MEDIZINISCHE UNIVERSITÄT WIEN

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StaDt Wien

Analytic Techniques Utilised for Drug Checking

Challenges and Current Developments

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***checkit!* is a scientific collaboration of**

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Bundesministerium
Arbeit, Soziales, Gesundheit
und Konsumentenschutz

Integrated Drug Checking (IDC)

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Analytical & toxicological measures

- Substance analysis
- Individual risk categorisation

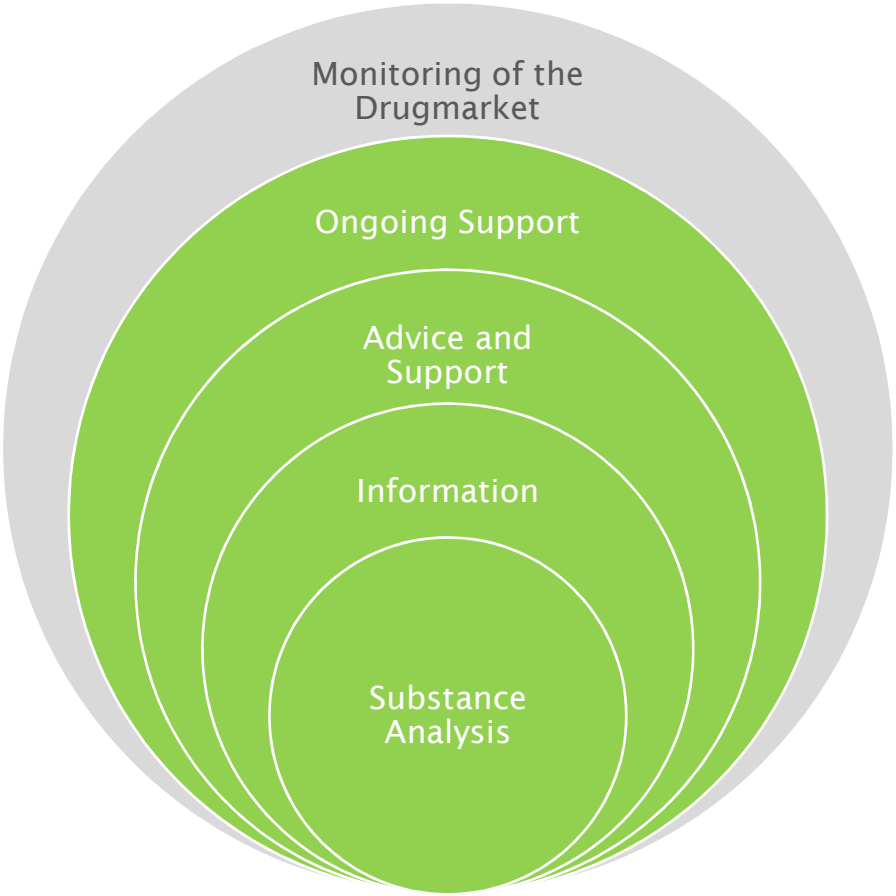
⟷

Psychosocial interventions

- Information
- Advice & support

source: © Boran Ilic Fotografie

Integrated Drug Checking (IDC)



Requirements for comprehensive individual risk assessment and effective harm reduction:

- Identity of pharmacologically active substances
- Quantitative composition of the drug (dosage)
- Fast analysis and presentation of results at the venue

Source: checkit!, Suchthilfe Wien gGmbH

Mobile Drug Checking Methods

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Requirements and challenges for mobile Drug Checking (DC)

- Mobile use
- Robustness
- Detection of all pharmacologically active components esp. in substance mixtures
- Low detection limits
- Quantitative determination
- Wide (quantitative) measuring range
- High sample throughput
- Identification of unknown substances
- Discrimination between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- Allows adaptations to market changes

Rational acquisition- & operating-costs

Mobile Drug Checking Methods

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Reagent testing:

Source: http://izutti.com/blog/astonishing-sci-fi-apartment-design-by-a-cero/

Benefits: Fast and easy to use, low costs

Limitations: High risk of misinterpretation & false negative results

- ✓ Mobile use
- ✓ Robustness
- ✗ Detection of all pharmacologically active components (substance mixtures)
- ✗ Low detection limits
- ✗ Quantitative determination
- ✓ High sample throughput
- ✗ Identification of unknown substances
- ✗ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ~ Allows adaptations to market changes

Mobile Drug Checking Methods

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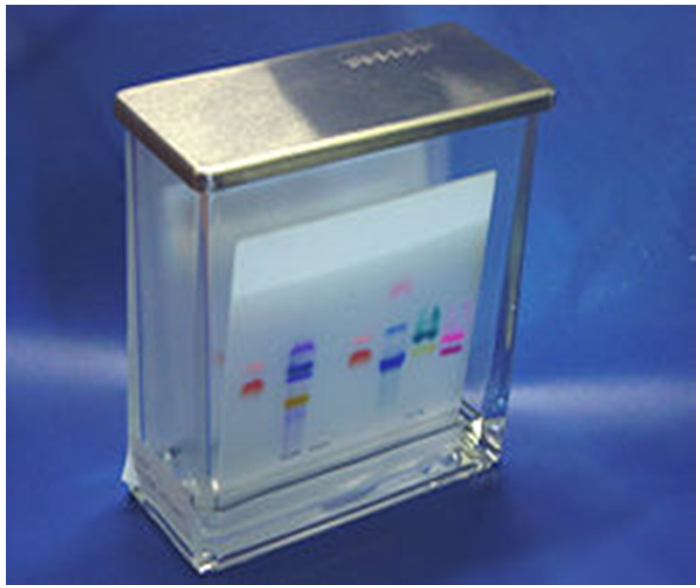
TLC (Thin Layer Chromatography)



Source: http://www.chemgapedia.de

Benefits: Low costs & separation of substances, combination with Direct MS possible

- ✓ Mobile use
- ✓ Robustness
- ✗ Detection of all pharmacologically active components (substance mixtures)
- ✗ Low detection limits
- ~ Quantitative determination
- ✓ High sample throughput
- ✗ Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ✓ Allows adaptations to market changes

Mobile Drug Checking Methods

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FTIR (Fourier-Transform Infrared Spectroscopy)

Source: https://www.bruker.com

Source: https://www.thermofisher.com

Benefits: No sample preparation & high throughput

Limitations: Deciphering substance mixtures

- ✓ Mobile use
- ✓ Robustness
- ✗ Detection of all pharmacologically active components (substance mixtures)
- ✗ Low detection limits
- ~ Quantitative determination
- ✓ High sample throughput
- ~ Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ✓ Allows adaptations to market changes

Mobile Drug Checking Methods

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UHPLC-UV
Ultra High Performance Liquid Chromatography - Ultra Violet

Source: checkit! Suchthilfe Wien gGmbH

- ✓ Mobile use
- ✓ Robustness
- ~ Detection of all pharmacologically active components (substance mixtures)
- ~ Low detection limits
- ✓ Quantitative determination
- ✓ High sample throughput
- ✗ Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ✓ Allows adaptations to market changes

Mobile Drug Checking Methods

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UHPLC-MS
Ultra High Performance Liquid Chromatography-Mass spectrometry

Source: checkit! Suchthilfe Wien gGmbH

Benefits: High discrimination power, identification of unknown substances possible, low detection limits

- ✓ Mobile use
- ~ Robustness
- ~ Detection of all pharmacologically active components (substance mixtures)
- ✓ Low detection limits
- ✓ Quantitative determination
- ✓ High sample throughput
- ~ Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ✓ Allows adaptations to market changes

Mobile Drug Checking Methods

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GC-MS
(Gas Chromatography - Mass spectrometry)

Source: http://www.bruker.com

Benefits: Low detection limits & Identification of unknown substances

Limitations: Elaborate sample preparation, not for thermally unstable compounds

- Mobile use
- Robustness
- ~ Detection of all pharmacologically active components
- Low detection limits
- Quantitative determination
- ~ High sample throughput
- Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- Allows adaptations to market changes

Mobile Drug Checking Methods

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Direct masspectrometric techniques (DESI, MALDI, DART, etc.)

Source: https://www.ionsense.com

Benefits: Short analysis time & low detection limits

Limitations: no separation (substance mixtures)

- Mobile use
- Robustness
- Detection of all pharmacologically active components (substance mixtures)
- Low detection limits
- Quantitative determination
- High sample throughput
- Identification of unknown substances
- Discrimination between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- Allows adaptations to market changes

Mobile Drug Checking Methods

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HR-MS^n (High Resolution Mass Spectrometry)

Sources: checkit! Suchthilfe Wien gGmbH

Benefits: High amount of structural information & very low detection limits

Limitations: not for mobile use (yet)

- ✗ Mobile use
- ✗ Robustness
- ~ Detection of all pharmacologically active components
- ✓ Low detection limits
- ✓ Quantitative determination
- ✓ High sample throughput
- ✓ Identification of unknown substances
- ~ Discriminate between isomers (e.g. 2-MMC, 3-MMC, 4-MMC)
- ✓ Allows adaptations to market changes

Mobile Drug Checking Methods

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	Reagent Testing	TLC	FTIR	(U)HPLC-UV	(U)HPLC-MS	GC-MS	Direct MS	HR-MS
Mobile use	+	+	+	+	+	+	+	-
Robustness	+	+	+	+	~	+	~	-
Detection of all components	-	-	-	~	~	~	~	~
Low detection limits	-	-	-	~	+	+	+	+
Quantitative determination	-	~	~	+	+	+	~	+
High sample throughput	+	+	+	+	+	~	+	+
Identification of unknowns	-	-	~	-	~	+	+	+
Discrimination between isomers	-	~	~	~	~	~	-	~
Adaptability to market changes	~	+	+	+	+	+	+	+
Costs	+	+	~	~	-	-	-	-

Current challenges for DC

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- ✓ **Increasing number of different new psychoactive substances (NPS) on the market**
- ✓ **High complexity of samples**
- ✓ **High variability of dosage**
- ✓ **Appearance of highly potent substances**

2018
UHPLC-DAD-MS &
MALDI-IT-MS

2012
HPLC-DAD-MS

2008
HPLC-DAD

2002
HPLC-UV

1997
Remedy

Mobile DC Methods
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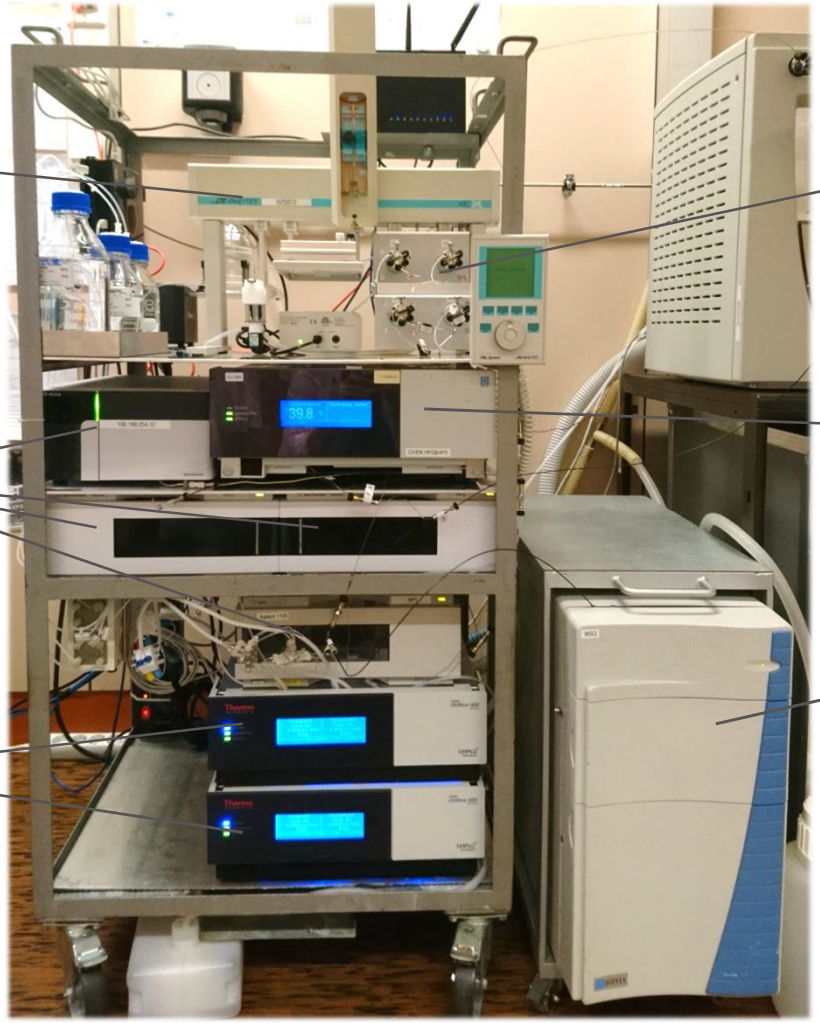
Mobile UHPLC-DAD-MS System



Source: checkit! Suchthilfe Wien gGmbH

Mobile DC Methods
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Source: checkit! Suchthilfe Wien gGmbH

Source: checkit! Suchthilfe Wien gGmbH

Mobile DC Methods
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Source: checkit! Suchthilfe Wien gGmbH

Specifications

- ✓ Four parallel UHPLC-DAD-systems
- ✓ One of them coupled with MS
- ✓ Automated sample preparation
- ✓ Runtime per system: less than 10 min
- ✓ Throughput: up to 40 samples/h
- ✓ Screening for over 300 different substances
- ✓ Currently up to 58 quantitative parameters

Increasing number of NPS

Substance	First identified in Vienna	Substance	First identified In Vienna
mCPP	2006	Dibutylone	2014
TFmPP	2007	Pentylone	2014
4-Fluoramphetamine	2009	4-chloromethamphetamin	2015
pFPP	2009	4-CMC	2015
Butylone	2009	4-Methylpentedrone	2015
Methylone	2009	5-MAPB	2015
Mephedrone	2010	bk-MDDMA	2015
2C-E	2011	4-EMC	2015
4-MEC	2011	3-MMC	2015
2C-I	2011	**3-MeO-PCP**	**2016**
MPA	2011	**4-CEC**	**2016**
Ethylphenidat	2011	**3-FPM**	**2016**
Flephedrone	2011	**4-Fluormethamphetamine**	**2016**
DOC	2012	**4-Methylmethamphetamin**	**2016**
25B-NBOMe	2013	**Deschloroketamine**	**2016**
25C-NBOMe	2013	**Furanylfentanyl**	**2016**
25I-NBOMe	2013	**TH-PVP**	**2016**
5-MeO-MiPT	2013	**MPHP**	**2016**
25H-NBOMe	2014	**N-Ethylhexedrone**	**2016**
2-MXP	2014	**N-Ethylpentylone**	**2016**

Increasing number of NPS

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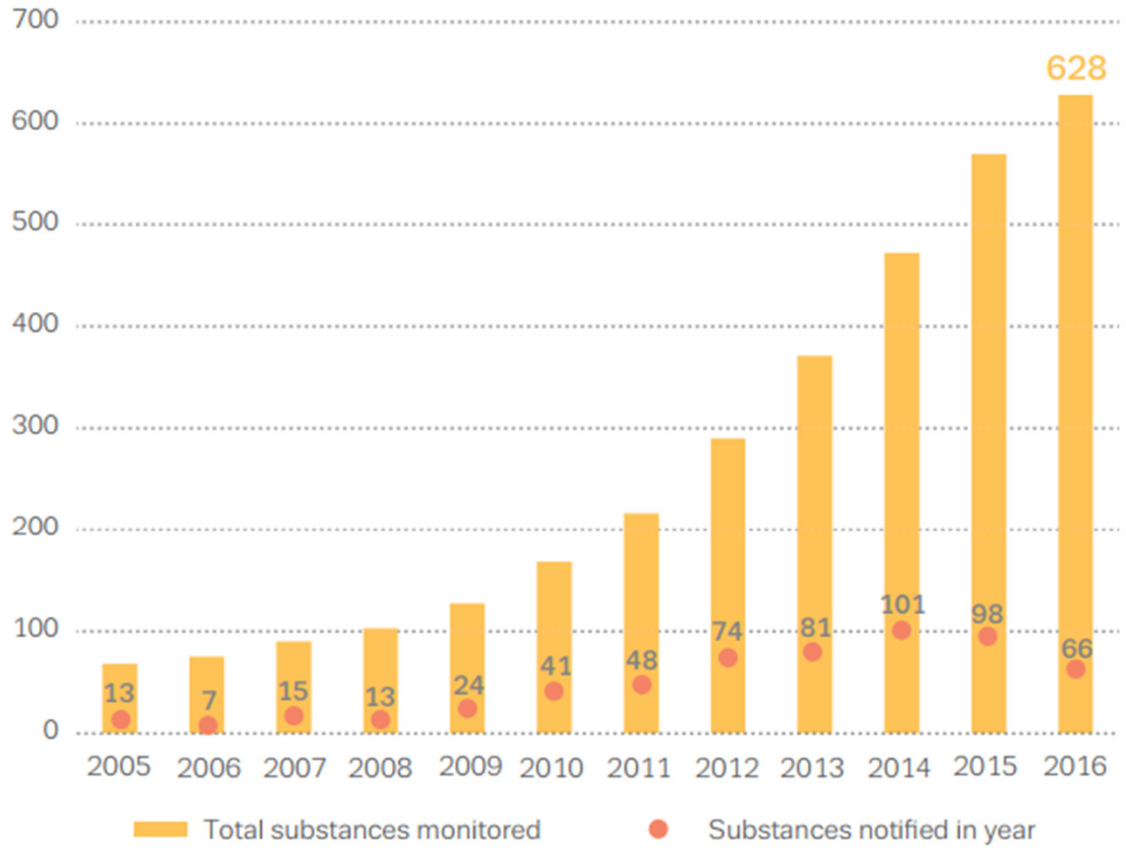
Number of new psychoactive substances formally notified for the first time in Europe (dots) and total number of new psychoactive substances monitored by the EMCDDA, 2005–16 (bars)



Source: EMCDDA-Europol 2016, Annual Report on the implementation of Council Decision 2005/387/JHA

Complexity of samples

Highly potent substances
Need for low detection limits

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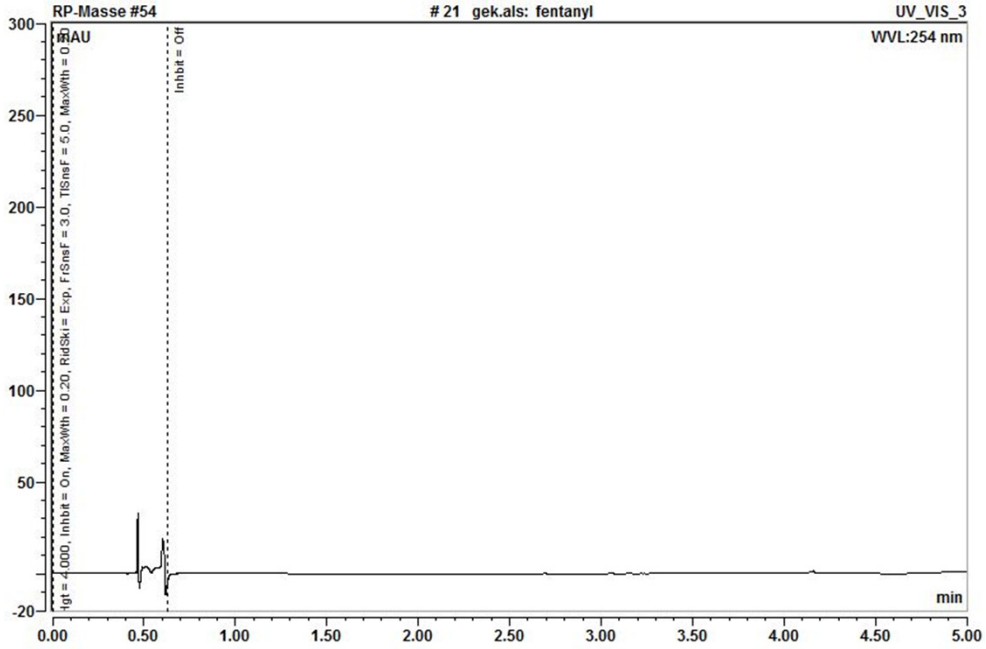
Sample submitted as: Fentanyl

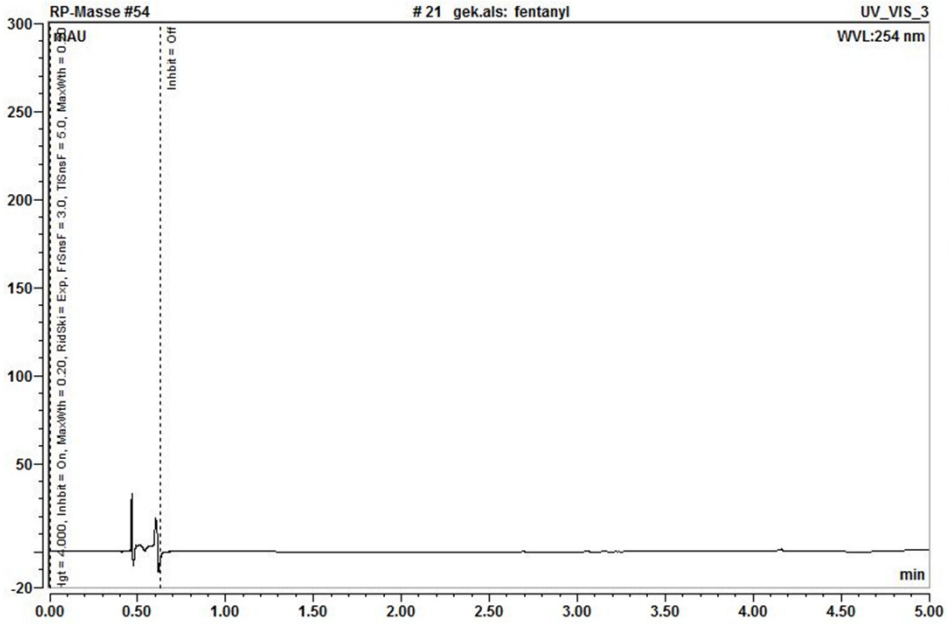
Suchergebnis	
Datum	[redacted]
Event	[redacted]
gekauft als	Fentanyl
Straßenname	k.A.
Konsistenz	k.A.
Farbabstufung	normal
Farbe	weiß
bedenkliches Ergebnis	
Ergebnis der Probe	

UHPLC-UV chromatogram @ 254 nm

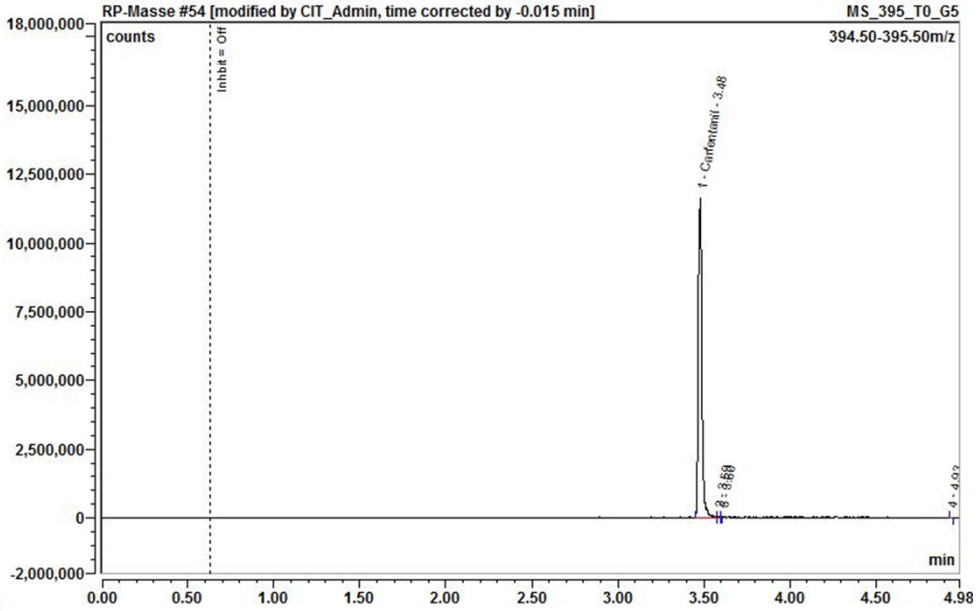


Highly potent substances
Need for low detection limits

UHPLC-UV chromatogram @ 254 nm



UHPLC-MS chromatogram (SIM scan; m/z 395)



Highly potent substances
Need for low detection limits

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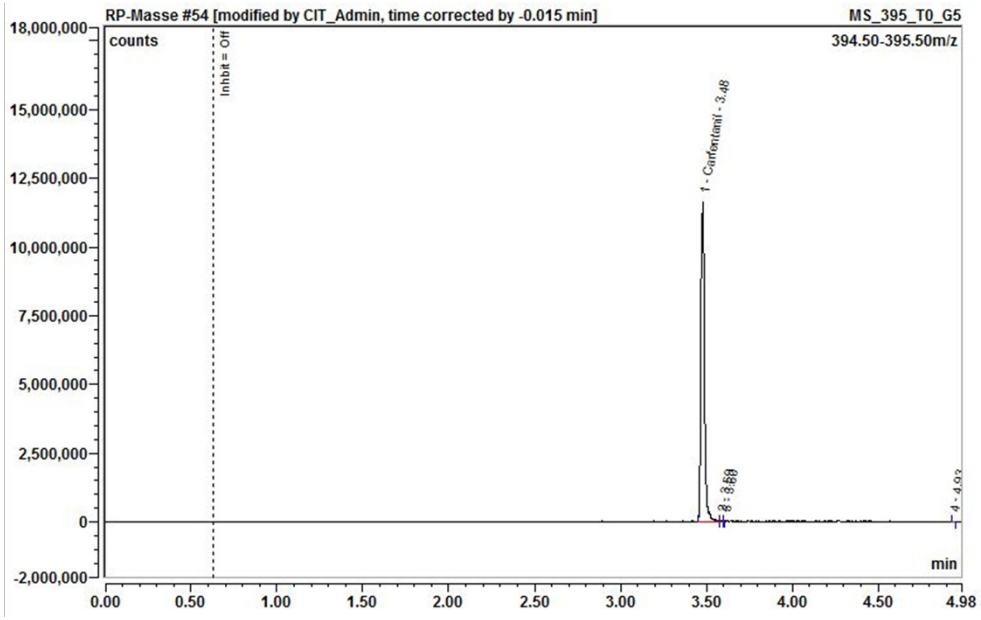
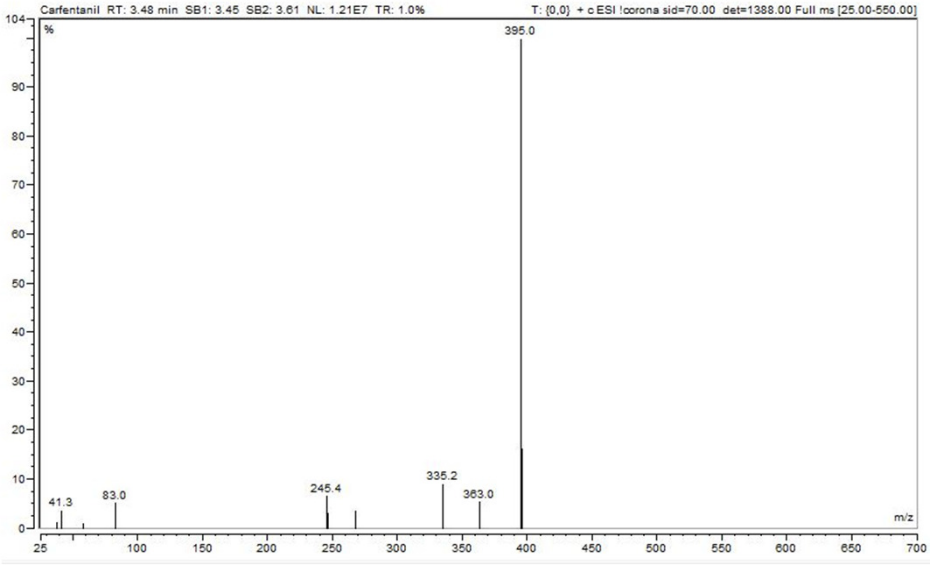
UHPLC-MS chromatogram (SIM scan m/z 395)



Mass spectrum @ RT 3.48 min



Highly potent substances
Need for low detection limits

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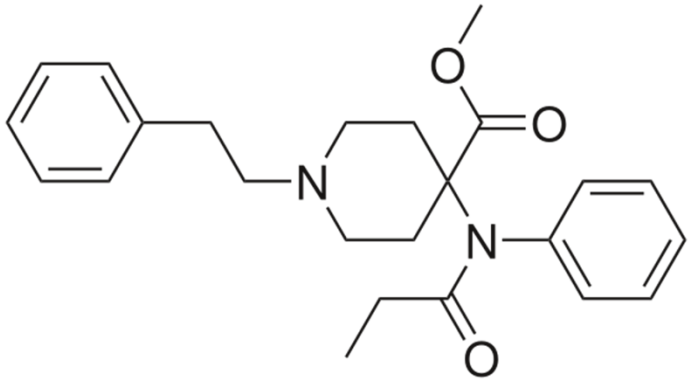
Carfentanil

Highly potent synthetic opioid (4.000 to 10.000 fold more potent than morphine)



4[(1-Oxopropyl)-phenylamino]-1-(2-phenylethyl)-4-piperidin-carbonsäuremethylester

Source: http://www.huffingtonpost.ca/2017/05/02/fentanyl-carfentanil_n_16397030.html

Highly potent substances
Need for low detection limits

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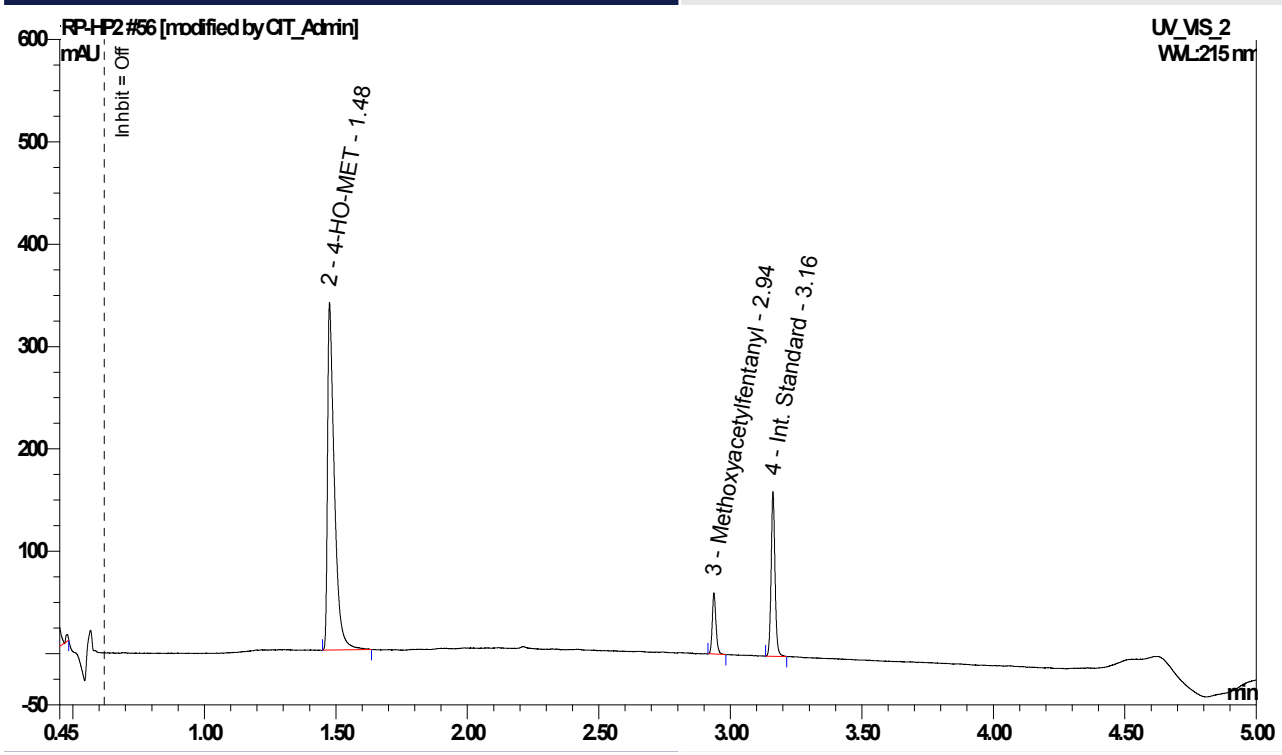
Brought to analysis as:	Actual constituents
4-HO-MET	4-HO-MET & Methoxyacetylfentanyl
Fentanyl	Carfentanil
Mephedrone / 4-MMC	4-CMC + 4-CEC
unknown Research Chemical	U-47,700
	U-47,700
	U-47,700
	Cyclopentylfentanyl
	Ethylphenidat + N-Ethylbuphedrone + Caffeine
	4-CEC + 4-CMC + 3-MMC

Highly potent substances
Need for low detection limits

Brought to analysis as:	Actual constituents
4-HO-MET	4-HO-MET & Methoxyacetylfentanyl
	one + Caffeine



Highly potent substances
Need for low detection limits

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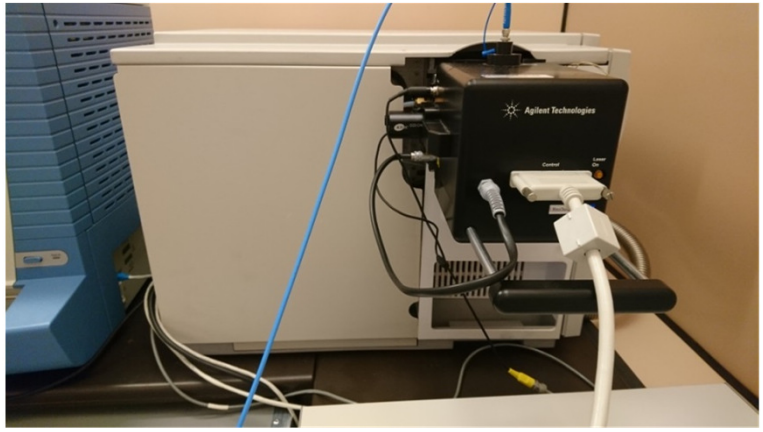
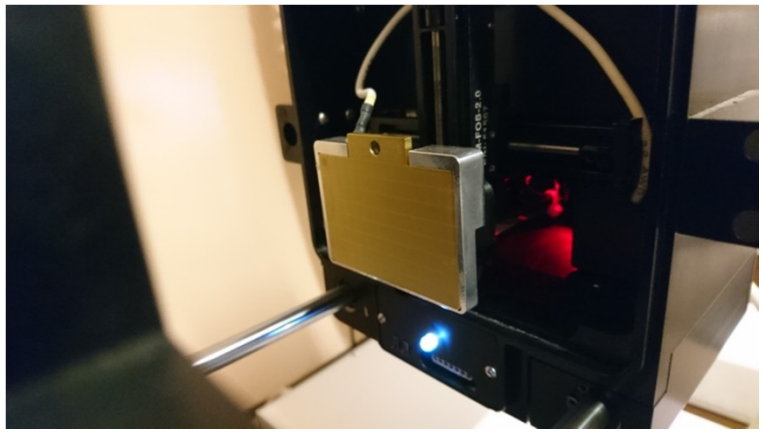
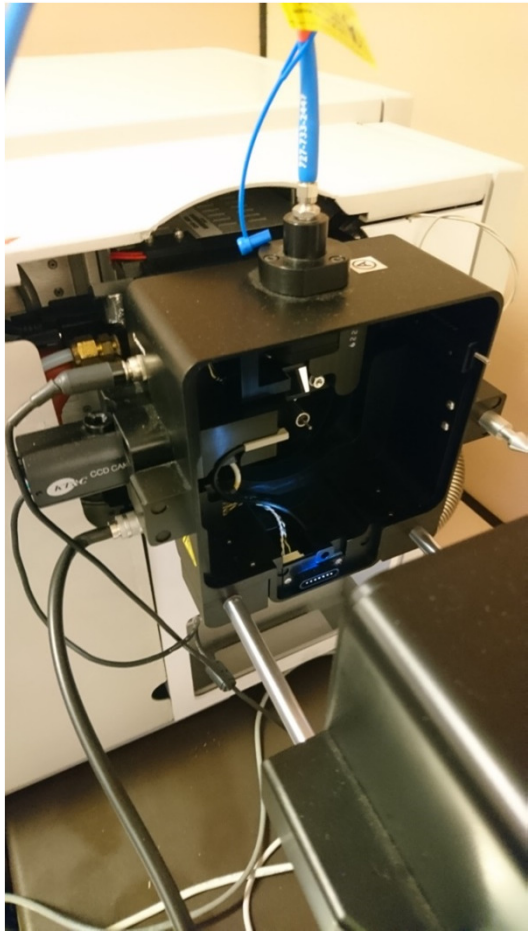
Direct MS: MALDI-IT-MS^n







Highly potent substances
Need for low detection limits

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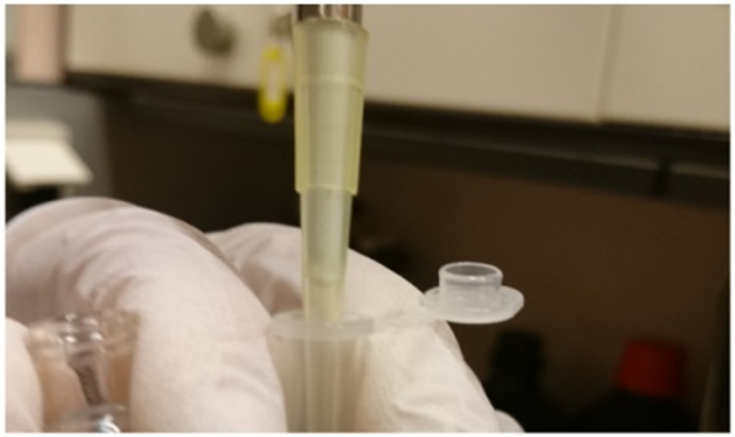
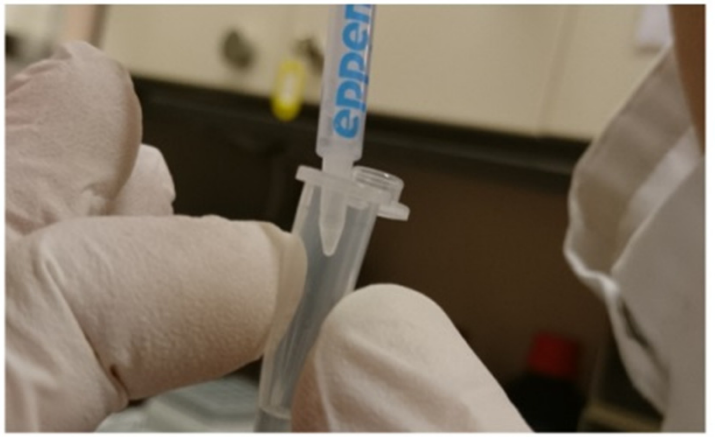
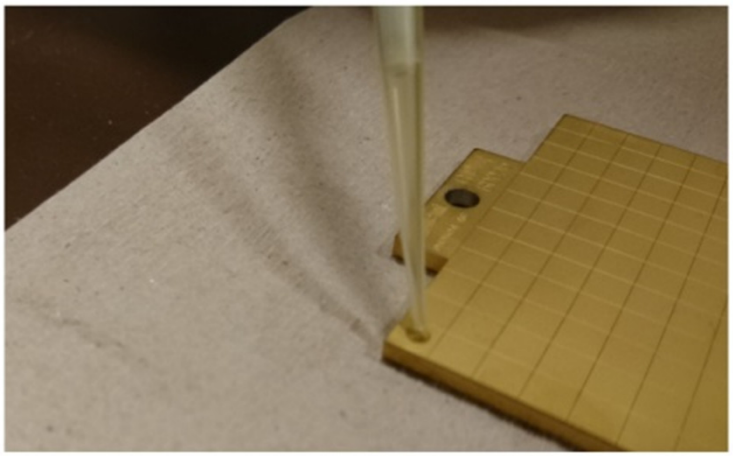
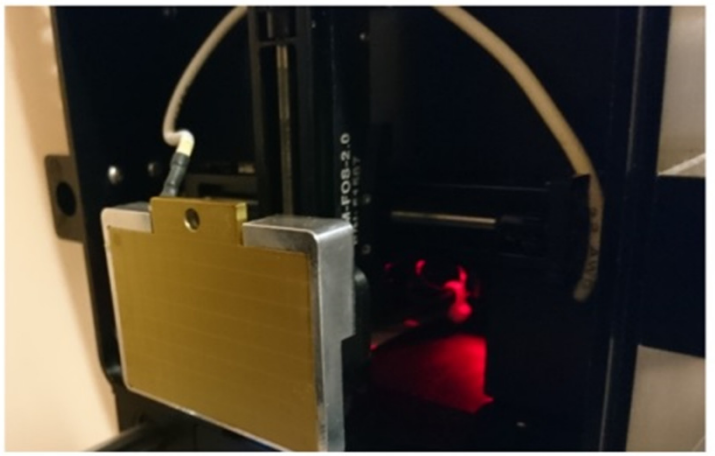
Direct MS: MALDI-IT-MS^n

Highly potent substances
Need for low detection limits

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Benefits of complementary MALDI-IT-MS^n analysis:

- Additional structural information
- Minimum sample preparation
- Instant analysis (60 sec/sample)
- Fast screening for synthetic opioids
- Very low detection limits

	(U)HPLC-UV	(U)HPLC-MS	Direct MS (MALDI)
Mobile use	+	+	(+)*
Robustness	+	~	~
Detection of all components	~	~	~
Low detection limits	~	+	+
High sample throughput	+	~	+
Identification of unknowns	-	+	+
Discrimination between isomers	~	~	-
Adaptability to market changes	+	+	+
Costs	~	-	-

* Proof of concept phase

High variability of dosage

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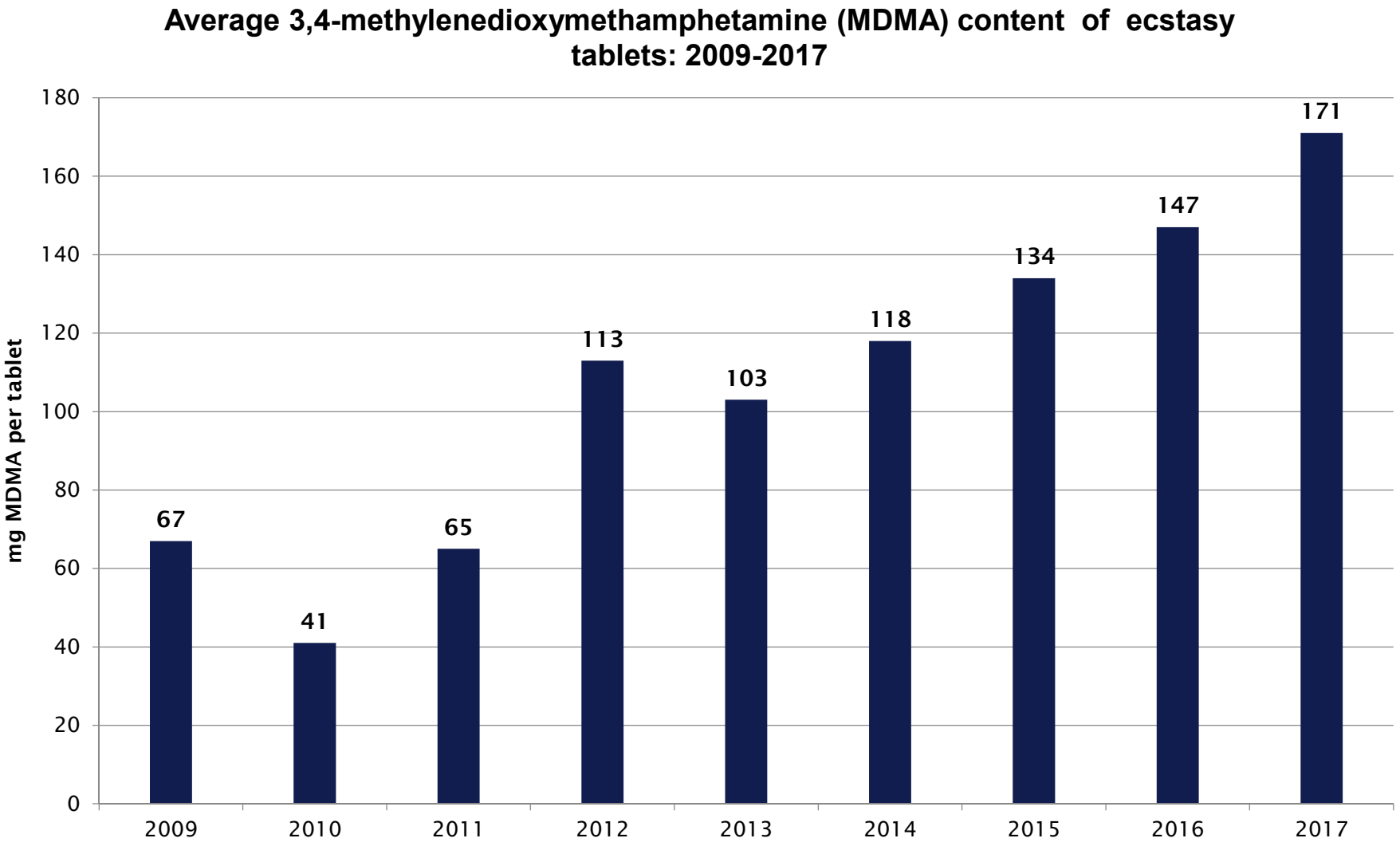
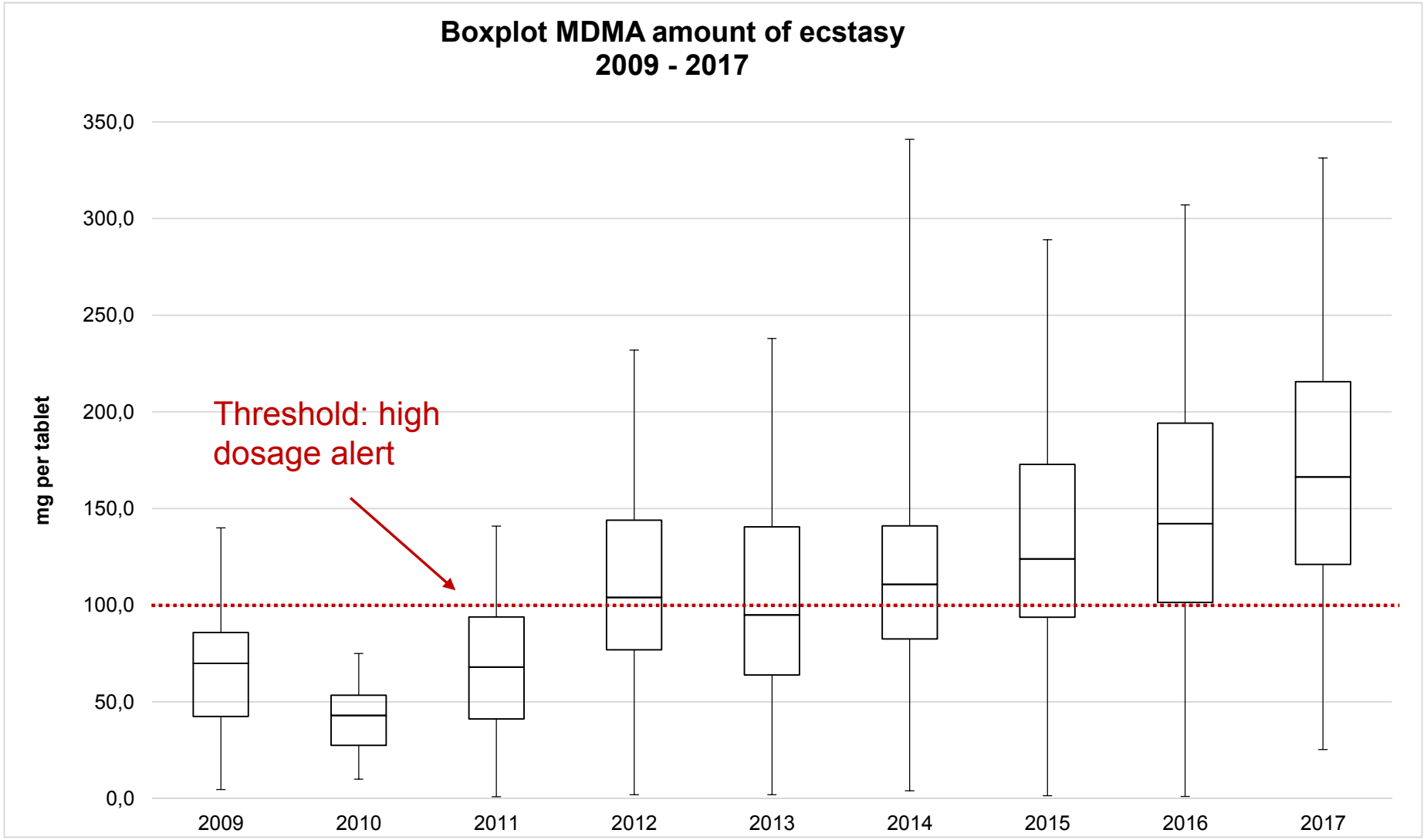


High variability of dosage



Mobile Drug Checking
Conclusions

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- Hardly any analytical technique applied alone meets all the requirements for mobile DC
- A combination of complementary methods increases the validity and thus the safety of the results
- Quantitative measurement is as important as identification of substances
- Constant method development is necessary to adapt to market changes

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Thank you!