Institution: Manchester Metropolitan University		
Unit of Assessment: A3 Allied Health Professions, Dentistry, Nursing and Pharmacy		
Title of case study: Interdisciplinary research at the heart of Greater Manchester's cross-sectoral, nationally commended response to New Psychoactive Substances		
Period when the underpinning research was undertaken: 2012 - 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Oliver Sutcliffe	Senior Lecturer	2012 - present
Ryan Mewis	Lecturer, Senior Lecturer	2014 - present
Period when the claimed impact occurred: 2014 – December 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

Manchester Metropolitan University has pioneered inter-disciplinary research around New Psychoactive Substances (NPS) detection, supply, use trends and harm reduction. The research underpins city-region police and public authority infrastructure, strategy, monitoring and operational decisions. A first-of-its-kind drugs early warning system now informs 700 frontline healthcare practitioners about substances in circulation, critical incidents and emergency care protocols, informed by our MANchester DRug Analysis and Knowledge Exchange service (MANDRAKE) that uses validated methods underpinned by our research to identify and characterise NPS or adulterants in samples. This provision is the foundation of intelligence-led intervention; it marks a significant step-change in UK harm reduction and has helped to safeguard lives during major incidents and at large events. The multi-agency collaborative approach is nationally recognised as best practice and has been commended in Parliament for its effectiveness. MANDRAKE also contributes to wider evidence-based policy-making, trends monitoring and enforcement through the UK Government's Advisory Council on the Misuse of Drugs, the European Monitoring Centre for Drugs and Drug Addiction, and the World Health Organization.

2. Underpinning research

New Psychoactive Substances (NPS) pose a significant health risk to many substance-using groups, for example vulnerable populations within custody and/or rough sleeping communities. More broadly, NPS use can threaten public health and safety. Their use can especially strain emergency services when new, potent NPS or toxic substances enter circulation and cause major public health incidents, such as those reported in Manchester by the media in recent years.

Manchester Metropolitan University is at the forefront of coordinated, interdisciplinary research to combat these challenges. The integrated work programme involves psychopharmaceutical chemistry, public health, criminology and social policy studies. Research findings directly underpin the exemplary 'Manchester model' – a cross-sectoral and inter-organisational strategic response to NPS across the city-region (see Section 4). Sutcliffe leads research to develop novel libraries of chemical probes and new rapid NPS identification and analysis methods, while criminologists Ralphs, Gray and colleagues have focused on complementary social studies of use trends, supply and societal impacts.

Manchester Metropolitan is one of only two UK universities licensed to possess, supply and produce schedule 1-5 controlled drugs. The research, therefore, makes an important UK contribution to the limited body of international research in this field. Since 2012, Sutcliffe has published approximately 40 peer-reviewed papers on NPS/drugs detection and identification.

Since his arrival, Sutcliffe has designed and synthesized novel NPS libraries, now containing over 400 compounds; he has used these to elucidate the human pharmacology and mechanism of action of synthetic cannabinoids (eight examples) **[1,2]** and opiates (22 examples) **[3,4]**. In these studies, Sutcliffe synthesised, purified and characterised reference standards and conducted preliminary chemical identification and analyses from source samples. Research collaborators at the University of Dundee performed *in vitro* and *in vivo* biological assays. Co-authors of these outputs included Greater Manchester Police (GMP) collaborators.

The NPS probes were also used to co-develop with industry collaborator, Oxford Instruments, the first automated, algorithm-based NMR approach to NPS identification. Sutcliffe collected, analysed and processed spectra using his NPS reference samples to create an NMR spectral

library. The system conducts multivariate chemometric analysis using novel application of artificial neural networks. Early testing of components present in seized drug samples showed that the NMR method could rapidly identify psychoactive compounds in samples within five minutes, according to their unique chemical structures and without the need for expensive laboratory-based forensic analysis. Studies showed the new technique had low levels of false-positives (less than 1%)**[5]**. Subsequently, GMP and HMP Holme House (Category C prison) used the patent-pending technology in two field trials to screen suspected contraband (interception analysis), with due-diligence to cross-validate the system using GC-MS. Further refinement has demonstrated the first automated quantification (in 2.5 min) of MDMA, in 20 suspect tablets, without the need for an internal standard and with a high degree of accuracy **[6]**.

As described in Section 4, the novel NMR methods **[5-6]**, rapid colorimetric (presumptive) and GC-MS (confirmatory) tests for fentanyl derivatives **[4]** are now deployed routinely at critical incidents in Greater Manchester where drugs may be a factor. Sutcliffe's research on synthetic cannabinoids **[1,2]** has provided key evidence on substance prevalence, purity and mechanisms of action for the MESUS and GM-TRENDS surveys.

3. References to the research

Note: Citations, Web of Science (citations versus expected citations) – Jan 2021

1. Antonides LH, Cannaert A, Norman C, Vives L, Harrison A, Costello A, Nic Daeid N, Stove CP, **Sutcliffe** OB, McKenzie C, (2019). Enantiospecific Synthesis, Chiral Separation, and Biological Activity of Four Indazole-3-Carboxamide-Type Synthetic Cannabinoid Receptor Agonists and Their Detection in Seized Drug Samples. Front. Chem. 7:321. DOI: 10.3389/fchem.2019.00321. *Citations: 18 (expected: 3.08).*
2. Antonides LH, Cannaert A, Norman C, NicDáeid N, **Sutcliffe** OB, Stove CP, McKenzie C, (2020). Shape matters: The application of activity-based in vitro bioassays and chiral profiling to the pharmacological evaluation of synthetic cannabinoid receptor agonists in drug-infused papers seized in prisons. Drug Test Anal. 2020:1– 16. DOI: 10.1002/dta.2965.
3. McKenzie C, **Sutcliffe** OB, Read KD, Scullion P, Epemolu O, Fletcher D, Helander A, Beck O, Rylski A, Antonides LH, Riley J, Smith SA, Nic Daeid N, (2018). Chemical synthesis, characterisation and in vitro and in vivo metabolism of the synthetic opioid MT-45 and its newly identified fluorinated analogue 2F-MT-45 with metabolite confirmation in urine samples from known drug users. Forensic Toxicol. 36(2):359-374. DOI: 10.1007/s11419-018-0413-1. *Citations: 9 (expected: 6.86).*
4. Gilbert, N, Antonides, LH, Schofield, CJ, Costello A, Kilkelly B, Cain AR, Dalziel PRV, Horner K, **Mewis** RE, **Sutcliffe** OB, (2020). Hitting the Jackpot – development of gas chromatography–mass spectrometry (GC–MS) and other rapid screening methods for the analysis of 18 fentanyl-derived synthetic opioids. Drug Test Anal. 2020:12:798-811. DOI: 10.1002/dta.2771. *Citations: 1 (expected: 0.48).*
5. Lysbeth H. Antonides LH, Brignall RM, Costello A, Ellison J, Firth SE, Gilbert N, Groom BJ, Hudson SJ, Hulme MC, Marron J, Pullen ZA, Robertson TBR, Schofield CJ, Williamson DC, Kemsley K, **Sutcliffe** OB, **Mewis** RE, (2019). Rapid Identification of Novel Psychoactive and Other Controlled Substances Using Low-Field ^{1}H NMR Spectroscopy. ACS Omega 4(4):7103-7112. DOI: 10.1021/acsomega.9b00302. *Citations: 7 (Expected: 2.79).*
6. Hena Hussain J, Gilbert N, Costello A, Schofield CJ, Kemsley K, **Sutcliffe** OB, **Mewis** RE, (2020). *Quantification of MDMA in seized tablets using benchtop ^{1}H NMR spectroscopy in the absence of internal standards*. Forensic Chemistry 20:100263. DOI: 10.1016/j.forc.2020.100263.

Patent

- GB2571817A. A method for screening psychoactive substances. Inventors: David Williamson [GB]; Oliver **Sutcliffe** [GB]; Ryan **Mewis** [GB]; Kate Kemsley [GB]. Assignee: Oxford Instruments Industrial Products Ltd. Filed: 10-01-2019. Status: Pending.

Funding

- Novel detection methods for new psychoactive substances, 2016-2019. Funder: Oxford Instruments. GBP50,000. PI: Sutcliffe.

4. Details of the impact

The global emergence of synthetic drugs and NPS has posed significant challenges to law enforcement, policy-makers and healthcare professionals, all blindsided by the sudden and significant harms arising from their use **[A]**. Manchester Metropolitan's coordinated

interdisciplinary research around NPS has directly underpinned the Greater Manchester (GM) response to the problem since 2017 (see complementary impact case study, UoA20) **[A]**.

The success of the research-led 'Manchester model' is evident in high-level performance indicators and commendations. The cross-sectoral infrastructure (see following) has enabled a rapid and coordinated response to six critical incidents involving 79 hospitalisations (no deaths) since April 2017 **[A]**. Mr Nick Hurd MP (Minister of State, Home Office) indicated in Parliament the significance of Manchester's approach, saying: *"Another very good example of multi-agency working has taken place in Manchester... the multi-agency approach there appears to be working … I commend the work in Manchester"* **[B]**.

Creating new infrastructure: the GM Drugs Early Warning System

The coordinated, interdisciplinary research programme has directly underpinned three key infrastructural developments across the city-region:

The Drugs Early Warning System (DEWS) was launched in 2017 by Police and Crime Commissioner, Tony Lloyd, on the basis of research recommendations from Ralphs (C20). It now connects 700 healthcare professionals and frontline staff across Greater Manchester. Sutcliffe and Ralphs are both members of the associated GM Drug Alert Panel; Sutcliffe also sits on the DEWS steering committee **[A]**. The Strategic Lead for Substance Misuse in Greater Manchester Combined Authority (GMCA) confirms: *"Our colleagues [in GMP/Manchester City Council] recommended that the detailed testing information, rapid turnaround associated with critical incidents (2-3h) and legal compliance could enhance the GM Drugs Early Warning System (GM DEWS). Based on their national standing in the field on drug and NPS research we invited Dr Sutcliffe to support us further and become ongoing member of the GM Drug Alert Panel and the GM DEWS steering committee."* **[A]** The GM Drug Alert Panel has issued nine public alerts about dangerous batches of drugs based upon analytical/test results from MANDRAKE. **[A]**

The MANchester DRug Analysis and Knowledge Exchange service (MANDRAKE) was established in 2017 with support from Greater Manchester Police (GMP). This service provides GMP with non-forensic analysis of drug samples **[C]**. MANDRAKE's rapid methods include the benchtop NMR system and other methods developed through Sutcliffe's research (references [4-6]). According to GMP's Chief Superintendent with responsibility for the DEWS, *"this rapid non-evidential testing function is the **first of its type** available within a UK police force, and has not only in-part safeguarded lives, but had significant positive policing outcomes both locally and nationally."* **[C]**

GM-TRENDS monitors drug use trends and reveals GMCA's commitment to evidence-led strategy. Led by Ralphs, with Sutcliffe providing substance analyses, the interdisciplinary project, "*will be used to inform and develop more responsive and tailored harm reduction policies, initiatives and services and to raise awareness of emerging drug trends and potential harms to a range of frontline professionals"* **[A,D]**.

This three-pronged, research-led infrastructure was showcased at Public Health England's National Intelligence Network on Drug Health Harms Briefing in 2019, an indicator of the national significance of the work as a model of best practice. Drawing analogy from the Harry Potter children's books, the DEWS co-ordinator described the combination of DEWS, MANDRAKE and MESUS (now GM-TRENDS) as the *"Deathly Hallows of local drugs intelligence"* **[E]**. GMCA's Strategic Lead for Substance Misuse affirms this view: "*The key role of MANDRAKE within the GM Drugs Early Warning System and the GM TRENDS project represents a **significant step-change in UK harm reduction**. The public-funding of a research-led drug-testing initiative in collaboration with a police force has never been adopted before in the UK and is expected to provide a model of best practice that other areas of the country can follow"* **[A]**.

Informing city-region strategy: community safety, policing and drugs

This infrastructure is now firmly embedded into three city-region strategies. Manchester's *Community Safety Partnership Strategy 2018-21* commends MANDRAKE's contribution to the training now delivered to workers as part of a rolling programme. This strategy commits to: a) maintain up-to-date knowledge of new and emerging drugs (i.e. MESUS/GM-TRENDS and MANDRAKE); b) work with partners around the analysis of substances to reduce harm, learn about composition and identify new substances (i.e. MANDRAKE); and c) continue to develop the DEWS, ensuring that relevant stakeholders are signed up **[F]**.

Standing Together is GMCA's current Police and Crime Plan. It confirms that MANDRAKE and DEWS have become *"a trusted source of information to advise would be drug users about the specific risks associated with using particular batches of drugs"* **[F]**. As GMP's Chief Superintendent affirms, MANDRAKE makes a significant contribution to strategic city-region and national intelligence-led policing from trends analysis to rapid incident response. **[C]**

The *Greater Manchester Drug and Alcohol Strategy 2019-21* also commits to on-going support of DEWS and highlights national recognition of its significance: *"A consistent approach for reporting on emerging drug trends and sharing our understanding of local drugs issues is crucial to reducing drug related harms. That is why we have developed and will build on Greater Manchester's Drugs Early Warning System, which is recognised nationally as best practice*." The strategy highlights GMCA's commitment to "*conducting research with key informants and routine testing of substances to monitor purity levels, adulterants and the emergence of new drugs"* **[F]**.

Operational outcomes: reducing harms and safeguarding lives

MANDRAKE has tested 3,278 samples from across GM. GMCA's Strategic Lead for Substance Misuse remarks: *"We would like to emphasise that our partnership with MANDRAKE has been instrumental in ensuring that the right information is shared to the 700 professional stakeholders, through the GM DEWS, at the right time in relation to critical incidents and hospital admissions, where drugs are a factor"* **[A]**. He highlights MANDRAKE's positive support since 2017 to the police, medical professionals and GMCA in managing six critical incidents **[A]**.

MANDRAKE supported the police with rapid testing for harm reduction at the Parklife music festival, Manchester Pride (2017-2019, approximately 170,000 attendees/year) and five Warehouse Project (WHP) nights (48,624 patrons in total) **[G]**. DEWS issued two safety warnings during Pride (2017, 2018) and an alert about MDMA tablets following rapid testing at WHP (2019). Warnings were also shared via mainstream news media (the 2018 Manchester Pride alert had a total potential reach of over 40,000,000) **[H]**. The WHP alert on Twitter was viewed 16,500 times with 174 retweets **[G]**. WHP Operations Director says*: "We are particularly proud that as a result of both the testing by MANDRAKE and our social media alert there were no hospitalisations on the night and subsequently no deaths… implying that as a result of the alert, users became aware of the dangers"* **[G]**. WHP owner and GMCA's Night Time Economy Adviser, Sacha Lord, tweeted MANDRAKE saying: "*Thank you again, for keeping 10,000 people safe. Another successful night"* **[G]**.

MANDRAKE provided significant support during another major incident involving three teenagers in Bury, who took what they thought was Ecstasy. Preliminary medical examination (10pm, 17 Jan 2019) was inconclusive and GMP declared a major incident (3.45am, 18 Jan). An external service provider could not identify the substance present (11am). Gold Command authorised analysis by MANDRAKE (2pm), which confirmed the presence of alpha-PVP at 8-times the safe dose at 4.30pm (see reference [4]). The information was passed to the hospital and GM DEWS issued a public alert (6pm). All three individuals made a full recovery and no more cases were reported, indicating effective communication to potential users. The Chief Superintendent suggests MANDRAKE's support *"was key to the positive outcome."* The senior investigating officer stated: *"Without the expert work from our colleagues, we could have been dealing with a very different story this morning so please do not ignore these warnings"* **[A,C]**.

The Chief Superintendent confirms that GMP is currently in the process of formalising MANDRAKE as a part of its forensic procedure in relation to critical incidents where consumption of drugs/unknown substances may have resulted in collapses/hospitalisations or deaths. He states: *"The rationale behind this is that we are able to quickly make available valid information for dissemination both internally and via the Drugs Early Warning system after the method was proven to work in a number of previous incidents where unknown substances had believed to be responsible for one of aforementioned outcomes. An example of this was seen in the City Centre in August 2020 when a number of individuals collapsed within a period of half an hour. Samples were recovered and analysed enabling an Alert to be sent out within 2 hours"* **[C]**.

GMP also confirms that MANDRAKE's rapid testing supported an 88% improvement in operational efficiency. Although MANDRAKE analyses cannot inform decisions to charge people in custody, they do indicate whether forensic testing is required; this intelligence-led decision-making releases officers from processing duties and increases their time on the ground **[C]**.

The novel NMR system also reduced harms at HMP Holme House and was acknowledged as "best practice" by prison inspectors. The benchtop system detected and correctly identified

illicit substance in 64% of suspected contraband (verified using GC-MS). Crucially, the screening confirmed that Spice-impregnated paper was a significant supply route **[I]**. HM Prison Service's Drug Recovery Prison Programme Lead says the system led to quick and reliable identification of illicit substances and improved intelligence to inform adjudication decisions. Consequently, HM Prison Service developed a new Mail Management guidance policy and reviewed its policy on Local Searching Strategies **[I]**. HM Chief Inspector of Prisons has since cited use of the benchtop system as *"good practice".* He confirmed that the technology had disrupted the supply of illicit items and had, in part, led to a reduction in positive drug test findings from over 30% in 2017 to below 5% at the time of inspection, with parallel improvements in safety on-site **[I]**.

Informing public discourse

The research by Sutcliffe and Ralphs (C20) and their direct contribution to Greater Manchester's NPS response established them as the "go to" experts to enrich and inform media discourse. Between 2016 and 2020, Dr Sutcliffe's research and MANDRAKE featured in at least 164 media items, including a Spice "primer" article first published by The Conversation (370,000 reads), along with articles in The Guardian and appearances on BBC1 News, BBC Crimewatch and Radio 5 Live (e.g. Victoria Derbyshire phone-in). Total media reach was approximately 240,000,000 people across ten countries including Germany and the United States **[H]**. Sutcliffe and Ralphs also provided their research insights in the feature-length Unilad original documentary *The Dark Side Of Britain: Spice*. This film has had over 2,500,000 views on YouTube, with 15,000 likes. It is Unilad's fifth most watched YouTube video of all time (out of 200), with over 6,000 viewer comments (ranked second highest for comments). Public reaction has been sustained over two years, with thoughtful and emotional viewer comments posted every week since its release **[H]**.

Contributions to national policy and international drugs monitoring

Published research from MANDRAKE testing of seized and surrendered samples informs national and international drugs harms and trends monitoring to inform strategic responses. The UK's Advisory Council for Misuse of Drugs used MANDRAKE findings to assess the prevalence of SCRAs (Spice) in its 2020 drug harms assessment and review of classification and scheduling **[J]**. The European Monitoring Centre for Drugs and Drug Addiction, and WHO used published research in reports on MDMB-4en-PINACA as part of global trends monitoring **[J]**.

5. Sources to corroborate the impact

A. Statement from Strategic Lead for Substance Misuse, GMCA, *provides evidence of critical incidents in Greater Manchester and the impact of MANDRAKE, DEWS and GM TRENDS on the city-region's strategic and emergency responses.*

B. Hansard, HC Deb. vol. 645, Col. 836-46 *reports Mr Nick Hurd MP's commendation of Manchester's multi-agency response to NPS*.

C. Statement from Chief Superintendent, Greater Manchester Police, *describes the significance of MANDRAKE's rapid non-forensic drug identification in GMP operations and outcomes.*

D. GMCA news story about GM-TRENDS *is evidence of GMCA's use of Manchester Metropolitan research to steer evidence-led strategic responses to substance use trends.*

E. 'Developing and enhancing the drug early warning system and trend analysis in Greater Manchester' presentation to Public Health England's National Intelligence Network on Drug Health Harms Briefing *is evidence of national showcasing of best practice.*

F. Copies of the Manchester Community Safety Partnership Strategy; Standing Together; and the Greater Manchester Drug and Alcohol Strategy *provide evidence of the integration of DEWS, MANDRAKE and GM-TRENDS into city-region intelligence-led harms reduction.*

G. Statement from WHP Operations Director, Manchester Pride attendance figures and tweets *provide evidence of MANDRAKE rapid testing, public alerts and significant harms reduction.*

H. Media analysis *provides evidence of volume, reach and international exposure of media coverage and Tweets.* YouTube pages *give data on audience engagement (views, likes and comments) for the Unilad* Dark Side of Britain: Spice *documentary*.

I. Statement from Drug Recovery Prison Programme Lead, HM Prison and Probation, and Report on an inspection of HMP Holme House by HM Chief Inspector of Prisons.

J. Copies of ACMS, EMCDDA and WHO reports *provide evidence that Manchester Metropolitan research findings contribute to national and international drug use trends monitoring.*