



# Synthesis and Purification of Reference Materials for NPS

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Chiron AS, Trondheim, Norway





# Chiron – Provider for reference materials

- Environmental analysis
- Petroleum analysis
- Food safety analysis
- **Pharmaceutical and forensic analysis**





# Reference materials for Pharmaceutical and Forensic analysis:

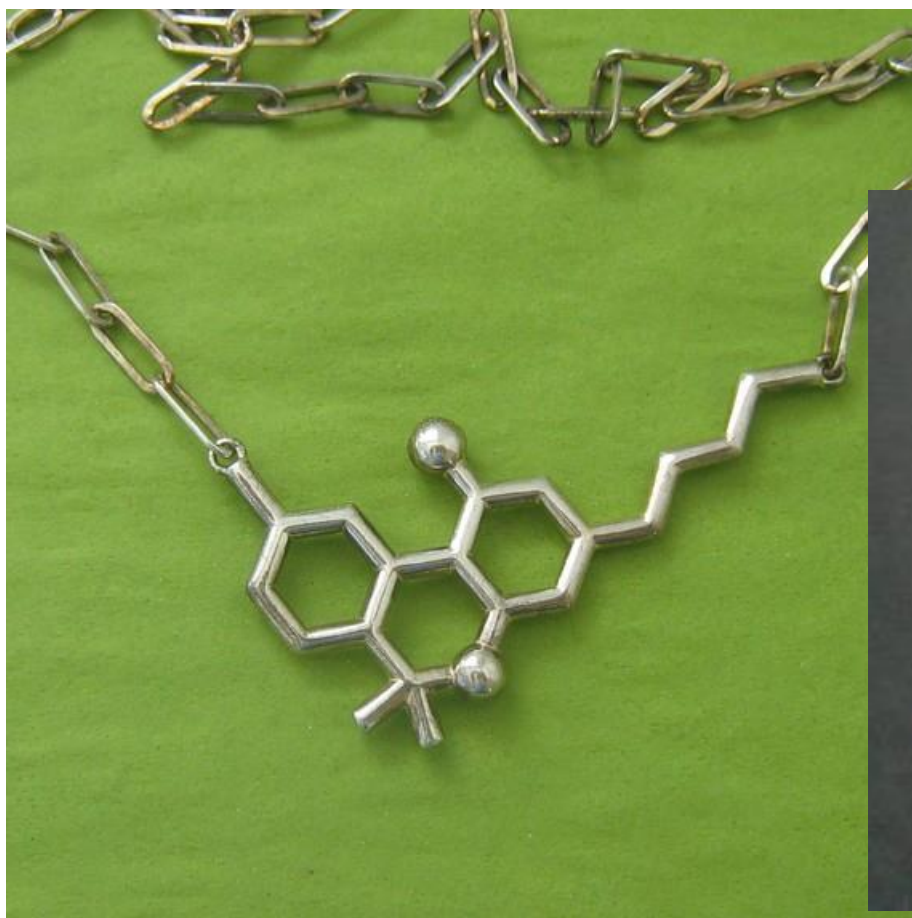
- Metabolites; Intermediates; Impurities
- Drugs of abuse:
  - Opioids
  - Cannabinoids
  - Cocaines
  - Amphetamines
  - New Designer Drugs





## Reference materials for NPSs:

- **2009: First to launch SPICE standards (JWH-018 and JWH-073)**
- **2012-13: Standards for SPICE metabolites**
- **2010-13: Cathinones and Amphetamines**
- **2014- :**



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CHIRON



## Reference materials for NPSs:


- **2009: First to launch SPICE standards (JWH-018 and JWH-073)**
- **2012-13: Standards for SPICE metabolites**
- **2010-13: Cathinones and Amphetamines**
- **2014- :  
new synthetic cannabinoids,  
designer benzodiazepines, GHB ...**



## Projects for NPS reference materials:

- **Industrial Ph.D (2012-2014)**
  - The Research Council of Norway
  - Cooperated with NTNU
- **ISOFOR (2012-2015)**
  - Innovation Norway
  - Cooperated with NIPH
- **Quantum SPICE (2013-2016)**
  - EuroStars, European Funding
  - Cooperated with Nal Van Minden



**THE GOLD STANDARD FOR FORENSIC ANALYSIS**



**<sup>13</sup>C**

<sup>13</sup>C Labelled internal standards (IS) are superior to DEUTERATED standards in UPLC-MS/MS analysis of drugs

The same RETENTION TIMES and RESPONSE FACTORS as the natives lead to  
**NO BIAS WITH ION SUPPRESSION**





# «QUANTUM SPICE»

- **EUROSTARS -**  
**A collaborative research project**  
**for European SMEs**
- **Chiron AS, Norway**
- **Nal von Minden GmbH , Germany**







## **Chiron AS:**

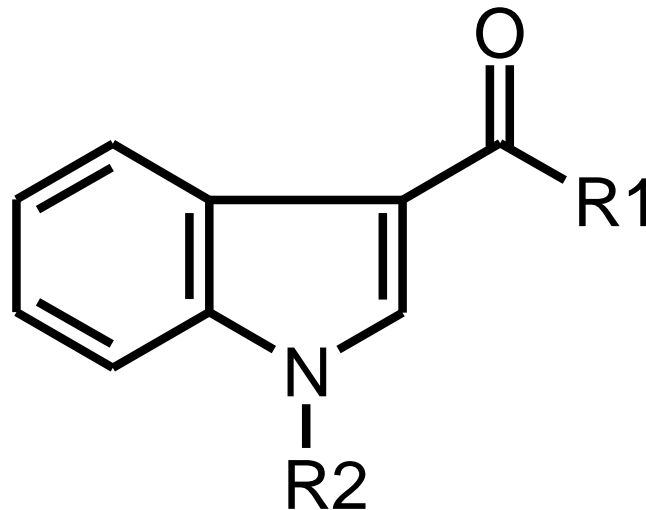
- **Synthesis of CRMs for the identification and quantification of «New Psychoactive Substances» by chromatography**

## **Nal von Minden GmbH:**

- **Preparation of POCT (point of care tests) or rapid tests for the same**

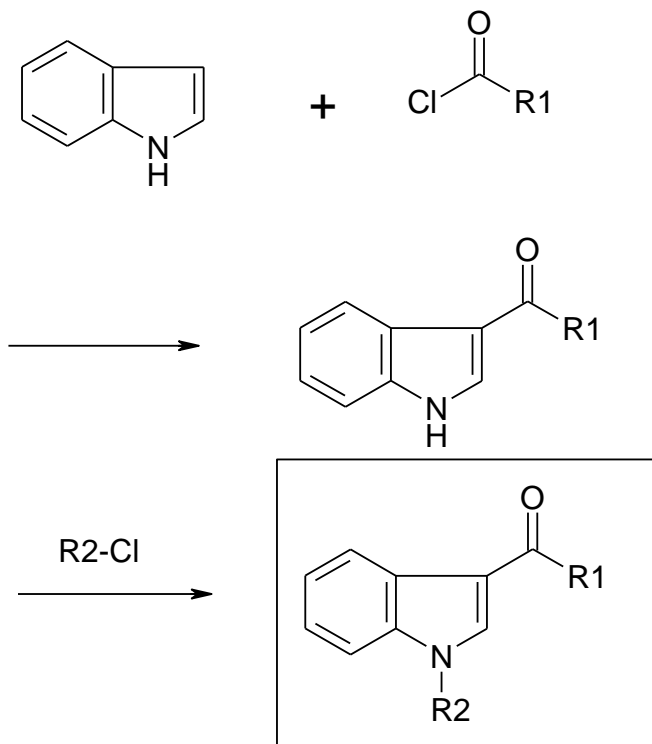


## SPICE (JWH) general structure:



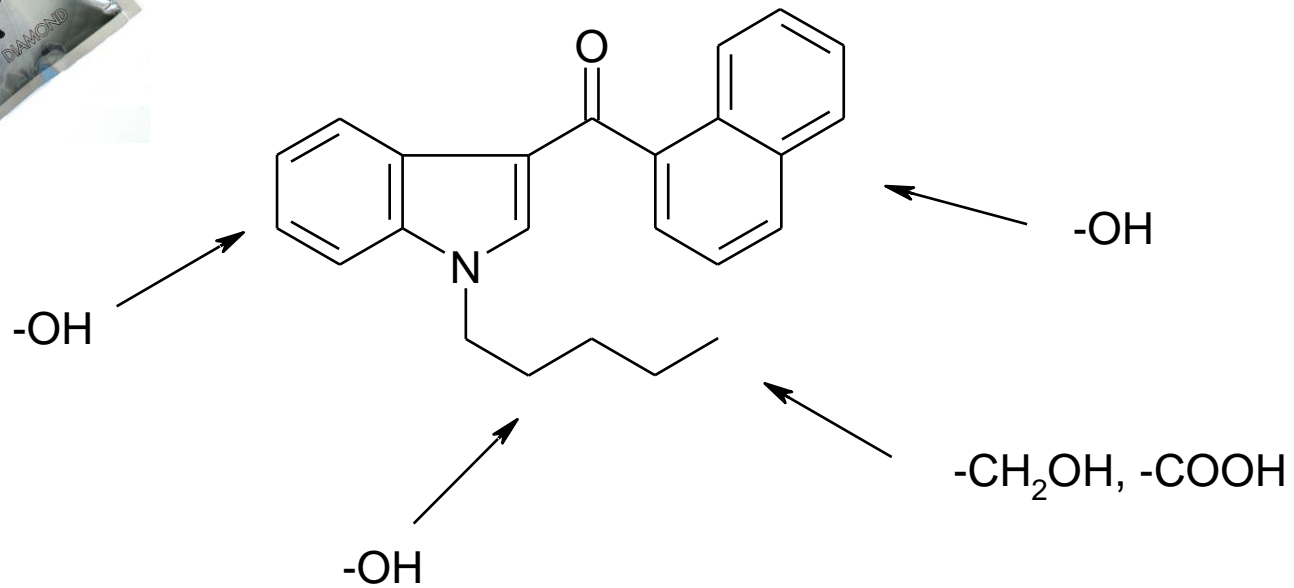


# SPICE general synthesis:



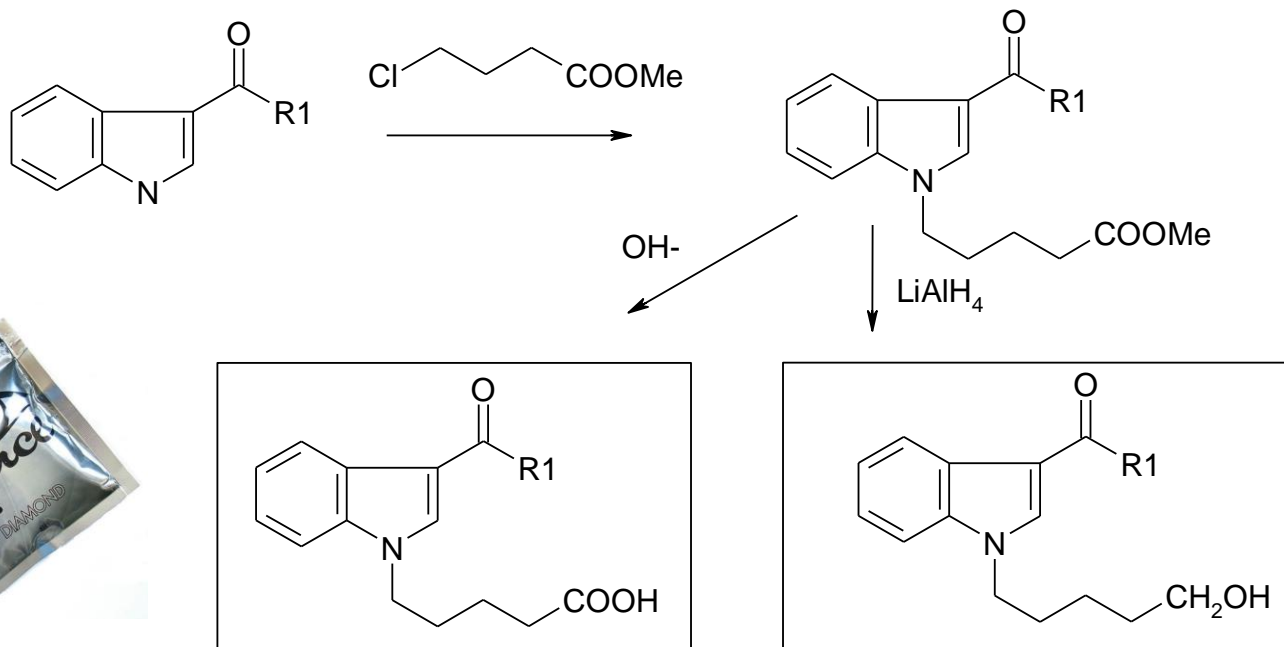


# Spice metabolites





# SPICE metabolite synthesis:





# First Norwegian list (2012)



AM-2201

JWH-018

JWH-073

JWH-081

JWH-122

JWH-203

JWH-210

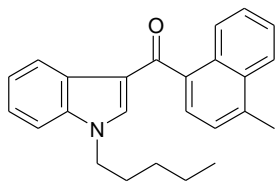
JWH-250



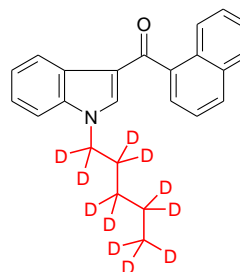


# JWH-018 type (C5-alkyl)

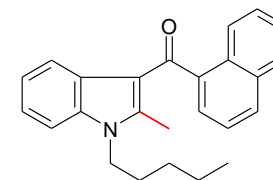
**JWH-018**



**JWH-018 d11**

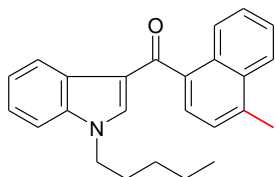


**JWH-007**

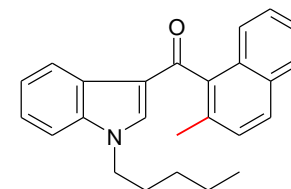


**JWH-018 2-Methylnaphthoyl**

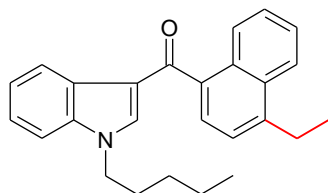
**JWH-122**



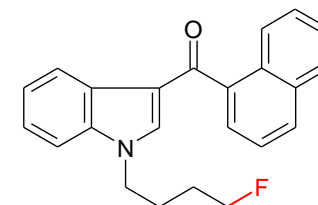
**JWH-122 d11**



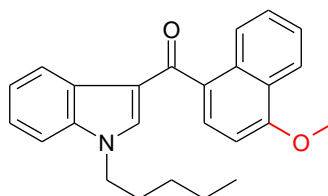
**JWH-210**



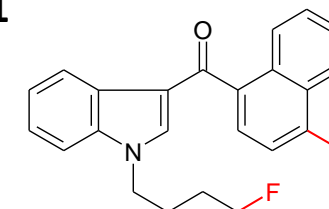
**AM-2201**



**JWH-081**



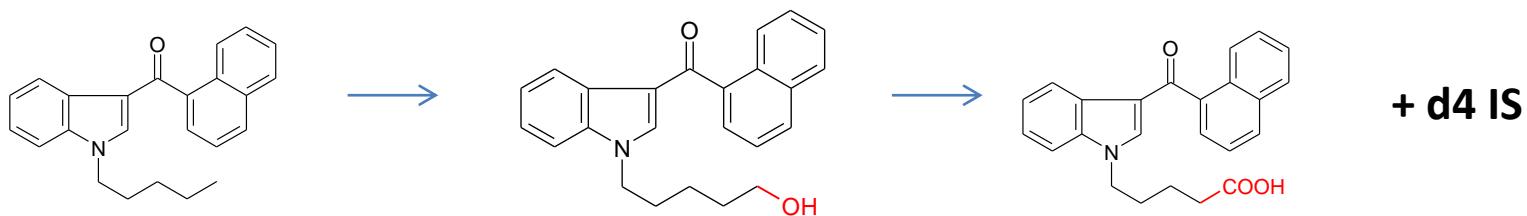
**MAM-2201**



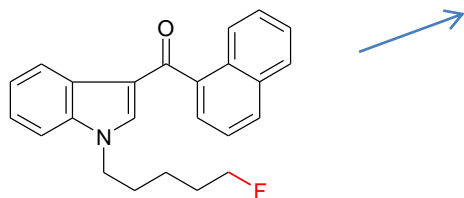


# JWH-018 type metabolites

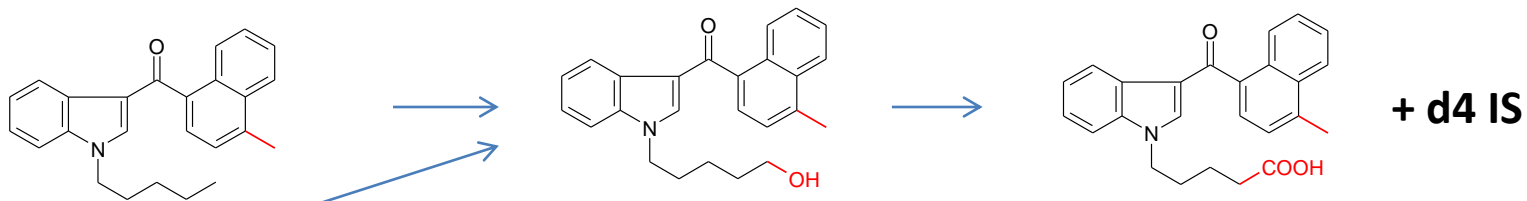
JWH-018



AM-2201



JWH-122



MAM-2201

JWH-210

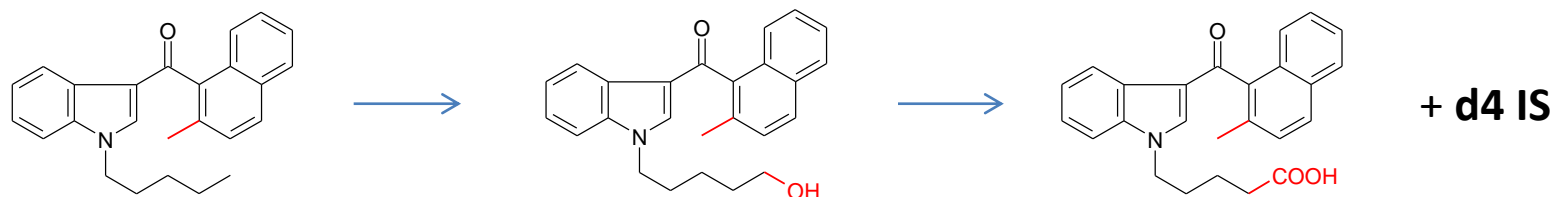






## cont. JWH-018 type metabolites

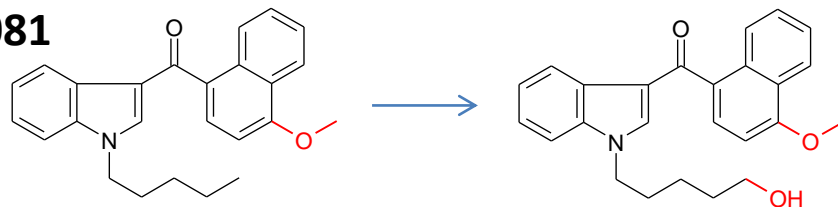
JWH-007



JWH-018 2-Methylnaphthoyl



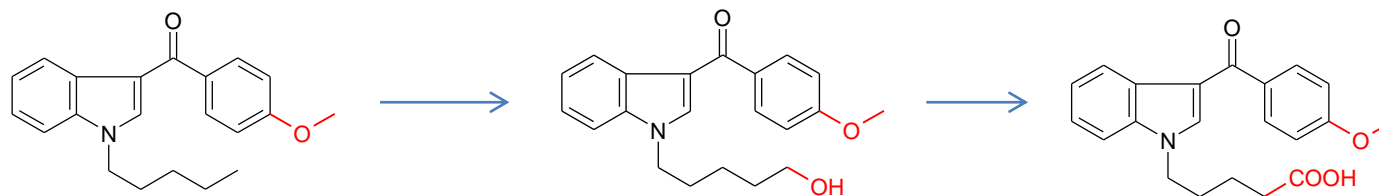
JWH-081





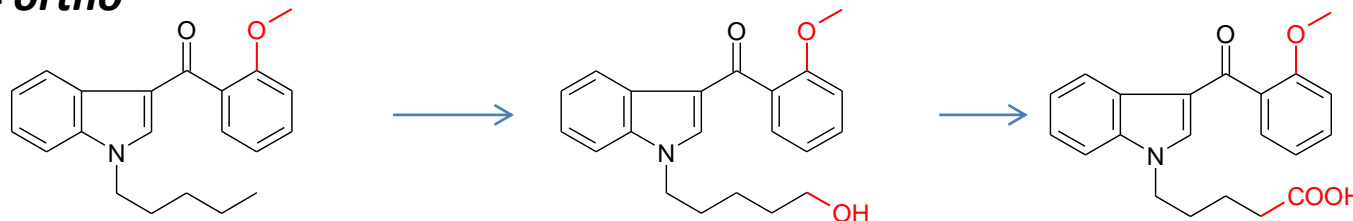
# RSC-4 metabolites

**RSC-4**



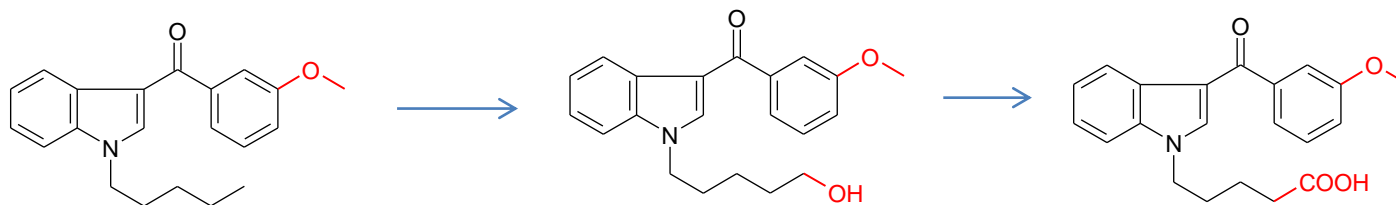
+ d4 IS

**RSC-4 ortho**



+ d4 IS

**RSC-4 meta**

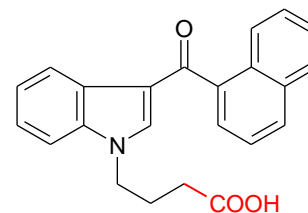
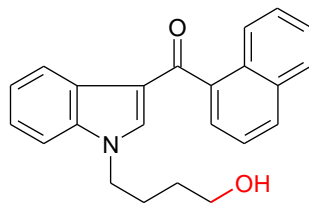
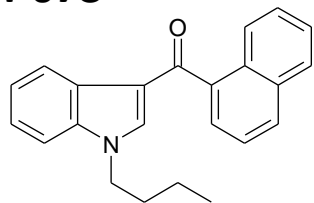


+ d4 IS



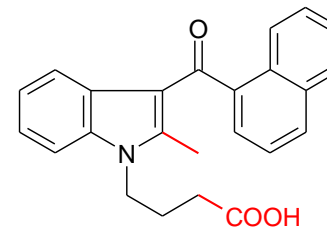
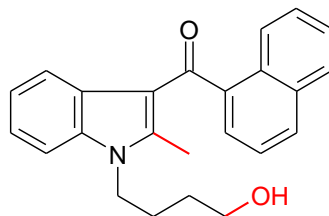
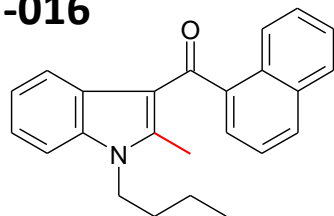
# JWH-073 type metabolites

**JWH-073**



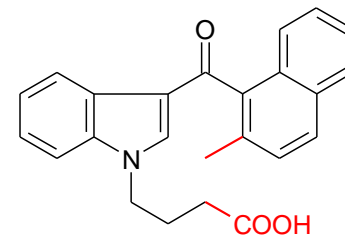
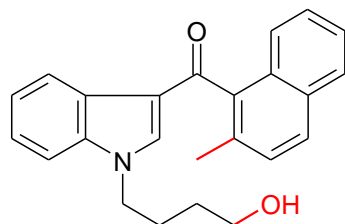
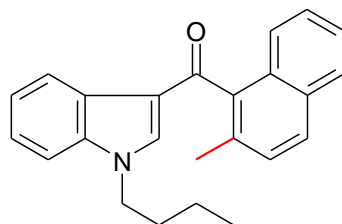
+ d4-IS

**JWH-016**



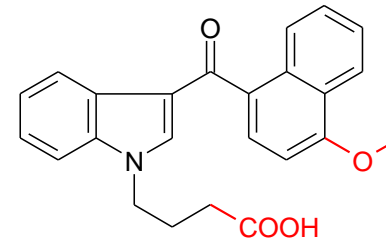
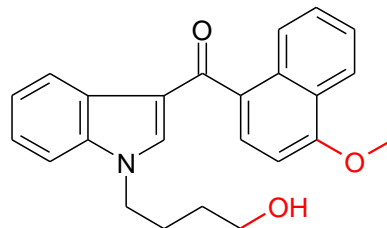
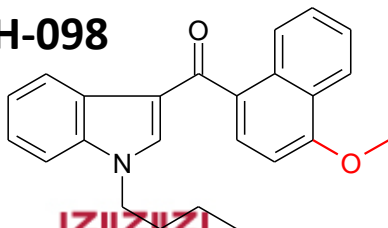
+ d4 IS

**JWH-073 2-Methylnaphthoyl**



+ d4 IS

**JWH-098**

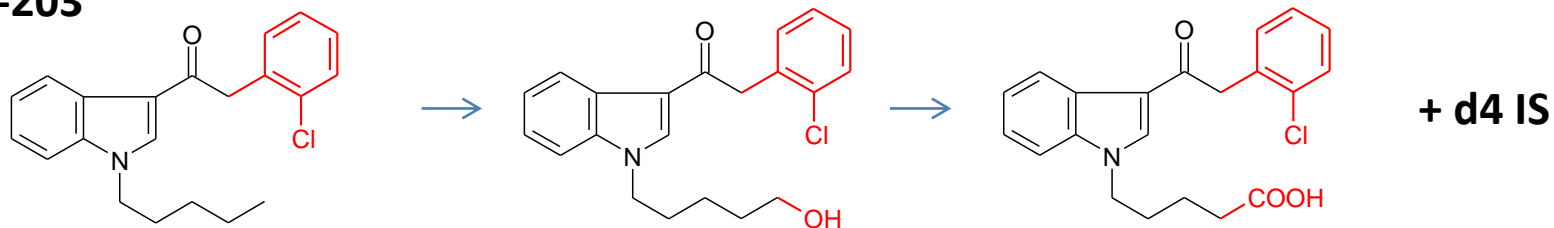


+ d4 IS

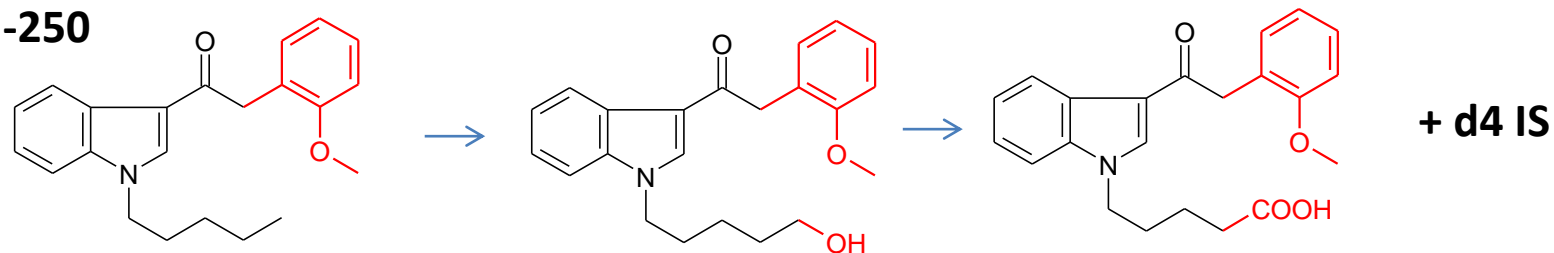


# Phenylethanone type metabolites

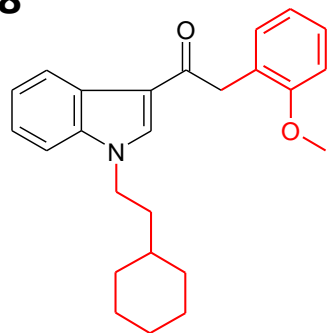
**JWH-203**



**JWH-250**

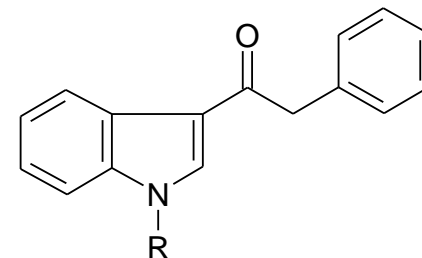
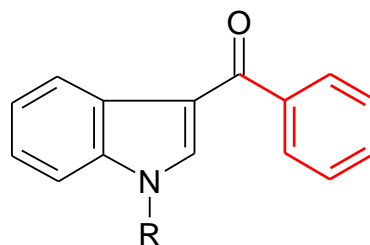
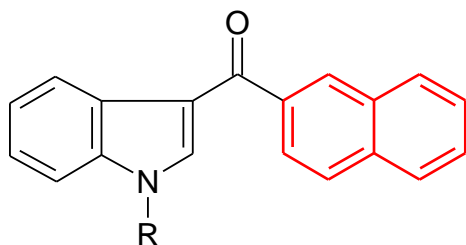


**RCS-8**

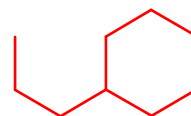




# Second Norwegian list (2013)



R=:

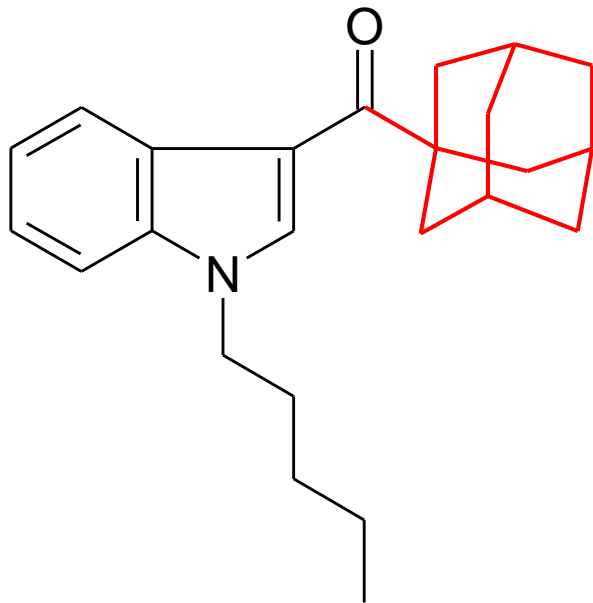


# JWH type NSPs not covered by the Norwegian regulations 2013:



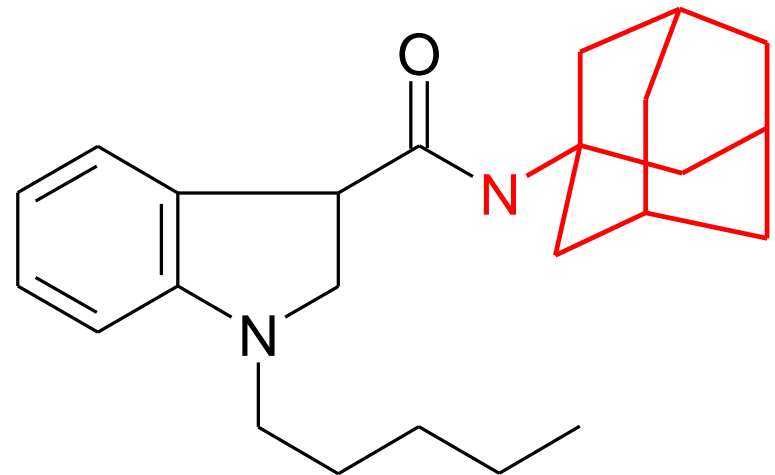
Adamantyltype:

AB-001



Amido-adamantyltype:

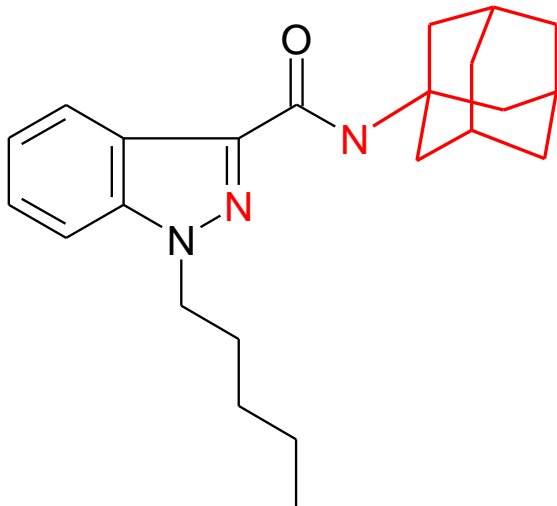
APICA



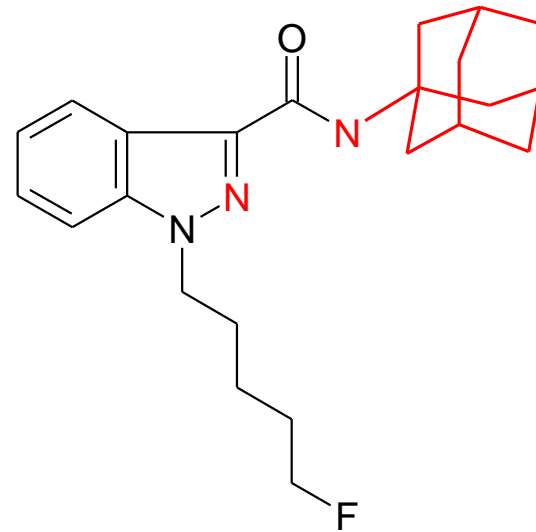
# JWH type NSPs not covered by the Norwegian regulations 2013:



APINACA



STS-135 (5F-APICA)

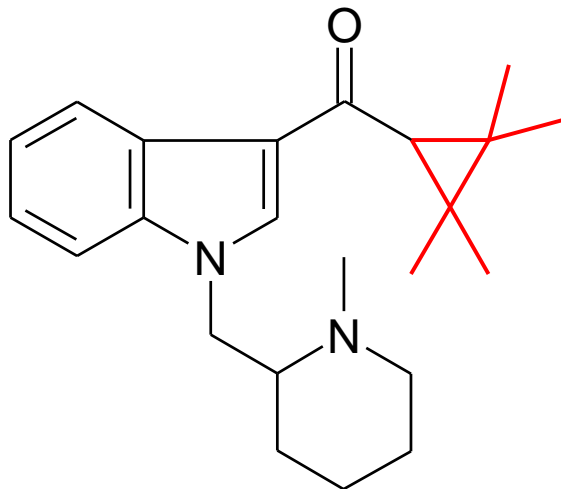


# JWH type NSPs not covered by the Norwegian regulations 2013:

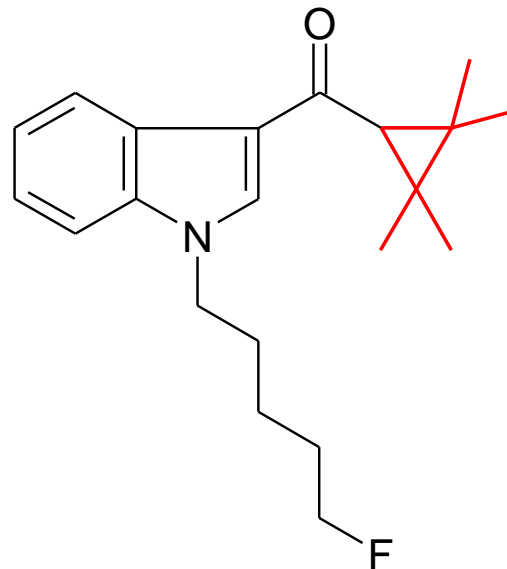


Cyclopropyltype:

AB-005



XLR-11



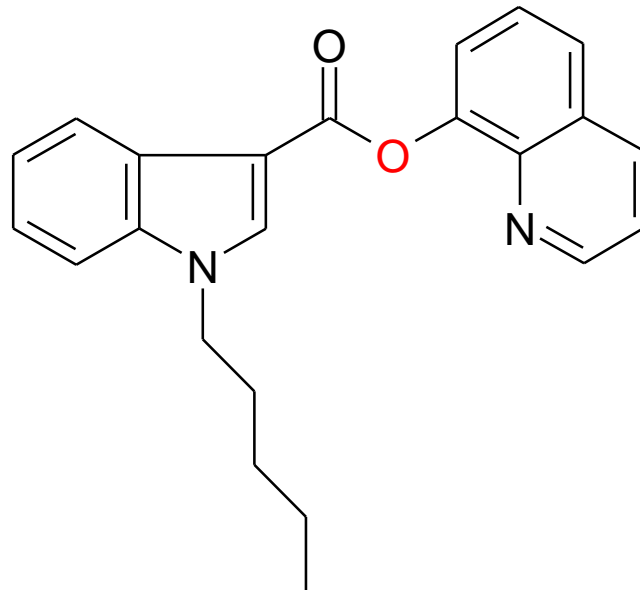


# JWH type NSPs not covered by the Norwegian regulations 2013:



Carboxylic ester type:

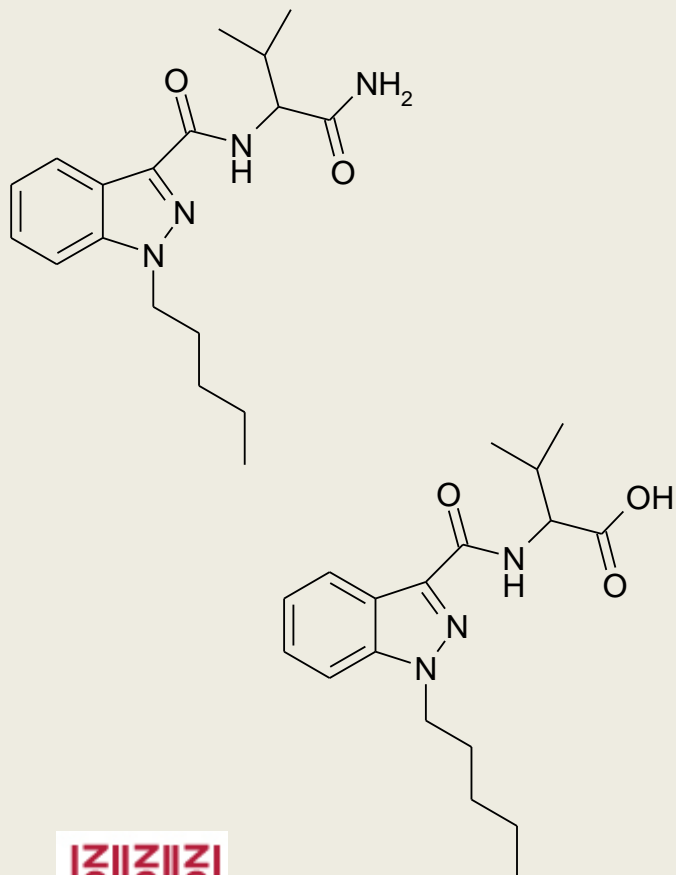
QUPIC



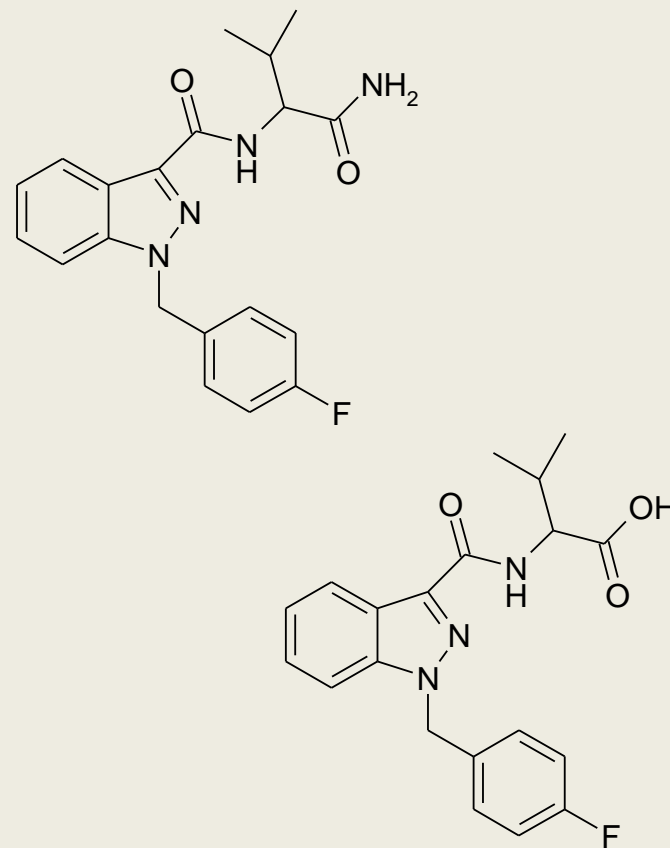


# Other compounds recently prepared:

AB-PINACA



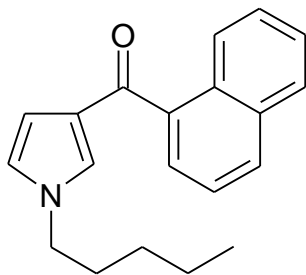
AB-FUBINACA



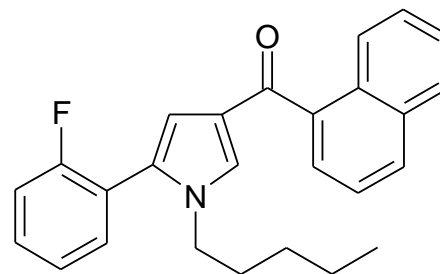


## Other compounds recently prepared:

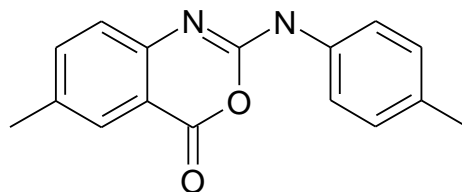
JWH-030



JWH-307

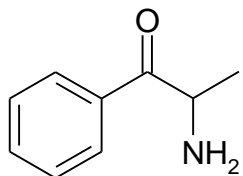


URB754

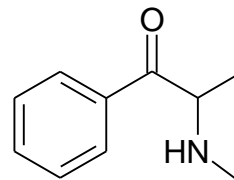




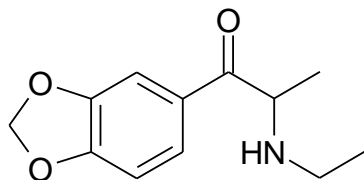
# Cathinones



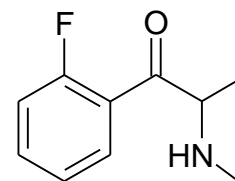
**Cathinone**



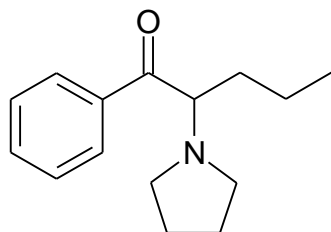
**Methylcathinone**



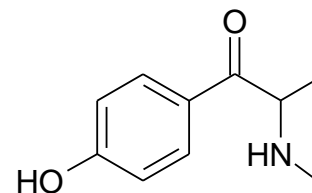
**Ethylone**



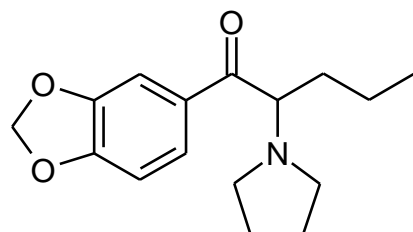
**2-FMC**



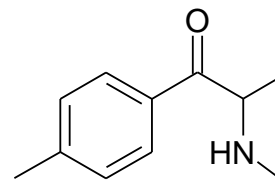
**$\alpha$ -PVP**



**4-Hydroxy-methcathinone**



**MDPV**

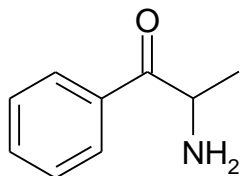


**Mephedrone**

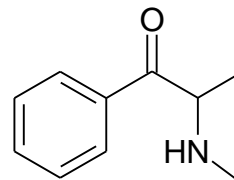




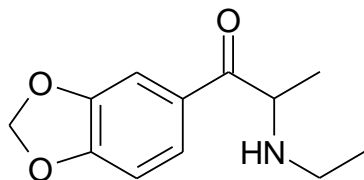
# Cathinones



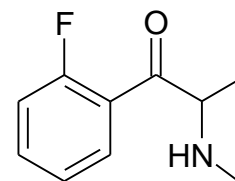
**Cathinone**



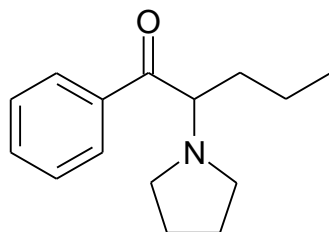
**Methylcathinone**



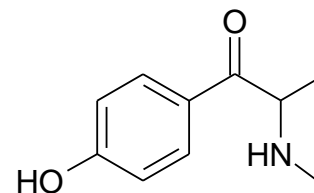
**Ethylone**



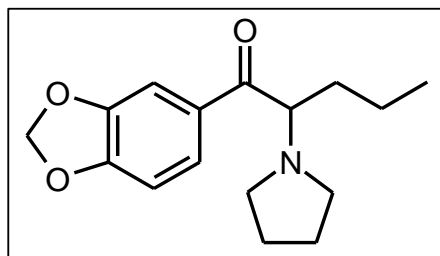
**2-FMC**



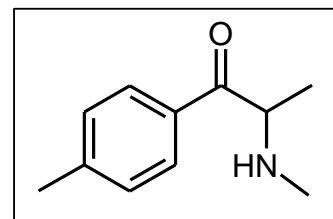
**$\alpha$ -PVP**



**4-Hydroxy-methcathinone**



**MDPV**

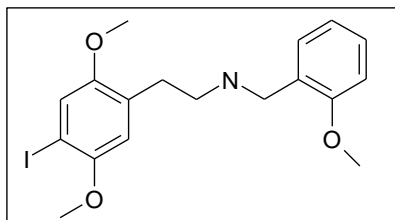


**Mephedrone**

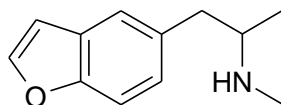


# NEW NPS-Compounds

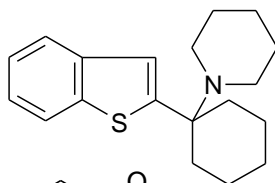
25NBOMe-series, e.g. 25INOBMe



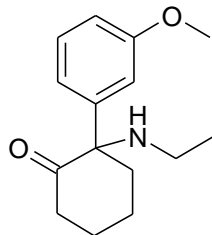
5MAPB



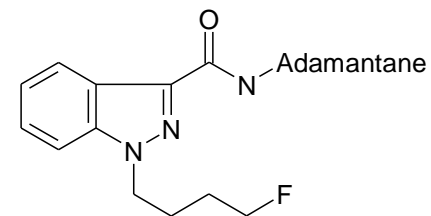
BTCP, BCP, Benoclidine



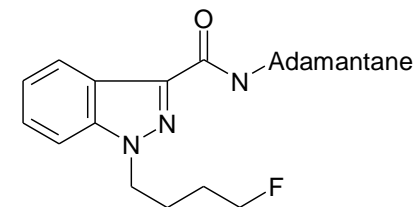
Methoxetamine, MXE



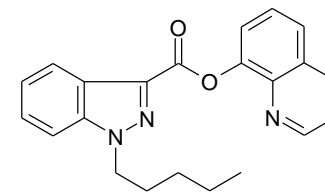
AKB-48, Apinaca



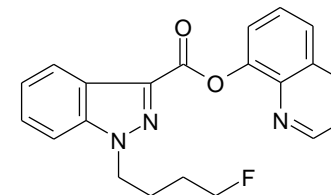
5F-AKB-48



PB-22, QUPIC



5F-PB22





# Identity

- **NMR**
- **Mass spectrometry**
- **UV-VIS spectrometry**
- **Comparison with authentic samples when available**
- **Other (mp, IR etc.)**



# Purity

- **Chemical purity by GC and/or LC**
- **Solvent content by GC-MS analysis (thermo desorption)**
- **Water content by Karl-Fisher analysis**
- **Inorganics by Ash content (sulphate ash)**





## **«Chiron Gold Label CRMs»**

- **A Chiron 2013 project aiming to produce highest quality CRMs through**
  - **ISO 17025 accreditation**
  - **ISO GUIDE 34 accreditation**
- **Will include the products from «ISOFOR» and «QUANTUM SPICE»**



# Challenges

- **Many products:  
new products, unknown metabolites**
- **Large variations in chemical classes**
- **Small quantities**



## **Future work on NSPs:**

- **Focus on important metabolites**
- **$^{13}\text{C}$  Labeling**
- **New compounds**



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