



**UNIVERSITÄTS  
KLINIKUM** FREIBURG

## Spice II Plus project conference

June 05<sup>th</sup> 2014, Lisbon, Portugal

# Key results of the online monitoring 2013/2014

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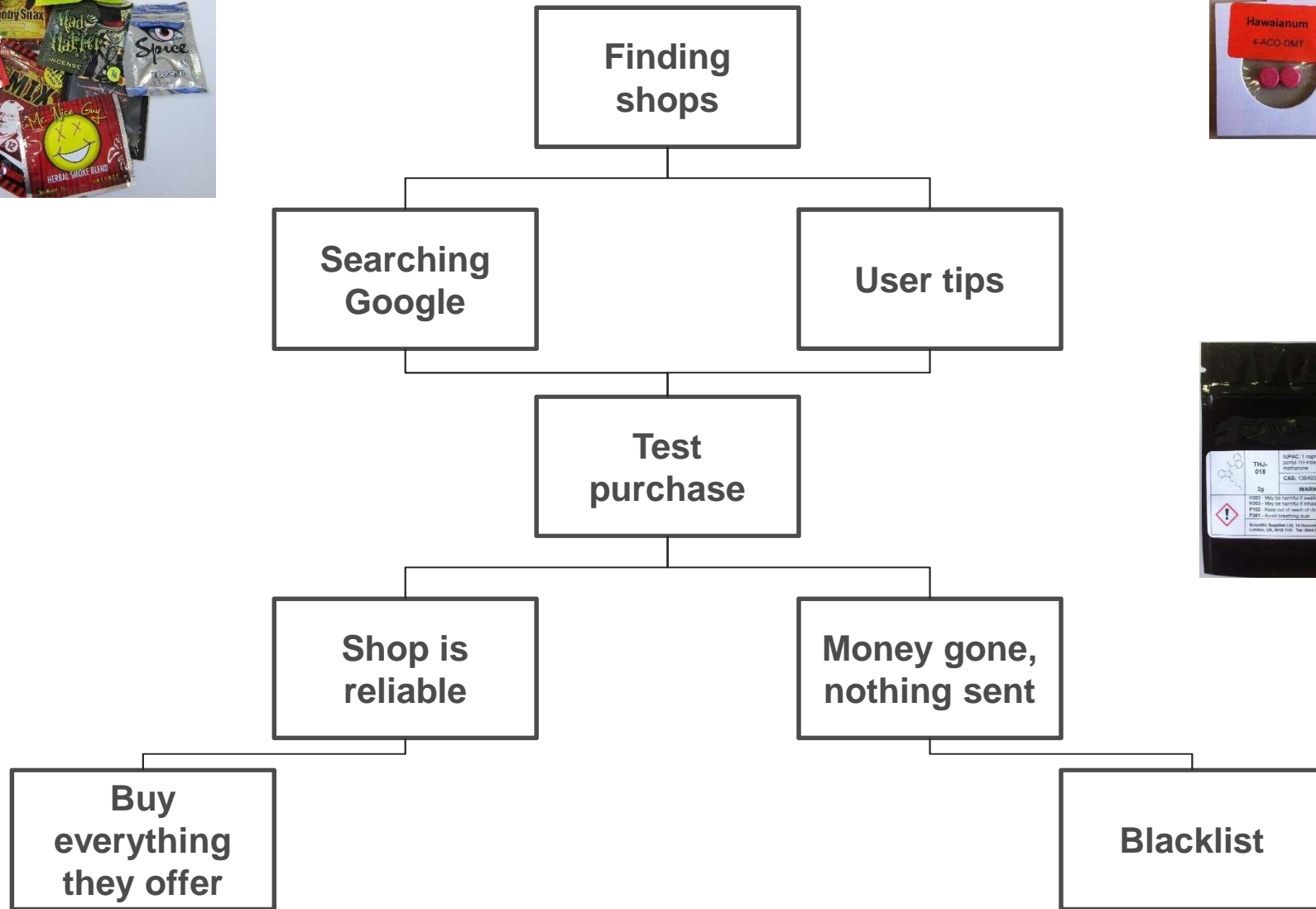


Bundesministerium  
für Gesundheit





# Monitoring - Procedure



# Monitoring - Procedure

How do we know which substances may be the next?

Most of the substances are synthesised in China → good to have a close look to the market in China

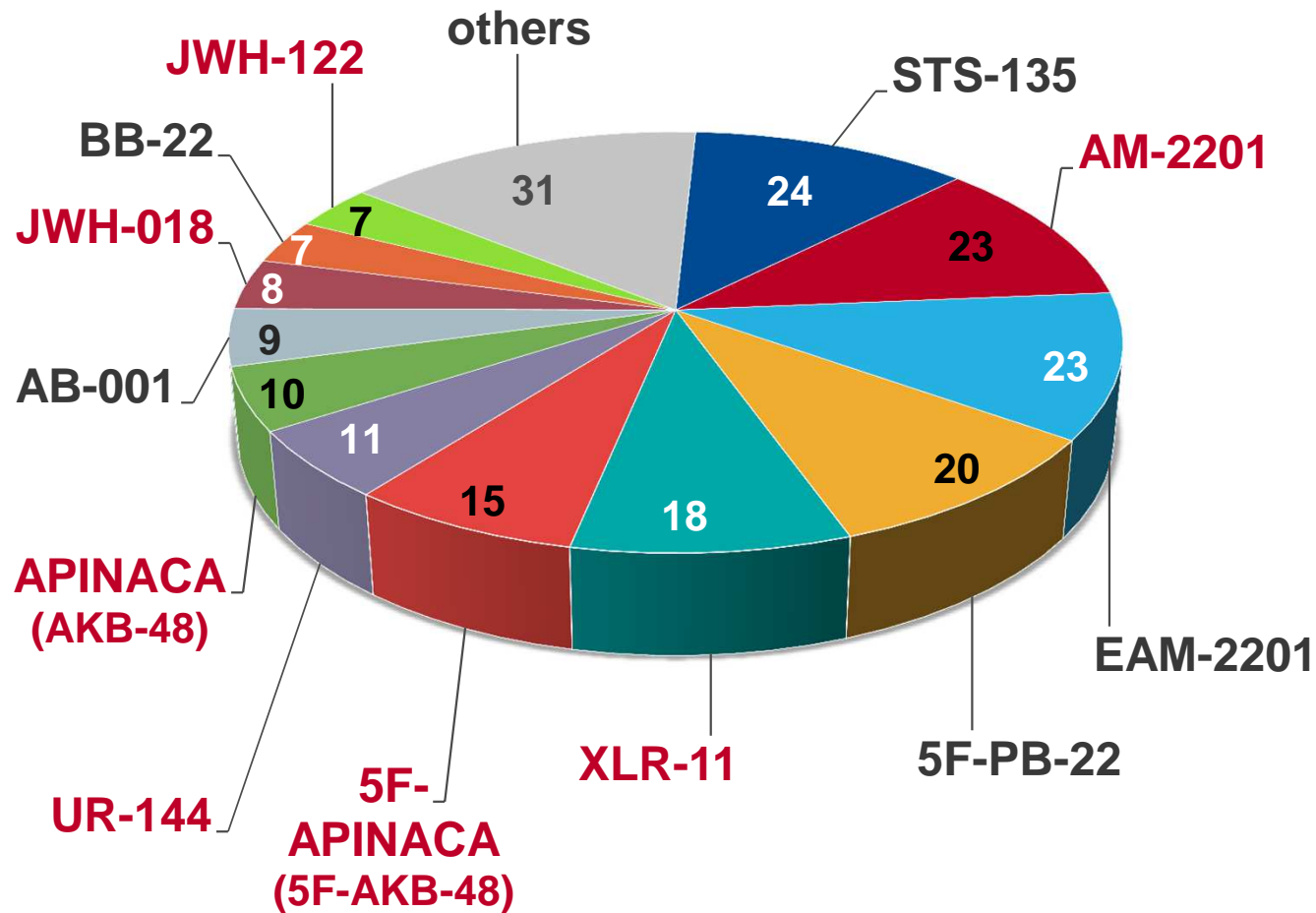
→ Tradekey



- Marketplace for wholesalers
- Possibility to buy a big variety of NPS as (pure) 'research chemicals'
- BUT: minimum quantity often  $\geq 100$  kg → negotiations about getting smaller samples (10 – 100 g)

# Synthetic Cannabinoids - Monitoring

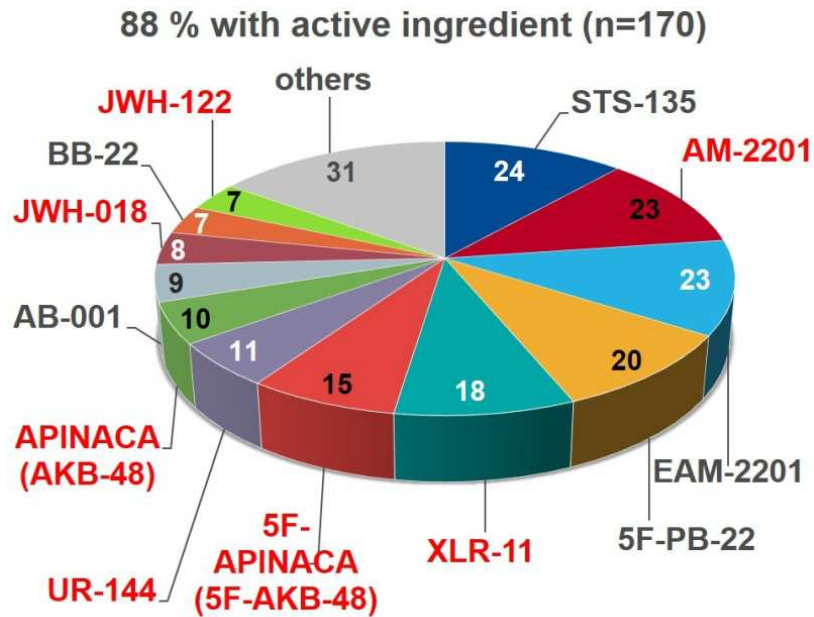
88 % with active ingredient (n=170)



Others:

- AB-FUBINACA
- APICA
- JWH-203
- AB-PINACA
- MAM-2201
- CRA-13
- JWH-073
- JWH-081
- JWH-210
- JWH-250
- AM-1220
- AM-2233

# Synthetic Cannabinoids - Monitoring



synthetic cannabinoids which have not been found during the last 1.5 years:

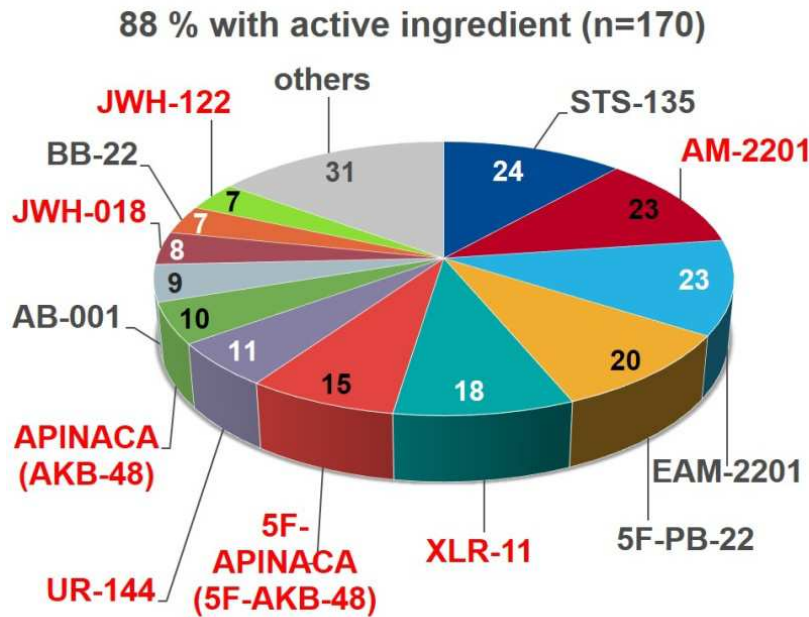
- AM-1220 azepane isomer
- AM-1248
- AM-2232
- AM-694
- JWH-019
- JWH-251
- JWH-307
- JWH-398
- RCS-4 + ortho Isomer



# Synthetic Cannabinoids - Monitoring

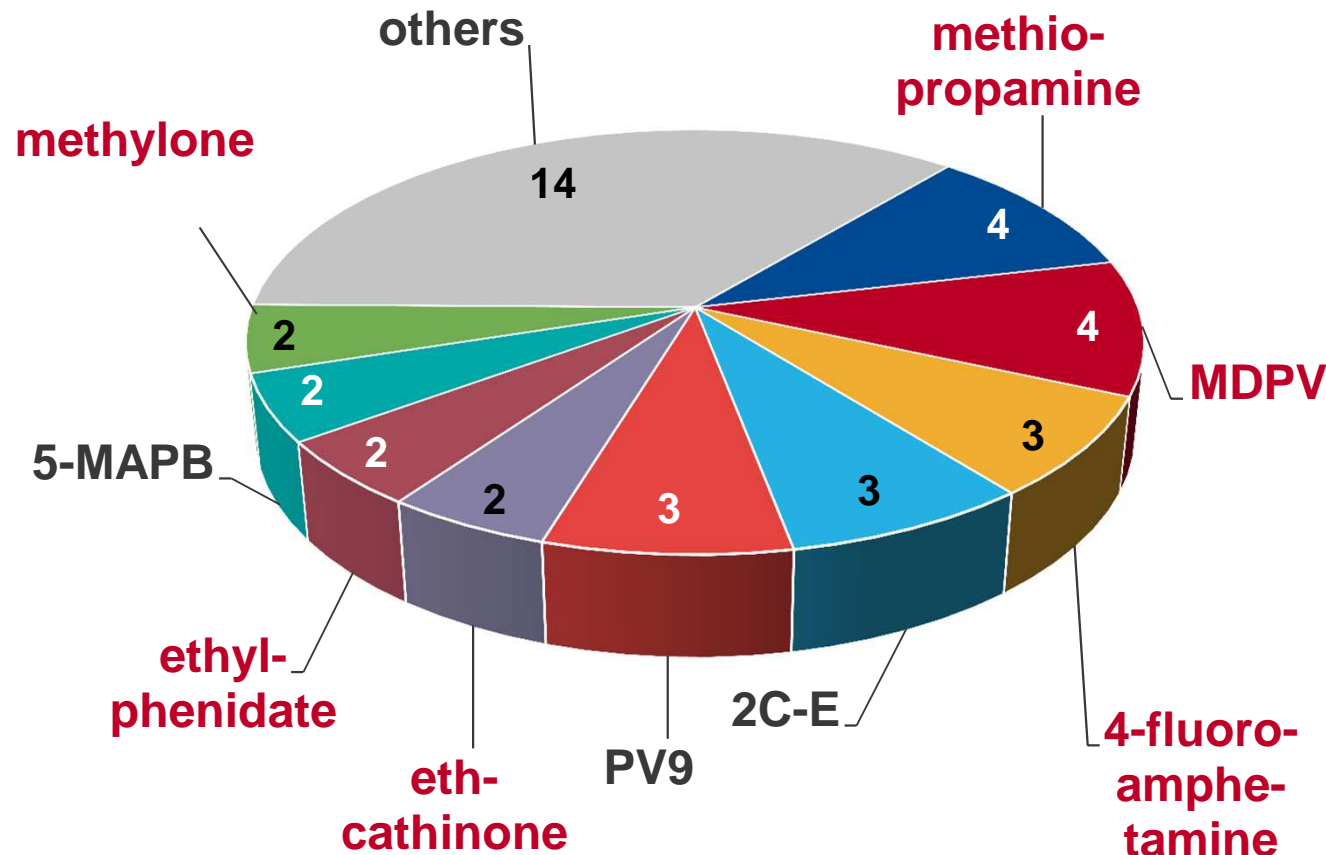
## NEW:

- **EAM-2201**: April 2013
- **5F-APINACA (5F-AKB-48)**: June 2013
- **5F-PB-22**: June 2013
- **BB-22**: September 2013
- **AB-FUBINACA**: January 2014
- **THJ-018** (as research chemical): January 2014
- **THJ-2201** (as research chemical): January 2014
- **AB-PINACA** (April 2014)



# Bath salts - Monitoring

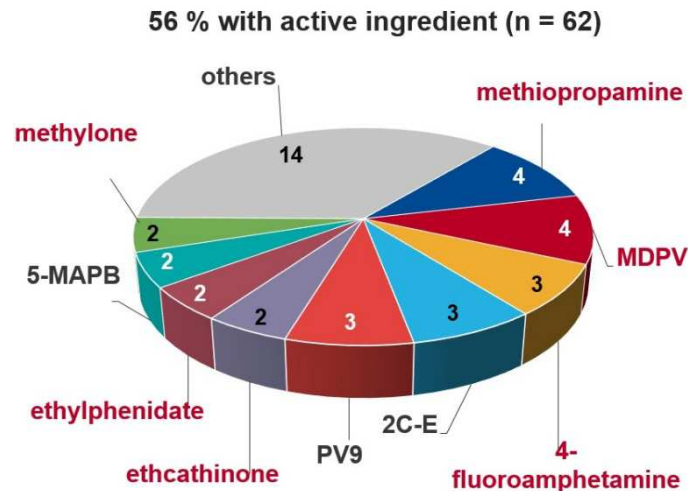
56 % with active ingredient (n = 62)



Others:

- 2-aminoindane
- 3/4-fluoromethcathinone
- 4-acetoxy-DMT
- 4-HO-MET
- 4-MEC
- 2C-D
- 25C-NBOMe
- 25I-NBOMe
- buphedrone
- ethylone
- MDPBP
- pentedrone/iso-pentedrone
- alpha-PVP

# Bath salts - Monitoring



## NEW:

- **5-/6-MAPB**: September 2013
- **4-HO-MET**: November 2013
- **PV9**: November 2013
- **4-acetoxy-DMT**: March 2014

Higher rate of products without any active ingredient (except caffeine)

→ Since August we started to buy research chemicals from online shops



# Research chemicals - Monitoring

- 100 % positive results (n=12)
  - until now: 'what we buy is what we get'
  - research chemical shops mostly located in GB
  - substances bought as research chemicals:
    - 2-aminoindane
    - 3,4-CTMP (dichloromethylphenidate)
    - bk-2C-B
    - benzocaine
    - etaqualone
    - ethylphenidate
    - mebroqualone
    - methiopropamine
    - methoxphenidine
    - methoxypiperamide
    - N-methyl-2-AI
    - nitracaine
- NEW:**
- **methoxypiperamide:** August 2013
  - **5-EAPB:** December 2013
  - **3,4-CTMP :** December 2013
  - **bk-2C-B:** December 2013
  - **N-methyl-2-AI:** December 2013
  - **methoxphenidine:** January 2014

# Latest products – E-liquids



New trend: Liquids for E-cigarettes

First bought in May 2014

Herballiquids.com (GB; picture left):

- Active ingredients listed
- 5F-APINACA



Nature World (CZ; picture right)

- Ingredients not listed
- 5F-APINACA

**BAD WEEDS GROW TALL...**

ANMELDEN | REGISTRIEREN | KONTO | EUR |

START SEITE | RÄUCHERMISCHUNGEN | RÄUCHERMISCHUNG BUNDLES | E-LIQUIDS | RESTPOSTEN

SUCHE

**NEU in unserem Shop!**

noch besser / noch ergiebiger / noch intensiver

**e-Liquids**

**Die neue Generation!**

Endlich da: Die neue Generation der e-Liquids



# Quantification of SCs in drug material

HPLC-DAD:

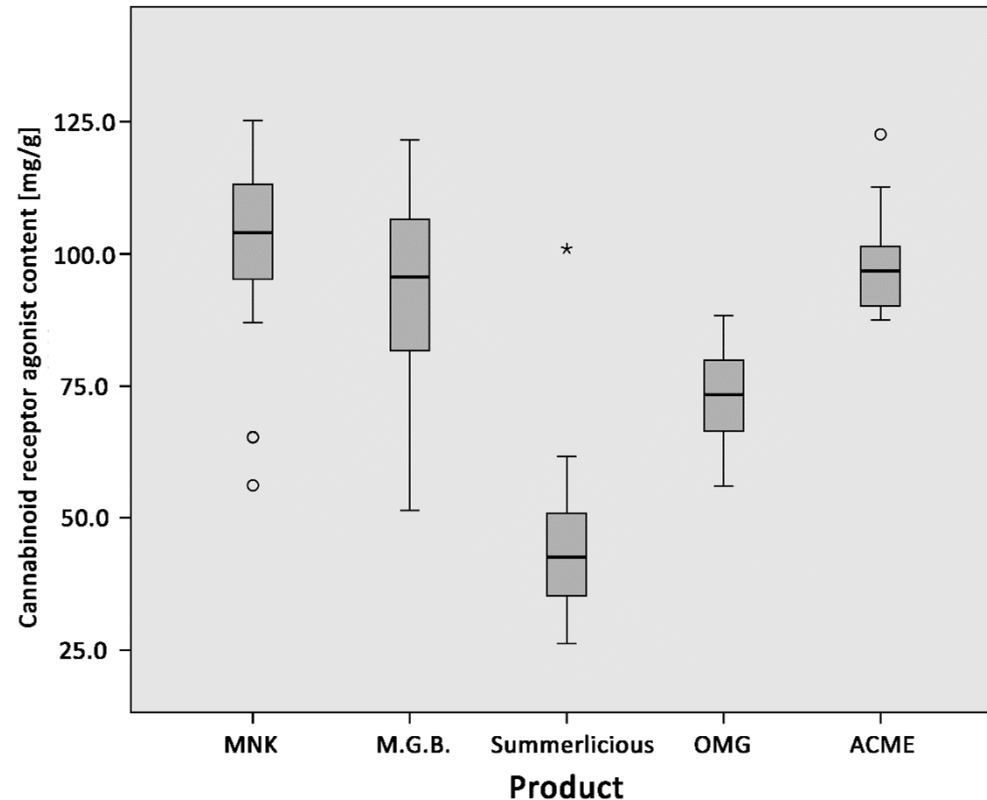
Analysis of 313 sachets (31 brands) from one single online retailer  
'Complete' analysis of 34 sachets (21 brands)



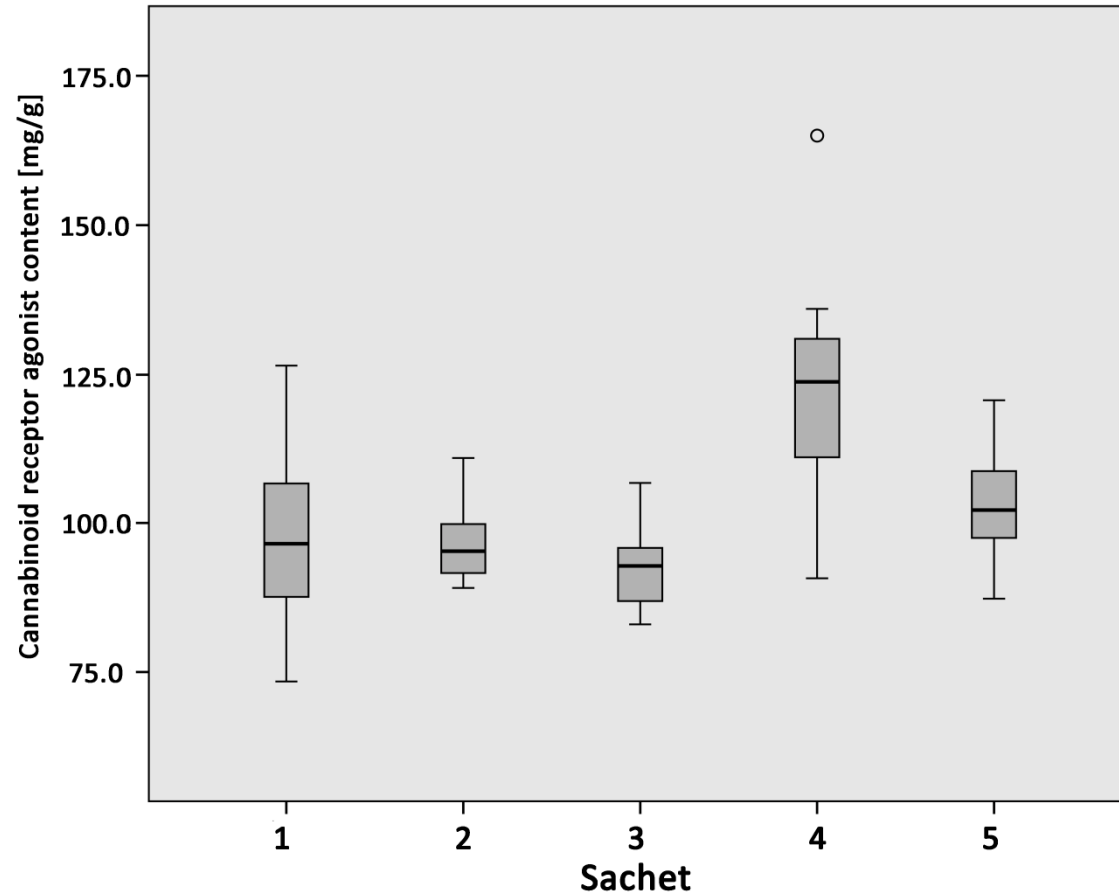
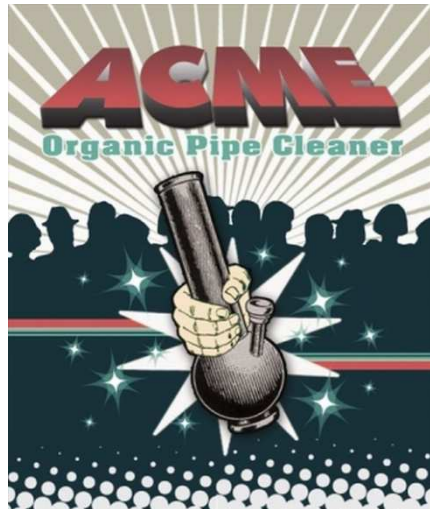
# Inter-package variability

313 sachets analysed (27 brands):

- highest standard deviation in product “Summerlicious” (AM-2232): 26 – 100 mg/g (n=23)
- five brands with the most sachets investigated:
  - MNK (n=55)
  - Monkees go Bananas (M.G.B. n=33)
  - Summerlicious (n=23)
  - OMG (n=22)
  - ACME (n=19)



# Inhomogeneities in the 'herbal mixture' ACME



Product weight: 2 g  
Aliquots: 200 mg  
SC: JWH-210  
 $K_i$  CB<sub>1</sub>: 0.46 ± 0.03 nM

# Replacement of the active ingredient

Product	Mean SC content [mg/g]	Synthetic cannabinoid	K <sub>i</sub> CB <sub>1</sub> [nM]
Blaze	160.7	JWH-307	7.7 ± 1.8
	152.8	JWH-210	0.46 ± 0.03
Peace	59.4	JWH-210	0.46 ± 0.03
	38.9	XLR-11	24
Vegas Titanium	49.2	JWH-210	0.46 ± 0.03
	45.9	XLR-11	24

The added amount of synthetic cannabinoids often stays the same despite significant differences in the binding affinity of the ,newly' added synthetic cannabinoid

→ Intoxications likely to occur



# German narcotics law

## synthetic cannabinoids

- CP 47,497
  - CP 47,497-C6-homolog
  - CP 47,497-C8-homolog
  - CP 47,497-C9-homolog
  - JWH-018
  - JWH-019
  - JWH-073
  - JWH-203
  - RCS-4 ortho isomer
  - AM-694
  - JWH-007
  - JWH-015
  - JWH-081
  - JWH-122
  - JWH-200
  - JWH-210
  - JWH-250
  - JWH-251
  - RCS-4
  - AKB-48 (APINACA)
  - AKB-48-5F
  - AM-1220
  - AM-1220-azepane isomer
  - AM-2201
  - AM-2232
  - AM-2233
  - JWH-307
  - MAM-2201
  - UR-144
  - XLR-11
  - AB-001
  - A 796,260
  - A 834,735
  - AB-001-5F
  - AB-005
  - AB-FUBINACA
  - AB-PINACA
  - ADB-FUBINACA
  - ADB-PINACA
  - ADB-PINACA-5F
  - ADBICA
  - ADBICA-5F
  - AM-1248
  - AM-2201 indazol isomer
  - AM-679
  - 2NEI (APICA)
  - BB-22
  - EAM-2201
  - FDU-PB-22
  - FUB-PB-22
  - JWH-020
  - JWH-022
  - JWH-030
  - JWH-080
  - JWH-176
  - JWH-180
  - JWH-182
  - JWH-213
  - JWH-368
  - JWH-370
  - JWH-387
  - JWH-398
  - JWH-412
  - JWH-412-5F
  - MN25
  - NNEI
  - NNEI-5F
  - PB-22
  - PB-22-5F
  - RCS-8
  - STS-135
  - THJ
  - THJ-5F
  - THJ-018
  - THJ-2201
  - UR-144 isomer
  - XLR-11 isomer
  - XLR-12
  - WIN 48,098
  - WIN 55,212-2
- already banned  
not listet yet

# German narcotics law

already banned  
not listet yet

## designer stimulants

### Annex I:

- DOB
- 2C-I
- 6-CI-MDMA
- 2C-T-2
- 2C-T-7
- DET
- DMA
- DOET
- DMMA
- DOM
- DMT
- DOC
- 4-Fluoroamphetamina
- Methcathinone
- Methiopropamine
- Methoxetamine
- Methoxyamphetamine
- 5-MeO-DiPT
- 5-MeO-DMT
- PMMA
- MDEA
- MDMA
- Mephedrone
- MPPP

- 1M-3PP
- MPTP
- 4-MTA
- MDA
- PCP
- TMA
- TMA-2
- 2C-B

### Annex II:

- 5-/6-APB
- Benzylpiperazine
- Buphedrone
- Butylone
- mCPP
- 3,4-DMMC
- Ethcathinone
- Ethylphenidate
- N-Ethylamphetamine
- Flephedrone (4-FMC)
- 4-Fluoromethamphetamine
- 3-FMC
- p-Fluorophenylpiperazin
- 4-Fluorotropacocaine
- Levamphetamine
- Methamphetamine

- Methedrone
- p-Methoxyethylamphetamine (PMEA)
- 4-Methylamphetamine
- Methylbenzylpiperazine (MBZP)
- MDPV
- 4-Methylethcathinone (4-MEC)
- Methylone
- Naphyrone
- Pentedrone
- Pyrovalerone
- $\alpha$ -Pyrrolidinovalerophenone

### Annex III:

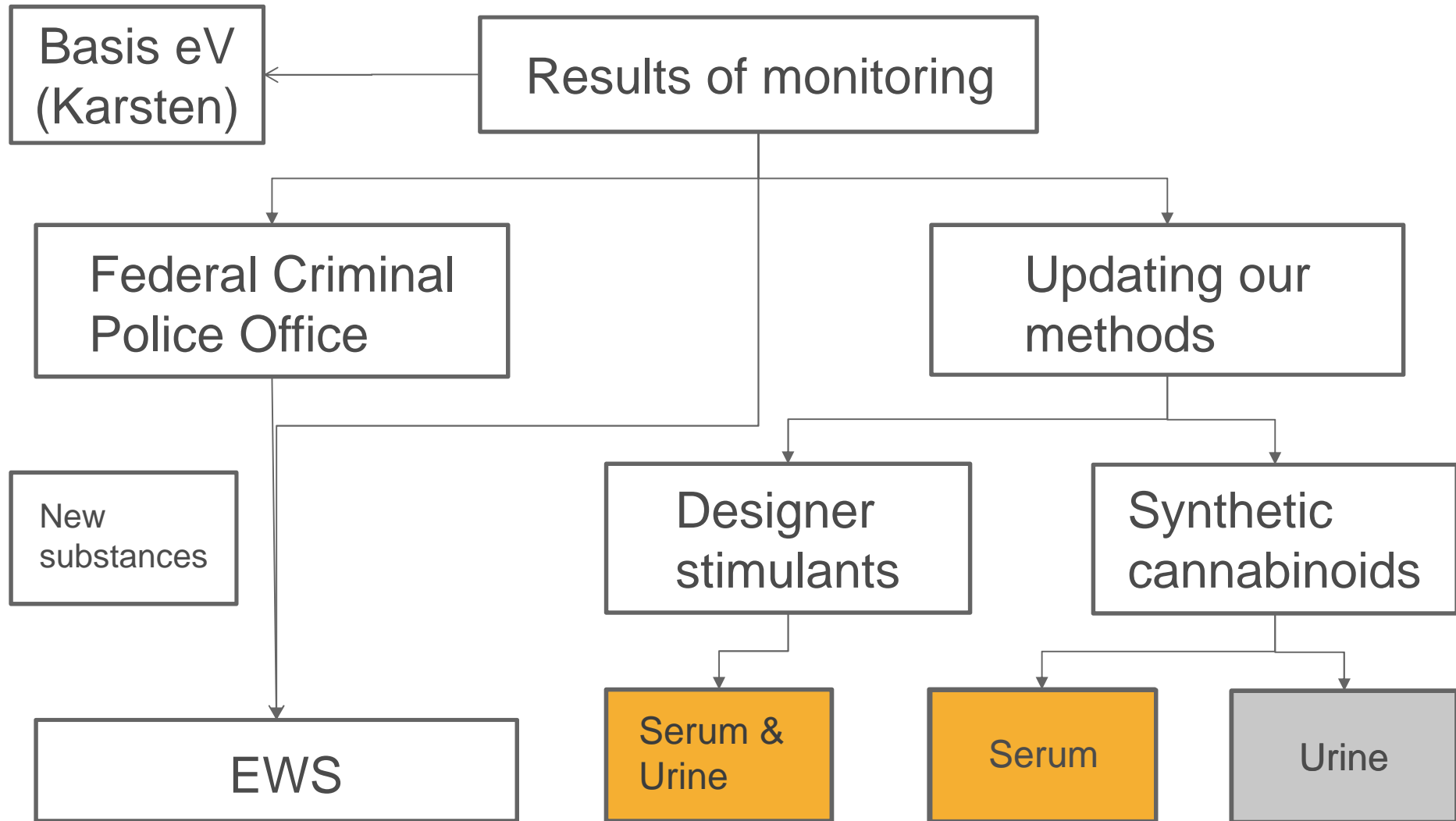
- Amphetamine
- Cathin (D-Norpseudoephedrine)
- Dexamphetamine
- Fenproporex
- Lisdexamphetamine
- Methylphenidate
- 2-AI
- 2C-C
- 2C-D
- 2C-E
- 2C-P
- 2-FMA

- 2-IAI
- 3-MMC
- 5-/6-APDB
- 5-EAPB
- 5-IT
- 5-/6-MAPB
- 5-MeO-DALT
- 5-MeO-DiPT
- Bromo-Dragonfly
- Dimethocaine
- DiPT
- DOI
- DOM
- Ethylone
- Ketamine
- MDAI
- MDPBP
- MDPPP
- NEB
- 25C-NBOMe
- 25D-NBOMe
- 25I-NBOMe
- Pentylone
- etc.





# What are we doing with the monitoring results?



# Designer stimulants - method

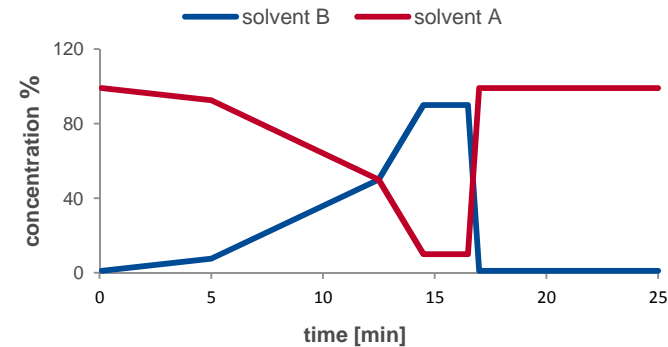
## Sample preparation:

- Automated solid phase extraction (SPE) of 1 mL serum/urine
- Evaporation to dryness
- Reconstitution
- LC-ESI-MS/MS



## Conditions:

- ABSciex Qtrap 4000<sup>®</sup>
- sMRM – positive mode



- Synergi Polar RP (100 mm × 2.0 mm, 2.5 μm particle size)
- 0.4 mL/min flow rate
- Solvent A: water with 0.1% formic acid/ 10 mM ammonium formate
- Solvent B: methanol with 0.1% formic acid
- Post column: isopropanol
- 25 min

# Designer stimulants - samples



1108 samples  
947 urine; 160 blood or serum, 1 hair  
964 male; 107 female

**negative**  
88 % (976)  
849; 98

**positive**  
12% (132)  
114; 10

**1 designer drug**  
75% (99)  
86; 7

**2 or more designer drugs**  
25% (33)  
28; 3

**Amphetamine**  
36% (36)

**MDPV**  
17% (17)

**Meth-amphetamine**  
14% (14)

**Others**  
31% (31)  
e.g.: desoxypipradrol;  
Methiopropamine



# Synthetic Cannabinoids – serum-method

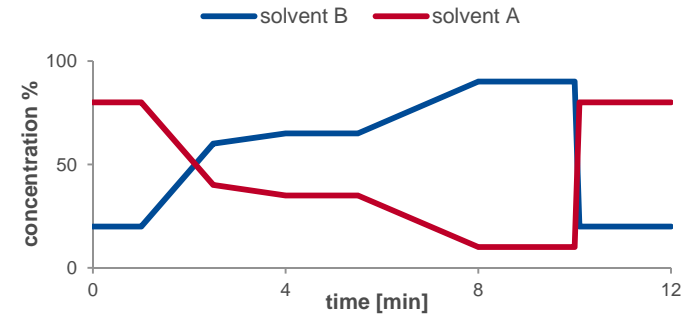
## Sample preparation:

- Liquid-liquid extraction (LLE) of 1 mL serum
- Centrifugation
- Evaporation to dryness
- LC-ESI-MS/MS



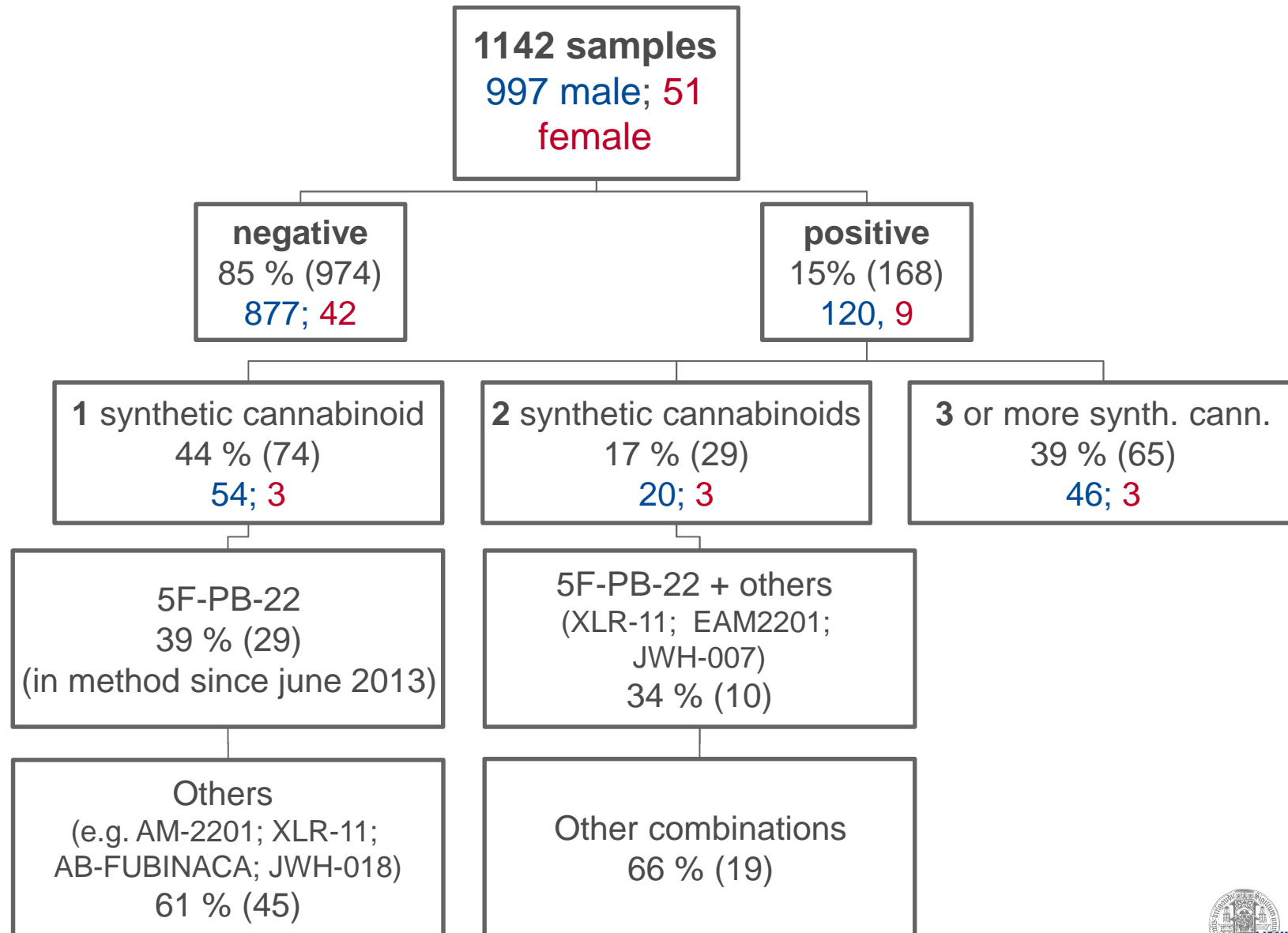
## Conditions:

- ABSciex Qtrap 4000<sup>®</sup>
- sMRM – positive mode



- Kinetex C18 column (100 mm × 2.1 mm, 2.6 µm particle size)
- 0.5 mL/min flow rate
- Solvent A: water with 0.1% formic acid/ 1% acetonitrile/2 mM ammonium formate
- Solvent B: acetonitrile with 0.1% formic acid/2 mM ammonium formate
- 12 min

# synthetic cannabinoids – samples since march 2013



# Thank you for your attention!

Thanks to:

Björn Moosmann

Folker Westphal

Michael Müller

Team Forensische Toxikologie



Bundesministerium  
für Gesundheit



This publication has been produced with the financial support of the Drug Prevention and Information Programme of the European Union (JUST/2011/DPIP/AG/3597), the German Federal Ministry of Health and the City of Frankfurt/Main.