575	C20H27FN2O3	362.4	218	362.200562	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CCCCF)C2=C1C=CC=C2
ADB-BENZINACA	CHEMSPIDER = 57621565	C21H24N4O2	364.4	91	364.189911	O=C(NC(C(N)=O)C(C)(C)C)C1=NN(CC2=CC=CC=C2)C3=C1C=CC=C3
4F-ABINACA	4-fluoro ABUTINACA/CAS = 1445580-39-1/CHEMSPIDER = 84400585	C22H28FN3O	369.5	219	370.2289	O=C(NC1(C2)C[C@H]3C[C@H](C[C@@H]2C3)C1)C4=NN(CCCCF)C5=C4C=CC=C5
4-cyano MMB-BUTINACA	AMB-4CN-BUTINACA 4-CN AMB-BUTINACA 4-CN MMB-BINACA 4-CN MMB-BUTINACA 4-cyano AMB-BUTINACA MMB-4CN-BUTINACA	C19H24N4O3	356.4	226	356.184845	O=C(N[C@@H](C(C)C)C(OC)=O)C1=NN(CCCCC#N)C2=C1C=CC=C2
5F-AEB	5-fluoro AEB/5-fluoro EMB-PINACA/CHEMSPIDER = 67167162	C20H28FN3O3	377.5	233	377.211456	O=C(N[C@H](C(OCC)=O)C(C)C)C1=NN(CCCCCF)C2=CC=CC=C21
ADB-P7AICA	34352	C19H28N4O2	344	LC-MS DATA ONLY	344.2212	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=CN(CCCCC)C2=C1C=CC=N2
4CN-AB-BUTICA	4CN-AB-BICA, AB-4CN-BUTICA, AB-4CN-BICA	C19H24N4O2	340	LC-MS DATA ONLY	340.1899	O=C(N[C@@H](C(C)C)C(N)=O)C1=CN(CCCCC#N)C2=C1C=CC=C2
ADB-4en-PINACA	ADMB-4en-PINACA, ADB-PENINACA	C19H26N4O2	342.4	213	343.2129	O=C(NC(C(C)(C)C)C)C(N)=O)C1=NN(CCCC=C)C2=C1C=CC=C2
ADB-HEXINACA	ADB-HINACA/ CHEMSPIDER - 109107958/33820	C20H30N4O2	358.5	229	358.236877	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=NN(CCCCCC)C2=C1C=CC=C2
MDA 77	1103774-21-5	C21H23N3O3	365.4		365.1739	COC1=CC(N(CCCCC)C(/C2=N\NC(C3=CC=CC=C3)=O)=O)=C2C=C1
BZO-HEXOXIZID	MDA-19/ MDA19/MDA 19/ 1048973-47-2/ CHEMSPIDER = 24689676	C21H23N3O2	349.4	244	349.179016	O=C(/C1=N\NC(C2=CC=CC=C2)=O)N(CCCCCC)C3=C1C=CC=C3

BZO-POXIZID	5C-MDA-19, Pentyl MDA-19	C20H21N3O2	335.4	105	335.163391	O=C(N/N=C1C(N(CCCCC)C2=C\1C=CC=C2)=O)C3=CC=CC=C3
5F-BZO-POXIZID	5-fluoro BZO-POXIZID/ 5F-MDA-19/ NO HITS ON CHEMSPIDER, CAYMAN OR NPS DISCOVERY	C20H20FN3O2	353.4	248.2	353.153961	O=C(N/N=C1C(N(CCCCCF)C2=C\1C=CC=C2)=O)C3=CC=CC=C3
BZO-CHMOXIZID	benzoic acid, (2Z)-2-[1-(cyclohexylmethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]hydrazide/ 1048973-67-6	C22H23N3O2	361.4	256.1	361.179016	O=C(C1=CC=CC=C1)N/N=C(C2=O)/C3=CC=CC=C3N2CC4CCCCC4
BZO-4en-POXIZID	4en-pentyl MDA-19/	C20H19N3O2	333.4	228.1	333.147736	O=C(N/N=C1C(N(CCCC=C)C2=C\1C=CC=C2)=O)C3=CC=CC=C3
5F-MDA-19-AD	NO HITS ON CHEMSPIDER	C24H30FN3O2	411.512			FCCCCCN1C(=O)/C(=N\NC(=O)C23CC4CC(C3)CC(C2)C4)/c2c1cccc2
5F-MDA-19-TMCP	Azidoindolene 1/ 1364933-69-6/ CHEMSPIDER = 34450866	C21H28FN3O2	373.464		373.216553	FCCCCCN1C(=O)/C(=N\NC(=O)C2C(C2(C)C)(C)C)/c2c1cccc2
CUMYL-NBMICA		C26H30N2O	386.5		386.235809	O=C(NC(C)(C)C1=CC=CC=C1)C2=CN(CC3C4CCC(C4)C3)C5=C2C=CC=C5
AMP-4en-PINACA	ABO-4en-PINACA/ ABO-PENINACA	C17H22N4O2	314.4	213.1	314.174286	O=C(N[C@@H](CC)C(N)=O)C1=NN(CCCC=C)C2=C1C=CC=C2
ADB-PHETINACA	ADB-PHTINACA	C22H26N4O2	378.5	249.1	378.205566	O=C(N[C@H](C(N)=O)C(C)(C)C)C1=NN(CCC2=CC=CC=C2)C3=C1C=CC=C3
MDMB-BENZICA		C23H26N2O3	378.5	234.1	378.194336	O=C(N[C@H](C(OC)=O)C(C)(C)C)C1=CN(CC2=CC=CC=C2)C3=C1C=CC=C3
Ethylbenzyl-PeGACLONE	CUMYL PeGACLONE Ethylbenzyl isomer	C25H28N2O	372.5		372.220154	O=C1C2=C(N(CCCCC)C3=C2C=CC=C3)C=CN1C(CC)C4=CC=CC=C4
EDMB-PINACA		C21H31N3O3	373.5	215	373.236542	O=C(N[C@H](C(OCC)=O)C(C)(C)C)C1=NN(CCCCC)C2=C1C=CC=C2
MMB-FUBGACLONE		C24H23FN2O3	406.4	292.1	406.169281	O=C1C2=C(N(CC3=CC=C(F)C=C3)C4=C2C=CC=C4)C=CN1C(C(OC)=O)C(C)C
4F-EDMB-BUTINACA	4-fluoro EDMB-BUTINACA	C20H28FN3O3	377.5		377.211456	O=C(N[C@H](C(OCC)=O)C(C)(C)C)C1=NN(CCCCF)C2=C1C=CC=C2

Cumyl-INACA		C17H17N3O	279.34	280.1?	279.1372	
Cumyl-TsINACA		C24H23N3O3S	433.53	434.1?	433.146	
CH-PIATA	Cyclohexyl-PIATA/ CHX-PIATA/ CH-PIACA/ CHX-PIACA	C21H30N2O	326.5	200	327.2431	O=C(NC1CCCCC1)CC2=CN(CCCCC)C3=C2C=CC=C3
ADB-5'Br-BINACA	ADB-5'Br-BUTINACA/ADB-BUT-5Br-INACA/5Br-ADB-BUTINACA	C18H25BrN4O2	409.3	279	409.1234	O=C(N[C@H](C(N)=O)C(C)(C)C)C1=NN(CCCC)C2=C1C=C(Br)C=C2
ADB-5Br-INACA	5Br-ADB-INACA/ ADB-5-bromo-INACA	C14H17BrN4O2	353.2	308	353.0608	O=C(N[C@H](C(N)=O)C(C)(C)C)C1=NNC2=C1C=C(Br)C=C2

Appendix 3 – Full NMR operating conditions

Table 4: Jeol ECX 400 Nuclear Magnetic Resonance Spectroscopy operating conditions

Operating conditions	
NMR System	Jeol ECX 400 Nuclear Magnetic Resonance Spectrometer (400 MHz)
Solvent	Deuterated chloroform (chloroform-d) (99.8%) with 0.05% v/v tetramethylsilane (TMS)
Probe	5 mm direct liquid probe
Software	Jeol Delta 5.0.4
^{1}H Proton (400 MHz)	
Samples	MJA3_221021_001_single_pulse-1-3 MJA5_191021_001_single_pulse-1-1 MJA6_191021_001_single_pulse-1-2
X Scans	8
X Offset	5 ppm
X Sweep	7.5 kHz
X Data points	16384
Samples	MJA6_single_pulse-2-3 MJA11_311019_001_proton-1-2 RANBY1_single_pulse-2-1 RANBY2_single_pulse-2-1
X Scans	32
X Offset	5 ppm
X Sweep	7.5 kHz
X Data points	16384
Samples	MJA20_271120_001_single_pulse-2-1 MJA21_271120_002_single_pulse-1-2 MJA22_271120_003_single_pulse-1-1 MJA23_271120_004_single_pulse-1-1 MJA24_271120_005_single_pulse-1-1 MJA25_271120_006_single_pulse-1-1 MJA26_271120_007_single_pulse-1-1 Methadone hydrochloride_021220_001_single_pulse-2-2
X Scans	64
X Offset	5 ppm
X Sweep	7.5 kHz
X Data points	16384
^{13}C Carbon (100.58 MHz)	
Samples	MJA3_221021_001_single_pulse_dec-1-1 MJA5_151001_single_pulse_dec-1-2
X Scans	1000
X Offset	100 ppm
X Sweep	31.4 kHz
X Data points	32768
Samples	MJA11_311019_001_single_pulse_dec-1-1
X Scans	20000
X Offset	100 ppm
X Sweep	31.4 kHz
X Data points	32768
^{19}F Fluorine (376.03 MHz)	
Samples	MJA3_single_pulse-5-1

X Scans	750
X Offset	0 ppm
X Sweep	189.4 kHz
X Data points	16384
$^{13}C\{^{1}H\}$/ppm Carbon_dept_dec 45°, 90° and 135°	
Samples	MJA3_dept_dec_5-1 MJA3_dept_dec_6-1 MJA3_dept_dec_7-1
X Scans	2000
X Offset	100 ppm
X Sweep	250 ppm
X Data points	32768
Pulse length	8.55 uS
Samples	MJA11_141019_001_dept_dec-5-1 MJA11_141019_001_dept_dec-6-1 MJA11_141019_001_dept_dec-7-1
X Scans	20000
X Offset	100 ppm
X Sweep	31.4 kHz
X Data points	32768
HMBC ^{1}H – ^{13}C	
Samples	MJA5_151001_HMBC_ft-1-1
Scans	2048
X Offset	100 ppm
Y Offset	100 ppm
X Sweep	7.5 kHz
Y Sweep	25.2 kHz
X Data points	2048
Y Data points	256
HMQC ^{1}H – ^{13}C	
Samples	MJA5_151001_HMQC_ft-1-1
Scans	1024
X Offset	5 ppm
Y Offset	85 ppm
X Sweep	7.5 kHz
Y Sweep	17.1 kHz
X Data points	1024
Y Data points	256
HSQC ^{1}H – ^{13}C	
Samples	MJA5_151001_HSQC_ft-1-1
Scans	1024
X Offset	5 ppm
Y Offset	85 ppm
X Sweep	7.5 kHz
Y Sweep	17.1 kHz
X Data points	1024
Y Data points	256
COSY ^{1}H-^{1}H	
Samples	MJA3_21221_001_1_COSY_ft MJA5_21221_002_1_COSY_ft
Scans	256
X Offset	5 ppm
Y Offset	5 ppm

X Sweep	7.5 kHz
Y Sweep	6 kHz
X Data points	1280
Y Data points	256

Appendix 4 - List of abbreviated synthetic cannabinoids

Table 5: List of synthetic cannabinoid abbreviations and full formal chemical names from Cayman Chemical Company (2020)

Abbreviation	Formal name
4F-MDMB-BUTINACA	methyl (S)-2-(1-(4-fluorobutyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate
5F-ADB or 5F-MDMB-PINACA	N-[[1-(5-fluoropentyl)-1H-indazol-3-yl]carbonyl]-3-methyl-L-valine, methyl ester
5F-AKB-48 or 5F-APINACA	N-((3s,5s,7s)-adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide
5F-MDMB-PICA	N-[[1-(5-fluoropentyl)-1H-indol-3-yl]carbonyl]-3-methyl-L-valine, methyl ester
5F-PB-22 or 5F-QUPIC	1-(5-fluoropentyl)-1H-Indole-3-carboxylic acid, 8-quinolinyl ester
MDMB-4en-PINACA	methyl (S)-3,3-dimethyl-2-(1-(pent-4-en-1-yl)-1H-indazole-3-carboxamido)butanoate
MDMB-CHMICA	N-[[1-(cyclohexylmethyl)-1H-indol-3-yl]carbonyl]-3-methyl-L-valine, methyl ester
MMB-022 or MMB-4en-PICA	methyl (1-(pent-4-en-1-yl)-1H-indole-3-carbonyl)-L-valinate
MMB-2201, 5-fluoro AMB-PICA or 5-fluoro MMB-PICA	N-[[1-(5-fluoropentyl)-1H-indol-3-yl]carbonyl]-L-valine, methyl ester
MMB-FUBINACA	N-[[1-[(4-fluorophenyl)methyl]-1H-indazol-3-yl]carbonyl]-L-valine, methyl ester

Appendix 5 – Pilot solvent extraction study results

Table 6: Summary table for the GC results from pilot solvent extraction studies of 5F-MDMB-PICA from MJA3, MJA5 and MJA6

	Acetone = Method 2					Methanol = Method 3					
Sample	Retention time (min)	Peak Area Ion Counts	Mean area	Area %RSD	Area SD	Sample	Retention time (min)	Peak Area Ion Counts	Mean area	Area %RSD	Area SD
MJA3(A)	19.632	275943				MJA3(1)	19.632	527201			
MJA3(B)	19.632	223205				MJA3(2)	19.614	481209			
MJA3(C)	19.614	303424	267524	12.44223	33285.9496	MJA3 (3)	19.614	373467	460625.7	13.98688	64427.17
MJA5(A)	19.738	100330728				MJA5(1)	19.738	97117336			
MJA5(B)	19.72	89453992				MJA5(2)	19.738	1.08E+08			
MJA5(C)	19.738	104110792	97965171	6.342066	6213015.515	MJA5(3)	19.738	1.12E+08	1.1E+08	5.999701	6340984
MJA6(A)	19.72	63386140				MJA6(1)	19.702	64372880			
MJA6(B)	19.685	73594880				MJA6(2)	19.702	70366352			
MJA6(C)	19.702	77734008	71571676	8.424657	6029668.032	MJA6(3)	19.702	62061004	65600079	5.335245	3499925
Mean	19.68678					Mean	19.68667				
SD	0.045932					SD	0.049621				

Appendix 6 – Full table for FTIR structural inferences

Table 7: Positive inference samples with their indicative structural assignments and corresponding wavenumbers

		Wavenumber (cm^{-1})									Inference
Samples	MJA3	3333	3054	2963	1739	1466	-	1157	-	748	MMB022 and 5F-MDMB-PICA
	MJA3_1	3324	3076	2965	1741	1466	-	1156	-	748	MMB022
	MJA5	3354	-	2957	1737	1466	1216	-	-	749	5F-MDMB-PICA
	MJA7	3419	-	2963	1737	*1473 (tentative)*	1213	-	-	751	4F-MDMB-BUTINACA
	MJA14	3411	3062	2922	1737	1467	1217	-	-	750	5F-MDMB-PICA and MDMB-4en-PINACA
	MJA38	3417	-	2928	1741	1471	-	1172	820	750	MMB-FUBINACA
	MJA40	3419	3070	2918	1736	1468	1216	-	-	751	MDMB-4en-PINACA
	Assignments	Secondary amide N-H stretch[ab]	Alkene RCH= CH_2 C-H stretch[cd]	CH_3 (sp^3) C-H stretch[ad]	Ester C=O stretch[ad]	CH_3 asymmetric deformation and CH_2 scissoring (tentative)[c]	CH_3 Deformation *Tert*-butyl (tentative)[e]	CH_3 Deformation Isopropyl (tentative)[e]	Para-distributed benzene ring (tentative)[c]	Ortho-benzene from the indole or indazole C-H bending (tentative)[e]	[a]*Housecroft and Constable (2006),* [b]*Heriot Watt (2023),* [c]*Bell (2006),* [d]*Merck (2023) &* [e]*Thermo Fisher Scientific Inc. (2008)*

Appendix 7 – NIST 2.0 Library results per peak for MJA11 GC chromatogram

Table 8: GC-MS results for MJA11 with corresponding NIST 2.0 library matches and uses per product

Retention time (minutes)	Name from NIST 2.0	NIST 2.0 match score	Uses
8.368	1-Tridecanol	837	Emollient, fragrance, and skin conditioner (PubChem, 2022g)
10.374	1-Chloro-dodecane	843	Surfactant (PubChem, 2022l)
10.744	Ethylene glycol monododecyl ether	841	Surfactant and haircare conditioner (PubChem, 2022m)
13.138	Diethylene glycol monododecyl ether	846	Surfactant and cleanser (PubChem, 2022n)
13.296	Diethylene glycol monododecyl ether	746	Surfactant and cleanser (PubChem, 2022n)
14.722	Diethylene glycol monododecyl ether	808	Surfactant and cleanser (PubChem, 2022n)
14.862	Lauryl glycidylether	707	Disinfectant (PubChem, 2022o)
15.232	Triethylene glycol monododecyl ether	843	Surfactant and haircare conditioner (PubChem, 2022p)
15.373	Triethylene glycol monododecyl ether	756	Surfactant and haircare conditioner (PubChem, 2022p)
16.640	Triethylene glycol monododecyl ether	751	Surfactant and haircare conditioner (PubChem, 2022p)
16.763	Lauryl glycidylether	688	Surfactant and emulsifier (PubChem, 2022o)
17.062	Diisooctyl phthalate	947	Plasticiser (PubChem, 2022a)
17.221	Triethylene glycol monododecyl ether	697	Surfactant and haircare conditioner (PubChem, 2022p)
18.875	Octaethylene glycol monododecyl ether	651	Surfactant and household cleaner (PubChem, 2022q)
19.685	2-Butyl-1-octanol	753	Conditioner, humectant and solvent (PubChem, 2022r)

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The identification of synthetic cannabinoids in English prisons

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ABSTRACT

Synthetic cannabinoids (SC) are extremely prevalent within the prison system and cause problems for prisoners, law enforcement and health services. SC are often soaked into paper then posted into prisons therefore one of the aims of this research is to collaborate with Rapiscan Systems Ltd. and local prisons in England to measure the effectiveness of trace detection methods for the indication of SC in prison post using the Itemiser 3E®. To ensure compounds did not go undetected, samples with Ion Trap Mobility Spectrometry™ peaks indicative of synthetic cannabinoids on the Itemiser 3E® were analysed using Gas Chromatography-Mass Spectrometry, Liquid Chromatography-Quadrupole Time-of-Flight Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy to identify chemical characteristics which allowed comparison to reference spectra. Sample data spanning three years from one prison's Itemiser 3E® were collated to identify trends in drug prevalence and the influence of library updates. To date, the method has identified four compounds: 5F-MDMB-PICA, MMB-4en-PICA, 4F-MDMB-BUTINACA and MDMB-4en-PINACA on prison post which were not already included on, or needed confirmatory analysis to update, the Itemiser 3E® library. As a result, the libraries on prison Itemiser 3E®s have been updated to ensure future detection of such compounds. Trends and influences from the processed Itemiser 3E® data were also reported back to the West Midlands Prison Group. This research directly benefitted both the West Midlands Prison Group and Rapiscan Systems Ltd. and it is anticipated that the continuation of this research could be expanded to a national scale.

1. Introduction

Drugs have been a known problem in prisons for decades with use of "traditional" and prescription drugs plaguing the prison service prior to the increased popularity of synthetic cannabinoids in the UK in 2008. In recent years, synthetic cannabinoids have become one of the most popular drugs used within European prisons as 22 European countries reported NPS being used by their prisoners in 2020 [1]. In the UK, it is estimated by prison officials that 60% of the prison population use synthetic cannabinoids [2], however it is estimated by prisoners to be closer to 90% [3]. This use can lead to new addictions [2], physical and mental health issues [4], organised crime, debt and bullying, which all result in a stretched prison service [3].

The Psychoactive Substances Act 2016 [5] deemed it illegal to supply, possess with the intent to supply, produce, import, export, or possess within a custodial institution any psychoactive substances. NPS are classified by the Psychoactive Substances Act 2016 [5] as any substance that induces a psychoactive effect to an administered person. The resultant psychoactive effect may affect the person's mental or physical capacity through stimulation or depression of the central nervous system [5]. The structure of the 2016 Act was deliberately laid out to reduce the occurrence of waves of new generations of substances being produced to circumvent legislation and has been largely successful in achieving this aim compared to other countries with different legislation types where more variation is seen in the types of NPS [6,7]. However, even with 'blanket ban' style legislation, the number of NPS deaths in England and Wales has continued to increase, reaching a maximum of 258 deaths from NPS use in 2021 [8]. Two key drivers in the development of new NPS are the legislation in those countries where NPS are manufactured, particularly legislation dictating what can be produced and exported [9], and the use of novel structures to circumvent detection at ports, in prisons and in mandatory drugs tests [10,11].

One of the greatest appeals to the users of synthetic cannabinoids in prisons is that they are easy to access and are perceived as difficult to identify. Under the Prison Act 1952 [12], mandatory drug testing (MDT) through random urine samples can be undertaken to determine whether prisoners are under the influence of psychoactive substances. It is therefore important to ensure that the toxicology

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Appendix 9 – Traditional drug groups Itemiser 3E® alarm list

Table 9: Table of total alarms per substance listed in the Itemiser 3E® library. The total counts have been generated from the data spanning 40 months.

Drug group	Name of substance	Total counts of alarms
Amphetamines and cathinones	Amphetamine	68
	Amphetamine DTK*	7
	MDA/4-MMC	9
	Cathine	29
	4-MMC DTK*	45
	Ephedrine/Pseudoephedrine	10
	Ethyl	53
	MDEA	707
	MDMA DTK*	70
	Methamphetamine DTK*	107
	MPA	25
	MPDT	150
Opiates and substitutes	Buprenorphine	36
	Heroin	8
	Heroin DTK*	78
	Heroin Mix	178
	Morphine	9
	Subutex	58
Benzodiazepines and similar	Tramadol	89
	Diazepam	0
	Diazepam DTK*	21
	Gabapentin and Gabapetin [sic]	300
	Nimetazepam	49
Stimulants and others	Cocaine	0
	Cocaine DTK*	1620
	Ketamine	7
	Ketamine DTK*	82
	LSD	62
	PCP	11

**Drug Testing Kit (DTK). These definitions were produced for when water-based sample dilution methods were used for bulk powder samples prior to Itemiser 3E® screening.*