New Psychoactive Substances - Are We Doing Enough?

July 2014

Science
for a safer world

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Background

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New Psychoactive Substances (NPS)

NPS (often called legal highs) cover a wide range of substances:

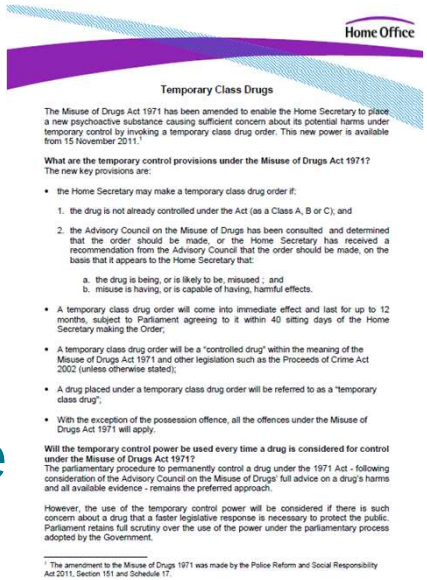
1. Products with names which give no indication of what they contain, Vertex Pirate Edition
2. Named and specific substances which are designed to be similar chemically and/or pharmacologically to known specific controlled drugs, for example many synthetic cannabinoids
3. Substances related to medicines, such as 2-MeO-2-deschloroketamine
4. Herbal and fungal materials or their extracts, salvia

Increasing Prevalence

- New psychoactive substances reported are increasing (EMCDDA)

Legal Status of Legal Highs

- Legislation is slow to react to new drugs
- Many NPS are not controlled
- Fast track system – ‘Temporary Class Drugs’ in place to cover supply of most serious compounds
  - Issued for benzofury (5/6 APB), NBOMe compounds and methoxetamine



Home Office

Temporary Class Drugs

The Misuse of Drugs Act 1971 has been amended to enable the Home Secretary to place a new psychoactive substance causing sufficient concern about its potential harms under temporary control by invoking a temporary class drug order. This new power is available from 15 November 2011.[1]

What are the temporary control provisions under the Misuse of Drugs Act 1971?
The new key provisions are:

- the Home Secretary may make a temporary class drug order if:
  1. the drug is not already controlled under the Act (as a Class A, B or C); and
  2. the Advisory Council on the Misuse of Drugs has been consulted and determined that the order should be made, or the Home Secretary has received a recommendation from the Advisory Council that the order should be made, on the basis that it appears to the Home Secretary that:
     a. the drug is being, or is likely to be, misused ; and
     b. misuse is having, or is capable of having, harmful effects.
- A temporary class drug order will come into immediate effect and last for up to 12 months, subject to Parliament agreeing to it within 40 sitting days of the Home Secretary making the Order;
- A temporary class drug order will be a "controlled drug" within the meaning of the Misuse of Drugs Act 1971 and other legislation such as the Proceeds of Crime Act 2002 (unless otherwise stated);
- A drug placed under a temporary class drug order will be referred to as a "temporary class drug";
- With the exception of the possession offence, all the offences under the Misuse of Drugs Act 1971 will apply.

Will the temporary control power be used every time a drug is considered for control under the Misuse of Drugs Act 1971?
The parliamentary procedure to permanently control a drug under the 1971 Act - following consideration of the Advisory Council on the Misuse of Drugs' full advice on a drug's harms and all available evidence - remains the preferred approach.

However, the use of the temporary control power will be considered if there is such concern about a drug that a faster legislative response is necessary to protect the public. Parliament retains full scrutiny over the use of the power under the parliamentary process adopted by the Government.

[1] The amendment to the Misuse of Drugs 1971 was made by the Police Reform and Social Responsibility Act 2011, Section 151 and Schedule 17.

Hot of the press:- Queen's Speech in UK at opening of new parliament

- New UK government approach to Legal Highs

The main elements of the Bill are:

- The Bill would make it an offence to produce, supply, offer to supply, possess with intent to supply, import or export psychoactive substances; that is, any substance intended for human consumption that is capable of producing a psychoactive effect. The maximum sentence would be seven years' imprisonment.

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Risks

- Legal does **NOT** mean safe
- Most (excl prescription) not tested in humans
- Health risks (short and long term) are often not understood
- Impairment outcomes are often not understood
- Not guaranteed that you are taking what you think you are - hence possible unexpected consequences

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Workplace Analytical

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Traditional Techniques

- Workplace drug testing
- Screened on clinical analysers or using point of care tests (POCT) using immunoassay
- Limited panel of substances
- High throughput
- Cheap
- New reagents can take a while to develop

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Alternative Approach

- High resolution accurate mass (HRAM) LCMS to cover much broader range of analytes.
- Quick and easy to update analyte coverage
- Expensive capital purchase
- Requires high level of technical expertise

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Findings

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City Centre Study

‘Night time’ economy study:

1. Pooled urine samples from urinals
2. Taken from night clubs and city centre
3. Alternative approach as opposed to self reporting
4. HRAM screening
5. 164 different substances found, including synthetic steroids, drugs of abuse, prescription and over the counter medication, and NPS

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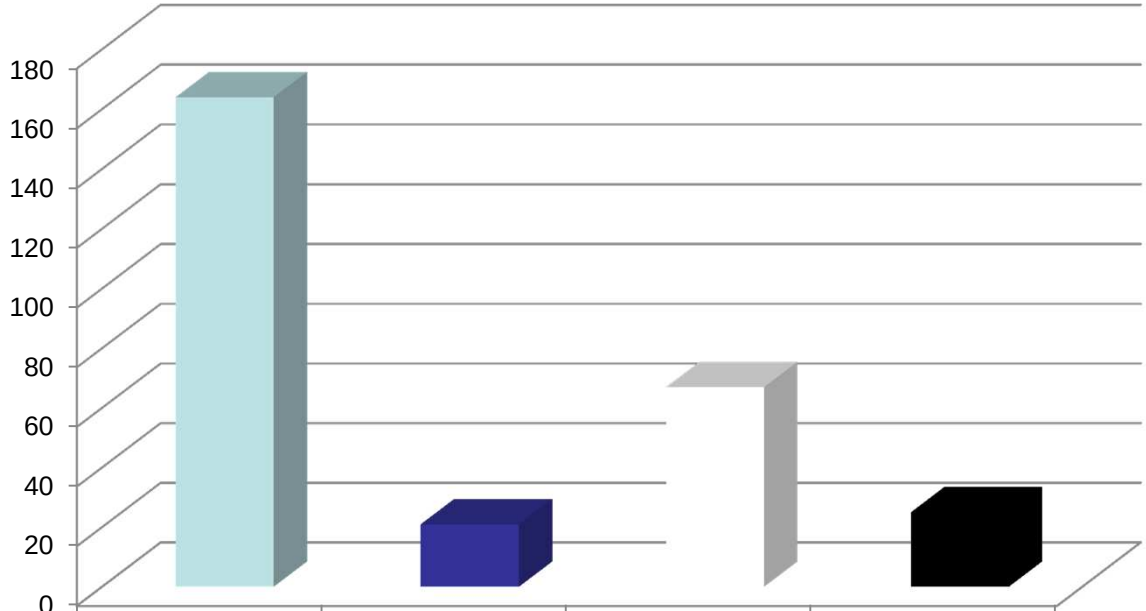
Compounds detected

1,4 methoxyphenylpiperazine	chlordiazepoxide	gabapentin	morphine	propranolol
4 methylethcathinone	chloroquine	guaifenesin	Nandrolone	pyrimethamine
4-ethylmethcathinone	chlorpheniramine	HMMA	naproxen	quetiapine
4-fluoroephedrine	Chlorthalidone	hordenine	nefopam	quinine
4-methylmethcathinone	cimetidine	hydrochlorthiazide	nevirapine	ranitidine
5/6-APB	citalopram	Ibuprofen	nicotine	risperidone
Ambroxol	clenbuterol	isometheptene	niflumic acid	salbutamol
Amisulpiride	clobazam	ketamine	nordazepam	sertaline
Amitriptylline	clomipramine	Ketoprofen	nortriptyline	sildenafil
Amphetamine	clozapine	lamotrigine	noscapine	sotalol
Ampyrone	codeine	lansoprazole	Olanzapine	Stanozolol
Arecoline	cotinine	Lidocaine	omeprazole	sulpiride
atenolol	cyclobenzaprine	MDA	opipramol	tamoxifen
Benzocaine	DEET	MDMA	oripavine	temazepam
Benzoylecgonine	desloratidine	Meclofenamic acid	orphenadrine	tetracycline
Benzydamine	dextromethorphan	mefenamic acid	oxazepam	tetramisole
bisoprolol	dextrorphan	methadone	oxprenolol	theobromine
bromhexine	Diazepam	methamphetamine	oxycodone	theophylline
Buprenorphine	diclofenac	methcathinone	oxytetracycline	tramadol
buprenorphine-nor	dihydrocodeine	methiopropamine	papaverine	Trazodone
Caffeine	dihydromorphine	methoxetamine	paracetamol	trenbolone
Camphor	diphenhydramine	methylhexaneamine	paroxetine	trifluoromethylphenylpiperazine
Capsaicin	dipyridamole	methylphenidate	pentedrone	trimethoprim
Carbamazepine	doxycycline	metoclopramid	pheniramine	vardenafil
Carboxy THC	enalapril	metoprolol	Phenylpropanolamine	venlafaxine
Cathine	ephedrine/pseudoephedrine	metronidazole	Pholcodine	xylometazolone
Cathinone	ethylphenidate	midazolam	pipradrol	Yohimbine
celecoxib	Etoricoxib	minoxidil	pregabalin	zolpidem
cetirizine	fluoxetine	mitragynine	prilocaine	methylone
chlorcylizine	furosemide	modafinil	Propoxyphene	ethylone

Coverage vs Traditional Workplace test

Enhanced vs traditional workplace test on samples analysed to date



	Drugs detected on enhanced workplace test	Traditional workplace test drugs detected on enhanced screen	Drugs with potential for abuse	'Legal Highs' not covered by traditional workplace test
Number of Drugs	164	21	67	25

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Population A

Specific study population – already undergoing 'standard' urine drug testing

1. Thousands of samples run
2. HRAM screening positive rate double the traditional type testing
3. Positives included controlled (classified) drugs not in routine testing panels – bufotenine
4. Non controlled substances which are suspected to have psychoactive outcomes not in routine testing – glaucine, 5F AKB-48.
5. Other substances (medication) available on prescription only not included in routine testing – zopiclone, gabapentin, pregabalin

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Population B

Specific study population – already undergoing urine drug testing

1. Thousands of samples run
2. Current programme includes rudimentary NPS screening
3. HRAM screening positive rate over 18% on samples previously screened as negative
4. Anabolic steroid positive rate over 10%

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Synthetic Cannabinoids detected in study

5F AB-PINACA	EAM-2201
5F AKB-48	FAM-2201
5F PB-22	MAM2201
5F UR-144	MDMB-CHMICA
AB-CHMINACA	STS-135
AM-2201	THJ-018
AM694	THJ-2201
Cumyl 5F PINACA	UR-144
BB-22	

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Challenges

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Challenges

- Standards
  - Often not available, purchase and purify
- Metabolites
  - Often none are published, In-vitro options
- Interpretation
  - Limited peer reviewed options
- Employment Policy
  - Often limited to ‘impairment’, controlled substances, or listed drugs
- Current
  - Keeping up to date, ‘white powder’ analysis

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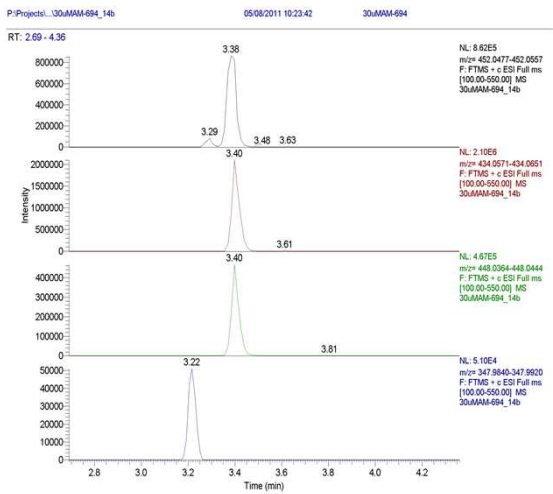
In Vitro Metabolism

- Knowledge of breakdown in the body is required – metabolism
- Many drugs only leave detectable concentrations of metabolites and not parent drug
- Metabolite information for many NPS are not available
- Able to mimic metabolism in a test tube using the drug and enzymes from liver cells
- Information is then used in testing process



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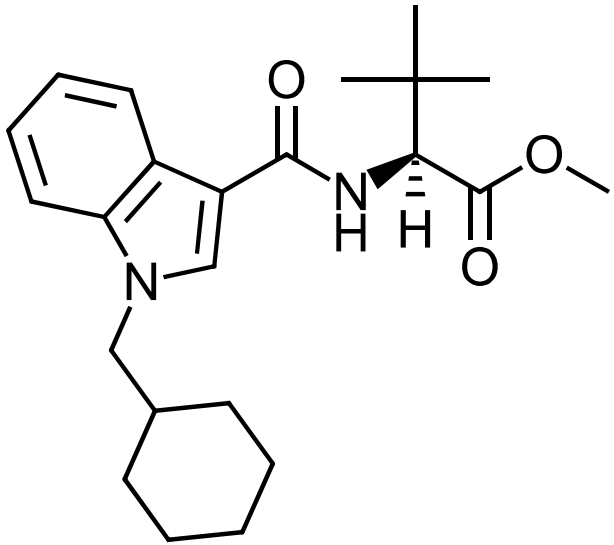
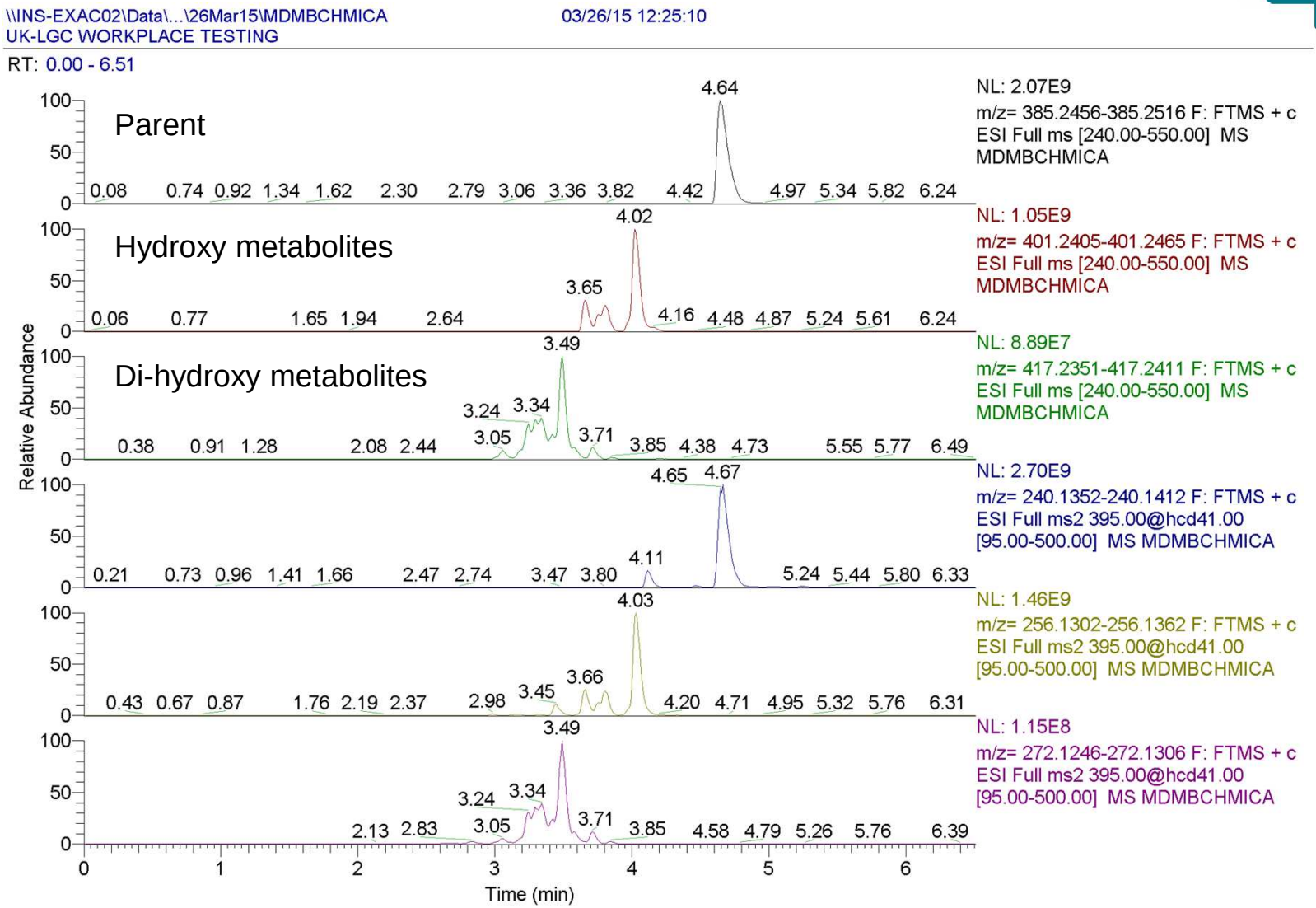
MDMB CHMICA

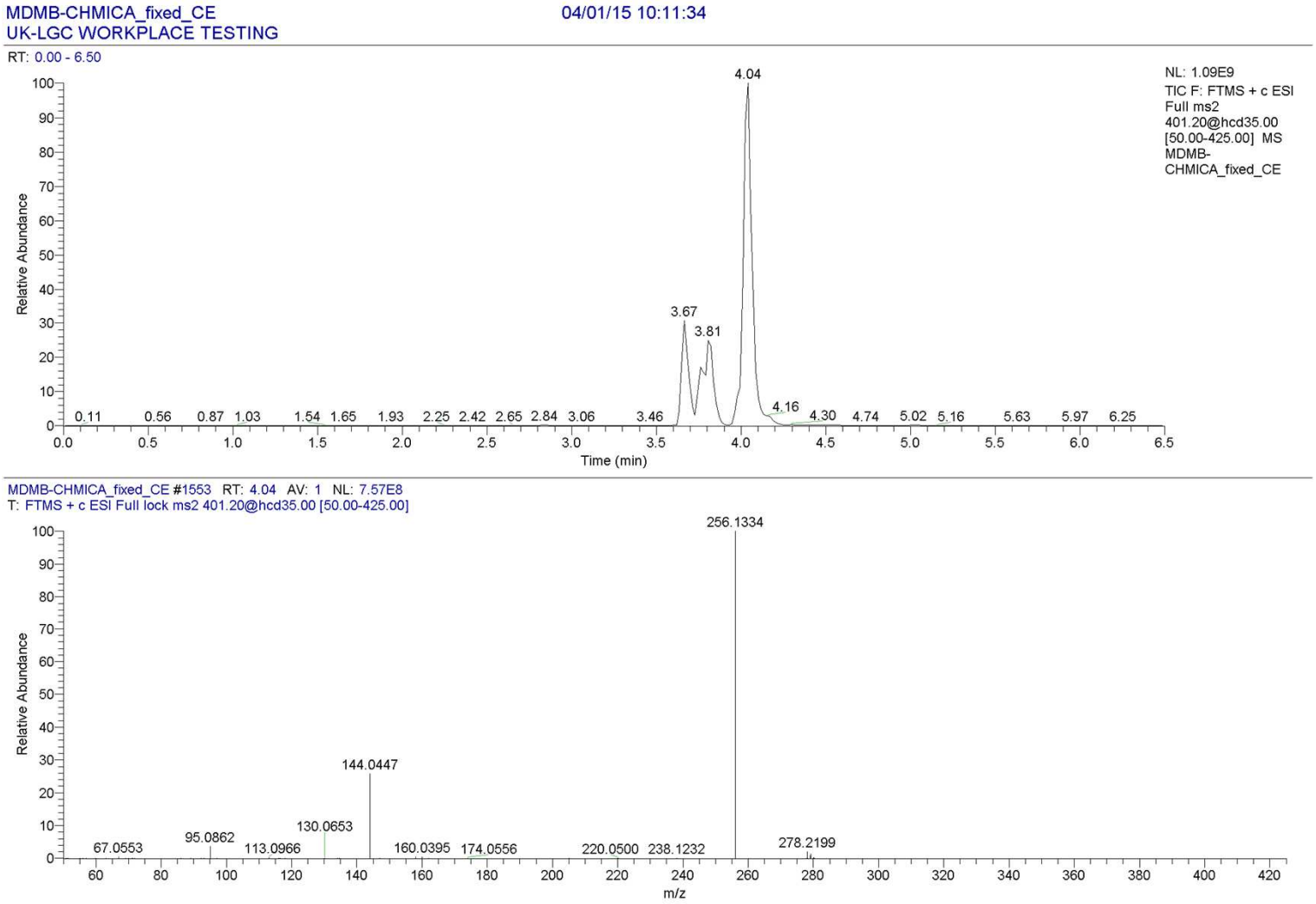


- Current synthetic cannabinoid in UK
- Related to deaths across Europe and USA
- No metabolism information
- No reference material for metabolite

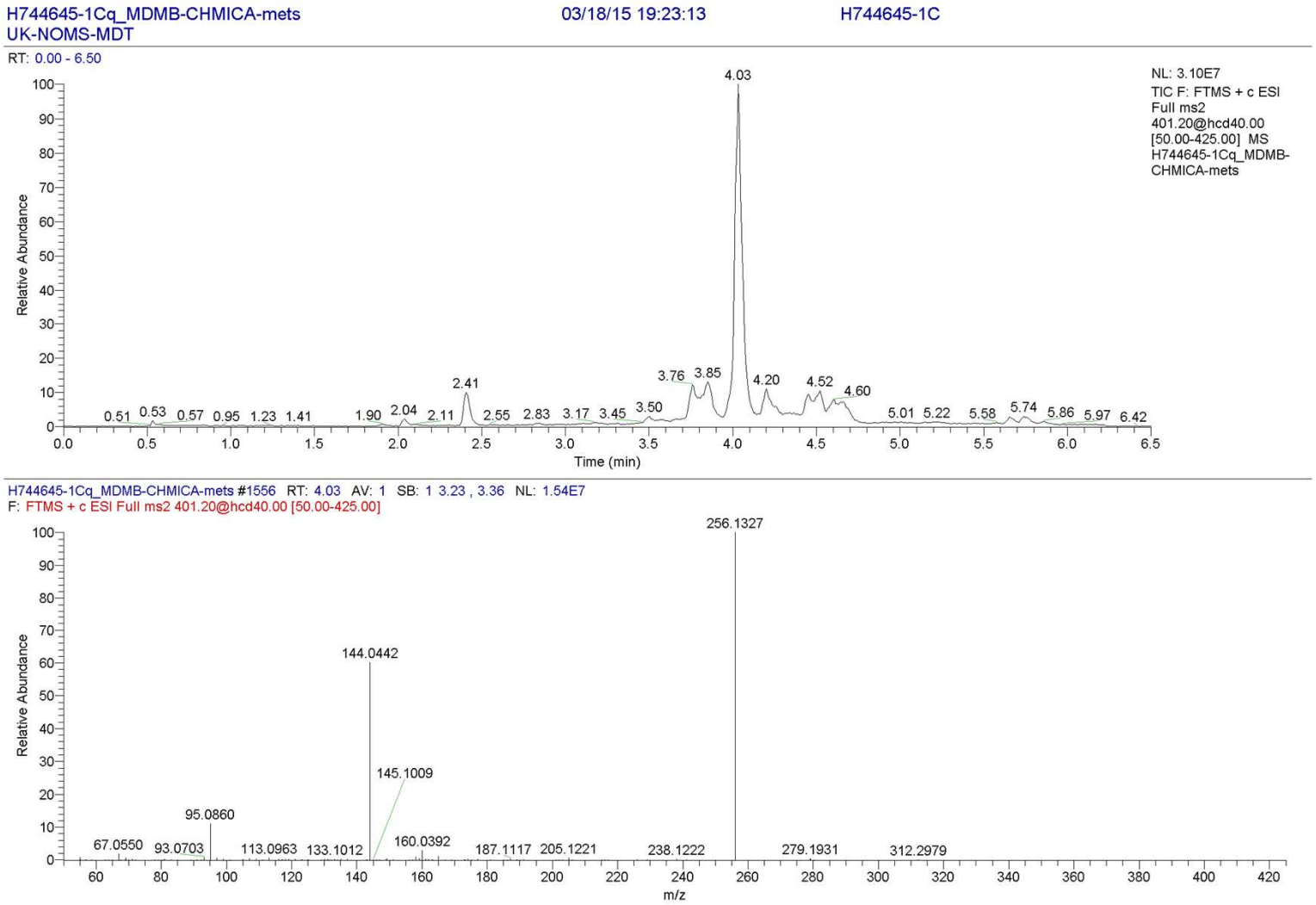
In vitro data for MDMB-CHMICA



MS/MS spectra on MDMB-CHMICA hydroxy metabolite



Major metabolite in positive urine



Questions?

- Can we use in vitro generated metabolites as reference materials where no other alternatives exist?

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