NOUVELLES SUBSTANCES PSYCHOACTIVES: ACTUALITÉ & DÉFIS ANALYTIQUES

Journal club de Toxicologie – 23 janvier 2020

Plan

- Introduction/rappels
- Actualité
- Actualité en Belgique
- Défi analytique
- Cas liégeois n°1: MDAI-EAPB
- Cas liégeois n°2: 2-AI
- Conclusion

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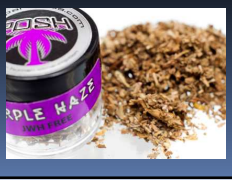
Les nouvelles drogues de synthèse « New Psychoactive Substances »

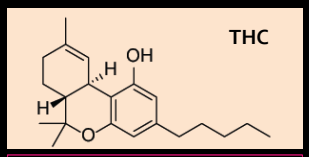
- Substances addictives, soit sous forme pure, soit sous forme de préparation, qui ne sont pas contrôlées *ou contrôlées depuis 2015* par la "Single Convention on Narcotic Drugs" de 1961 ou par la "Convention on Psychotropic Substances" de 1971, mais qui sont susceptibles de représenter une menace pour la santé publique
- Pas nécessairement de nouvelles inventions, mais disponibles sur le marché depuis peu
- Bath salts, research chemicals, legal highs, spice,…



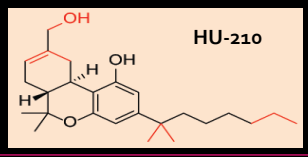
3

Les nouvelles drogues de synthèse

- Objectif: constituer une alternative légale aux drogues illicites

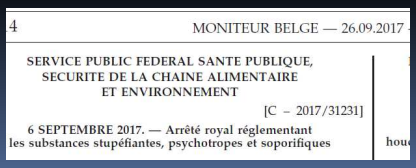


Psychoactif - Réglementé



Psychoactif - (Initialement) non réglementé

- MAIS



4 MONITEUR BELGE — 26.09.2017

SERVICE PUBLIC FEDERAL SANTE PUBLIQUE, SECURITE DE LA CHAINE ALIMENTAIRE ET ENVIRONNEMENT

[C − 2017/31231]

6 SEPTEMBRE 2017. — Arrêté royal réglementant les substances stupéfiantes, psychotropes et soporifiques

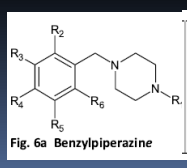


Fig. 6a Benzylpiperazine

R1 = H, CH_3, benzyl
R2 = H, halogène, OCH_3
R3 = H, CH_3, halogène , CF3
R4 = H, halogène, OCH_3
R5 = H, OCH_3,
R6 = H

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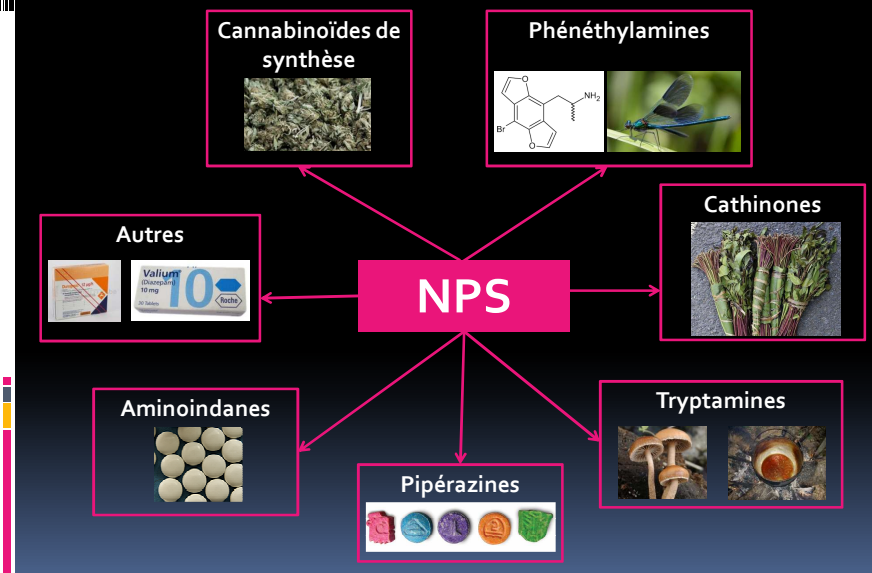
NPS - nombreuses catégories



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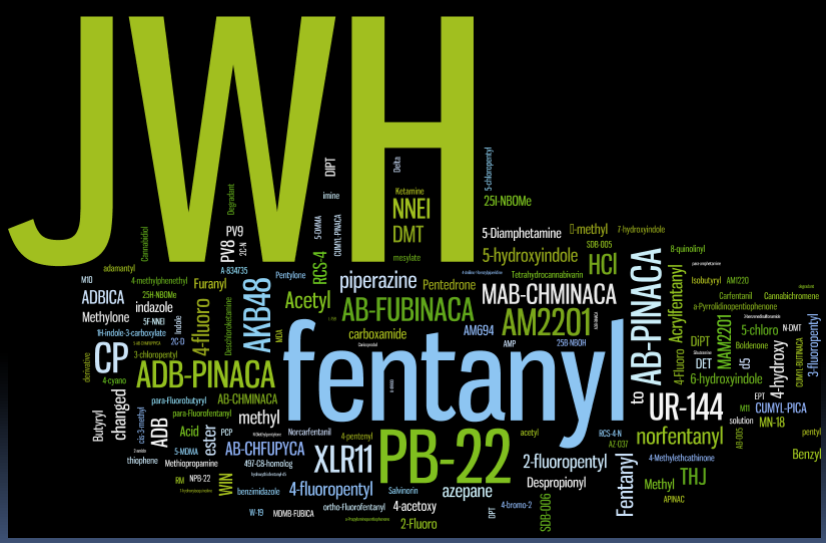
NPS - des centaines de molécules



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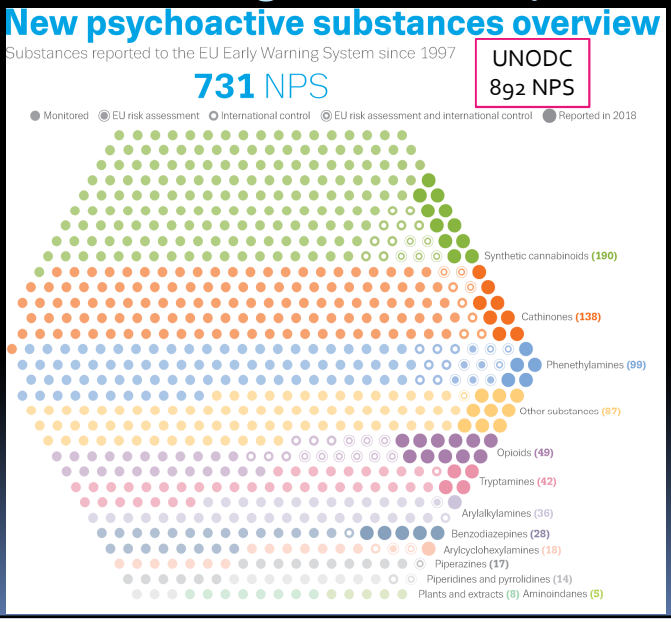
EMCDDA – EU Drug market report 2019



EMCDDA – EU Drug market report 2019

- Internet reste la source majoritaire d'approvisionnement
- La Chine reste le principal fournisseur, suivi par l'Inde
- Consommation de NPS < drogues classiques
- Groupes marginalisés, psychonautes
- Opioïdes: préoccupation croissante
- Augmentation de puissance
- Chevauchement avec le marché des médicaments contrefaits
- Epidémie de HIV liée aux cathinones

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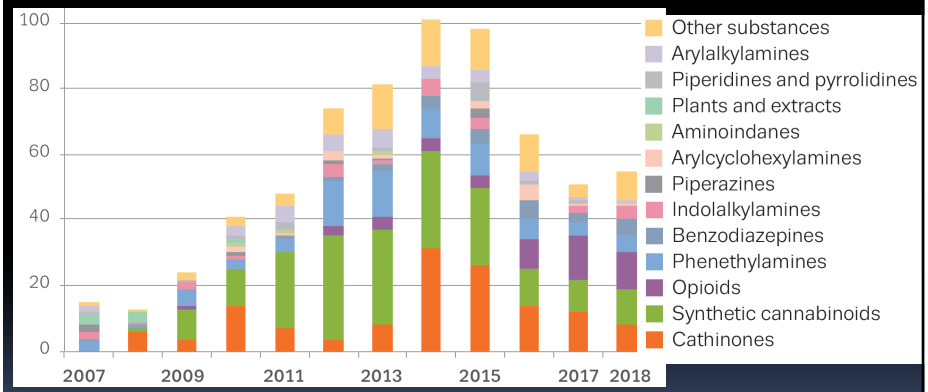
EMCDDA – EU Drug market report 2019

NPS notifiés pour la 1ère fois en EU



Identique au niveau mondial: 137 en 2015 → 78 en 2018 (UNODC)

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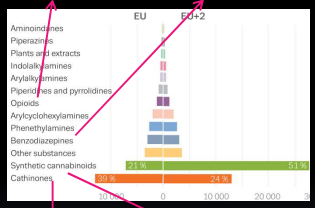
EMCDDA – EU Drug market report 2019

Opioid	Seizures	Powder (kg)	Tablets
Carfentanil	318	4.1	0
Furanylfentanyl	183	0.8	3 225
Cyclopropylfentanyl	131	2.8	329
U-47700	110	5.0	238
Ocfentanil (A-3217)	55	0.7	0

Benzodiazepines	Seizures	Powder (kg)	Tablets
Etizolam	1 634	25.06	2 218 797
Clonazolam/clonitrazolam	741	0.03	48 037
Norfludiazepam	365	0.25	28 234
Diclazepam	274	1.09	17 960
Phenazepam	102	0.05	13 757

Depuis 2015:
> 60000 → < 30000 saisies



Substance	Seizures	Powder (kg)	Tablets
N-ethylhexedrone	2 653	224	13
4-CMC/clephedrone	1 769	443	4
4-CEC	1 638	137	92
3-CMC	1 085	29	0
3-CEC	926	1	3
Ephylone	445	39	38 991

Substance	Number of seizures	Powder (kg)	Herbal (kg)
5F-MDMB-PINACA/5F-ADB	2 295	41.7	33
MDMB-CHMICA	1 438	0.6	10
AMB-FUBINACA	1 400	13.6	42
AB-CHMINACA	691	0.1	7
ADB-FUBINACA	542	0.4	3
CUMYL-PeGACLONE	303	5.0	7

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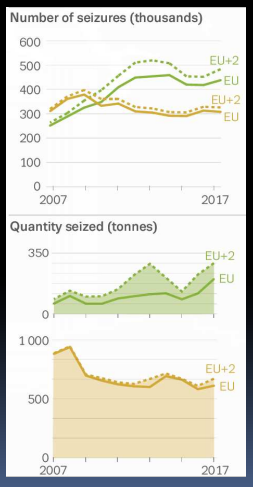
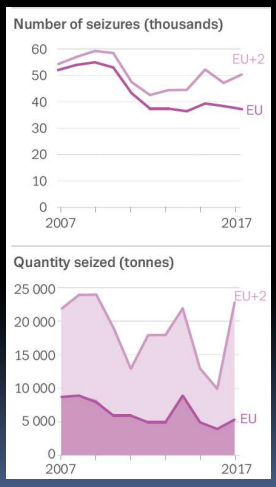
EMCDDA – EU Drug market report 2019

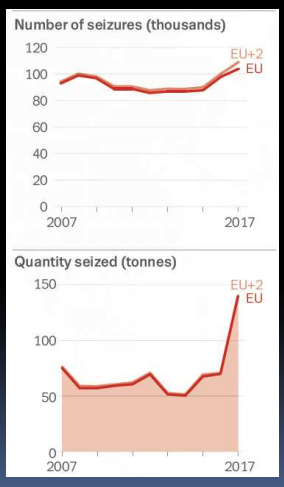
Herbe/résine



Héroïne



Cocaïne



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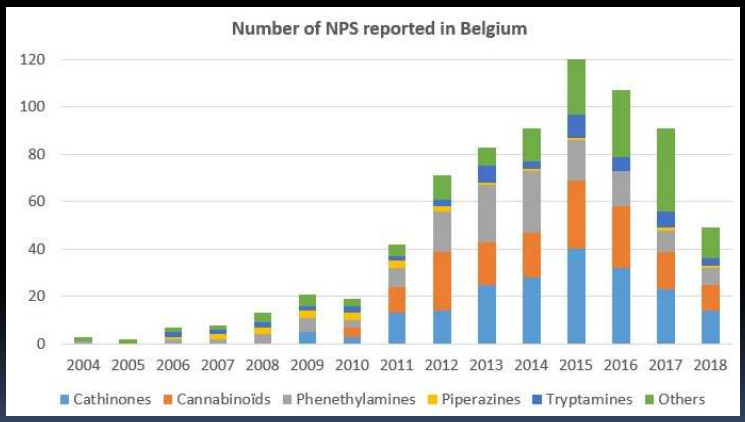
NPS notifiés en Belgique



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Données belges

sciensano — Belgian Early Warning System on Drugs (BEWSD) › Home

Belgian Early Warning System on Drugs (BEWSD) | Contact us! | Drugs Program (BMCDDA) | EWS Forum

All Site Content

Alerts by BEWSD

Type	Name	Modified By	Modified
	July 2019 - Highly dosed MDMA tablets	Blanckaert, Peter	10/07/2019 23:56
	July 2019 - Highly dosed MDMA tablets in circulation in Belgium	Blanckaert, Peter	18/07/2018 15:45
	July 2018 - Analysis of a powder containing ocfentanil and W-18	Blanckaert, Peter	18/07/2018 15:44
	January 2018 - Drugs contaminated with atropine in Belgium and The Netherlands	Blanckaert, Peter	22/03/2018 13:43
	December 2017 - Highly dosed MDMA tablets in circulation	Blanckaert, Peter	06/12/2017 23:20
	July 2017 - Highly dosed MDMA tablets and 2C-B in circulation	Blanckaert, Peter	12/07/2017 12:21
	June 2017 - One death after the consumption of 3-MeO-PCP	Blanckaert, Peter	12/07/2017 12:11
	June 2017 - Highly dosed MDMA tablets and 2C-B in circulation	Blanckaert, Peter	12/07/2017 12:00
	May 2017 - Highly dosed MDMA tablets in circulation	Blanckaert, Peter	12/07/2017 11:26
	March 2017 - Detection of highly dosed MDMA tablets, MDA and THJ-22011	Blanckaert, Peter	03/04/2017 10:38
	October 2016 - Detection of 25C-NBOME and a highly dosed MDMA tablet	Antoine, Jerome	16/12/2016 08:03
	December 2016 - Highly dosed MDMA tablets in circulation	Blanckaert, Peter	14/12/2016 12:36
	September 2016 - Detection of pCPP and series of highly dosed MDMA tablets	Antoine, Jerome	27/10/2016 09:05
	June 2016 - EMCDDA Alert U-47,700 in Europe	Antoine, Jerome	29/09/2016 10:50
	May 2016 - Highly dosed MDMA tablets detected by Modus Vivendi	Blanckaert, Peter	25/05/2016 11:30
	December 2015 - PMMA tablets	Blanckaert, Peter	24/12/2015 16:26
	December 2015 - Highly dosed MDMA tablets and liquid 2C-E	Blanckaert, Peter	11/12/2015 23:16
	October 2015 - Highly dosed ADE Amsterdam Dance Event ecstasy tablets	Blanckaert, Peter	12/10/2015 01:06
	September 2015 - Several new substances in ecstasy tablets	Blanckaert, Peter	12/10/2015 00:55
	September 2015 - Neurotoxic new substance found in ecstasy tablet	Blanckaert, Peter	09/09/2015 10:09

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Données belges - Gand

DRUG TESTING AND ANALYSIS

RESEARCH

Report

NPS or

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Peter Blan

Calenberg

First publis

DRUG TESTING AND ANALYSIS

RESEARCH ARTIC

Comprehe

Metabolic

AMB-FUBI

David Fabregat-

First published:

DRUG TESTING AND ANALYSIS

RESEARC

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valin

Elise Wo

First pub

DRUG TESTING AND ANALYSIS

RESEARCH ARTICLE

Application of an activity-based receptor bioassay to investigate the in vitro activity of selected indole- and indazole-3-carboxamide-based synthetic cannabinoids at CB1 and CB2 receptors

Carolina Noble, Annelies Cannaert, Kristian Linnet, Christophe P. Stove

First published: 02 October 2018 | https://doi.org/10.1002/dta.2517 | Citations: 14

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Données belges - Anvers

Journal of Pharmaceutical and Biomedical Analysis 153 (2018) 158–167

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

Journal of Pharmaceutical and Biomedical Analysis 117 (2016) 474–484

Contents lists available at ScienceDirect

Chemosphere 168 (2017) 1032–1041

Contents lists available at ScienceDirect

Chemosphere

Science of the Total Environment 573 (2016) 1527–1535

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Qualitative screening of new psychoactive substances in pooled urine samples from Belgium and United Kingdom

Juliet Kinyua [a], Noelia Negreira [a], Bram Miserez [b], Ana Causanilles [c], Erik Emke [c], Lies Gremeaux [d], Pim de Voogt [c,e], John Ramsey [b], Adrian Covaci [a], Alexander L.N. van Nuijs [a,*]

[a] Toxicological Center, Department of Pharmaceutical Sciences, Campus Drie Eiken, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium
[b] TICTAC Communications Ltd., St George's University of London, Cranmer Terrace, London SW170RE, United Kingdom
[c] KWR Watercycle Research Institute, Chemical Water Quality and Health, P.O. Box 1072, 3430 BB Nieuwegein, The Netherlands
[d] Programme Drugs, Operational Direction of Public health and Surveillance, Scientific Institute for Public Health, Juliette Wytsmanstraat 14, 1050 Brussels, Belgium
[e] Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, P.O. Box 94248, 1090 GE Amsterdam, The Netherlands

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Données belges - Population

DRUG TESTING AND ANALYSIS

RESEARCH ARTICLE

Prevalence of new psychoactive substances and prescription drugs in the Belgian driving under the influence of drugs population

S. M. R. Wille, C. Richeval, M. Nachon-Phanithavong, J. M. Gaulier, V. Di Fazio, L. Humbert, N. Samyn, D. Allorge

First published: 22 June 2017 | https://doi.org/10.1002/dta.2232 | Citations: 12

558 échantillons sanguins + 199 salives
7% de sang positifs et 11% de salives positives
Diphenidine, ketamine, 4F-amphétamine, 2-AI, methoxetamine, alpha-PVP, methiopropamine, 5-MAPB, 5-EAPB, TH-PVP, mephedrone, methedrone, 4-methylethylcathinone, 5-MeO-DALT, 4-acetoxy-DiPT, AB Fubinaca, FUB-JWH-018, JWH -020, trifluoromethylphenylpiperazine, ethylphenidate

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Données belges – Case report

Forensic Science International 266 (2016) 469–473

Contents lists available at ScienceDirect

Forensic Science International

Forensic Science International 266 (2016) 68–72

Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

Forensic Science International 299 (2019) 89–94

Contents lists available at ScienceDirect

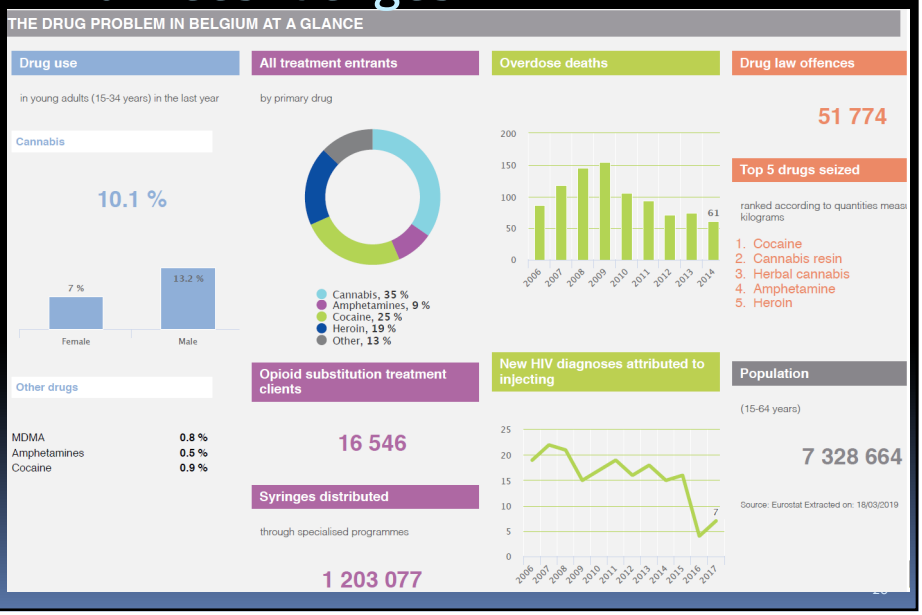
Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

Death following consumption of MDAI and 5-EAPB

Marine Deville[a,*], Nathalie Dubois[a], Ewa Cieckiewicz[b], Pascal De Tullio[c], Eric Lemaire[d], Corinne Charlier[a]

Données belges



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Défi analytique

- Nombre de substances
- Faible concentration
- Métabolisme

- Méthode de référence: MS-HR

- **Screening ciblé:** librairie
  - Avec temps de rétention: 329 composés
  - Sans temps de rétention:
    - Sciex: 2636 composés
    - Designer drugs: 530 NPS
- **Screening non ciblé:** Chemspider®

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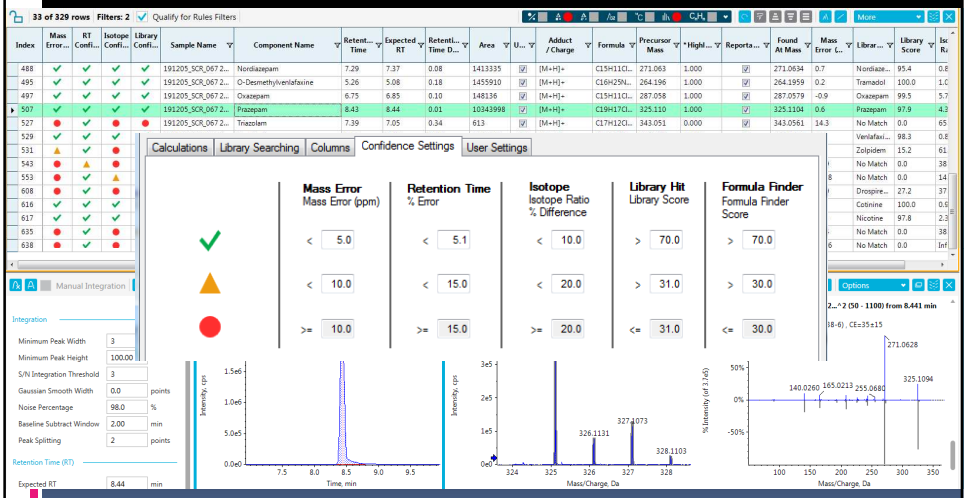
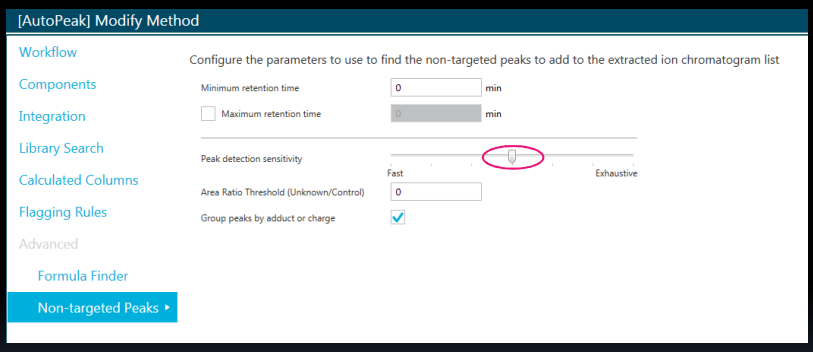
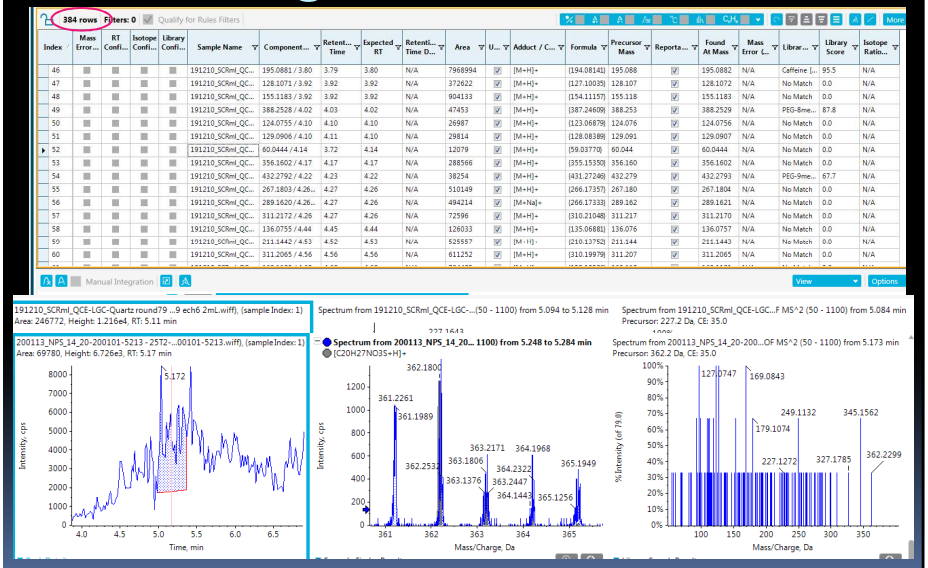
Screening ciblé



Screening non ciblé



Screening non ciblé



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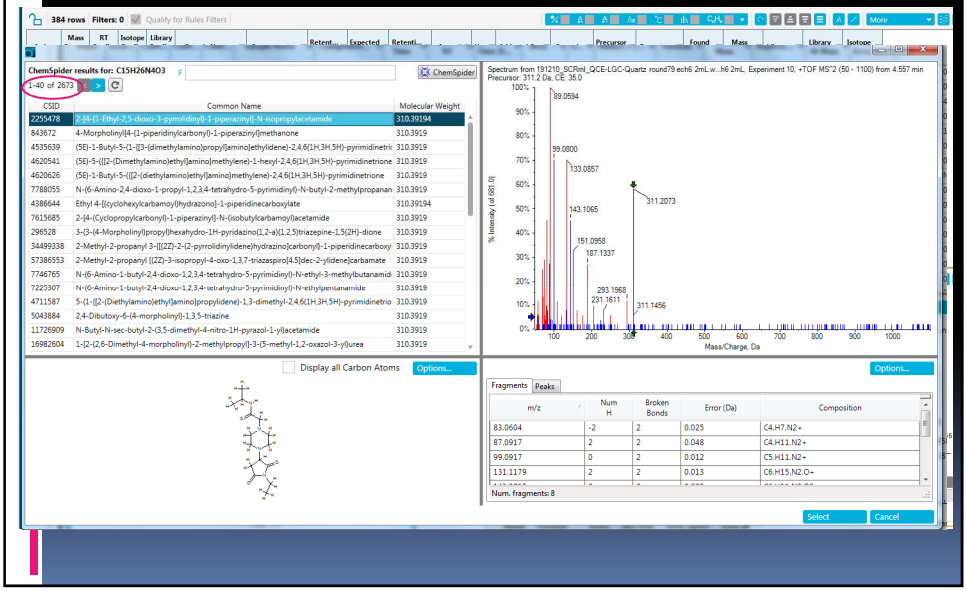
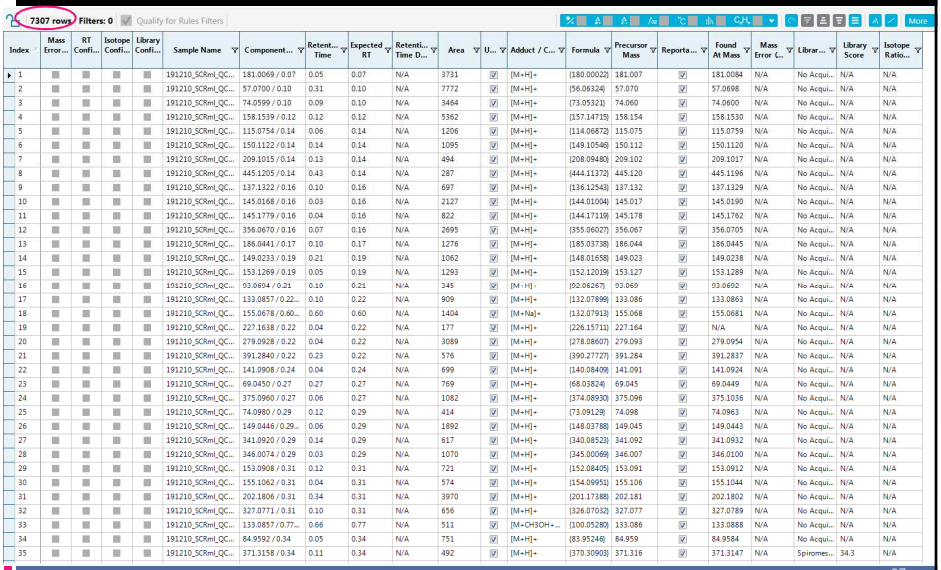


Screening non ciblé



Index	Mass Error ...	RT Confi...	Isotope Confi...	Library Confi...	Sample Name	Component ...	Retent... Time	Expected RT	Retenti... Time D...	Area	U...	Adduct / C...	Formula	Precursor Mass	Reporta...	Found At Mass	Mass Error (...	Librar...	Library Score	Isotope Ratio...
1					191210_SCRml_QC...	181.0069 / 0.07	0.05	0.07	N/A	3731		[M+H]+	(180.00022)	181.007		181.0084	N/A	No Acqui...	N/A	N/A
2					191210_SCRml_QC...	57.0700 / 0.10	0.31	0.10	N/A	7772		[M+H]+	(56.06324)	57.070		57.0698	N/A	No Acqui...	N/A	N/A
3					191210_SCRml_QC...	74.0599 / 0.10	0.09	0.10	N/A	3464		[M+H]+	(73.05321)	74.060		74.0600	N/A	No Acqui...	N/A	N/A
4					191210_SCRml_QC...	158.1539 / 0.12	0.12	0.12	N/A	5362		[M+H]+	(157.14715)	158.154		158.1530	N/A	No Acqui...	N/A	N/A
5					191210_SCRml_QC...	115.0754 / 0.14	0.06	0.14	N/A	1206		[M+H]+	(114.06872)	115.075		115.0759	N/A	No Acqui...	N/A	N/A
6					191210_SCRml_QC...	150.1122 / 0.14	0.14	0.14	N/A	1095		[M+H]+	(149.10546)	150.112		150.1120	N/A	No Acqui...	N/A	N/A
7					191210_SCRml_QC...	209.1015 / 0.14	0.13	0.14	N/A	494		[M+H]+	(208.09480)	209.102		209.1017	N/A	No Acqui...	N/A	N/A
8					191210_SCRml_QC...	445.1205 / 0.14	0.43	0.14	N/A	287		[M+H]+	(444.11372)	445.120		445.1196	N/A	No Acqui...	N/A	N/A
9					191210_SCRml_QC...	137.1322 / 0.16	0.10	0.16	N/A	697		[M+H]+	(136.12543)	137.132		137.1329	N/A	No Acqui...	N/A	N/A
10					191210_SCRml_QC...	145.0168 / 0.16	0.03	0.16	N/A	2127		[M+H]+	(144.01004)	145.017		145.0190	N/A	No Acqui...	N/A	N/A
11					191210_SCRml_QC...	145.1779 / 0.16	0.04	0.16	N/A	822		[M+H]+	(144.17119)	145.178		145.1762	N/A	No Acqui...	N/A	N/A
12					191210_SCRml_QC...	356.0670 / 0.16	0.07	0.16	N/A	2695		[M+H]+	(355.06027)	356.067		356.0705	N/A	No Acqui...	N/A	N/A
13					191210_SCRml_QC...	186.0441 / 0.17	0.10	0.17	N/A	1276		[M+H]+	(185.03738)	186.044		186.0445	N/A	No Acqui...	N/A	N/A
14					191210_SCRml_QC...	149.0233 / 0.19	0.21	0.19	N/A	1062		[M+H]+	(148.01658)	149.023		149.0238	N/A	No Acqui...	N/A	N/A
15					191210_SCRml_QC...	153.1269 / 0.19	0.05	0.19	N/A	1293		[M+H]+	(152.12019)	153.127		153.1289	N/A	No Acqui...	N/A	N/A
16					191210_SCRml_QC...	93.0694 / 0.21	0.10	0.21	N/A	345		[M-H]-	(92.06267)	93.069		93.0692	N/A	No Acqui...	N/A	N/A
17					191210_SCRml_QC...	133.0857 / 0.22...	0.10	0.22	N/A	909		[M+H]+	(132.07899)	133.086		133.0863	N/A	No Acqui...	N/A	N/A
18					191210_SCRml_QC...	155.0678 / 0.60...	0.60	0.60	N/A	1404		[M+Na]+	(132.07913)	155.068		155.0681	N/A	No Acqui...	N/A	N/A
19					191210_SCRml_QC...	227.1638 / 0.22	0.04	0.22	N/A	177		[M+H]+	(226.15711)	227.164		N/A	N/A	No Acqui...	N/A	N/A
20					191210_SCRml_QC...	279.0928 / 0.22	0.04	0.22	N/A	3089		[M+H]+	(278.08607)	279.093		279.0954	N/A	No Acqui...	N/A	N/A
21					191210_SCRml_QC...	391.2840 / 0.22	0.23	0.22	N/A	576		[M+H]+	(390.27727)	391.284		391.2837	N/A	No Acqui...	N/A	N/A
22					191210_SCRml_QC...	141.0908 / 0.24	0.04	0.24	N/A	699		[M+H]+	(140.08409)	141.091		141.0924	N/A	No Acqui...	N/A	N/A
23					191210_SCRml_QC...	69.0450 / 0.27	0.27	0.27	N/A	769		[M+H]+	(68.03824)	69.045		69.0449	N/A	No Acqui...	N/A	N/A
24					191210_SCRml_QC...	375.0960 / 0.27	0.06	0.27	N/A	1082		[M+H]+	(374.08930)	375.096		375.1036	N/A	No Acqui...	N/A	N/A
25					191210_SCRml_QC...	74.0980 / 0.29	0.12	0.29	N/A	414		[M+H]+	(73.09129)	74.098		74.0963	N/A	No Acqui...	N/A	N/A
26					191210_SCRml_QC...	149.0446 / 0.29...	0.06	0.29	N/A	1892		[M+H]+	(148.03788)	149.045		149.0443	N/A	No Acqui...	N/A	N/A
27					191210_SCRml_QC...	341.0920 / 0.29	0.14	0.29	N/A	617		[M+H]+	(340.08523)	341.092		341.0932	N/A	No Acqui...	N/A	N/A
28					191210_SCRml_QC...	346.0074 / 0.29	0.03	0.29	N/A	1070		[M+H]+	(345.00069)	346.007		346.0100	N/A	No Acqui...	N/A	N/A
29					191210_SCRml_QC...	153.0908 / 0.31	0.12	0.31	N/A	721		[M+H]+	(152.08405)	153.091		153.0912	N/A	No Acqui...	N/A	N/A
30					191210_SCRml_QC...	155.1062 / 0.31	0.04	0.31	N/A	574		[M+H]+	(154.09951)	155.106		155.1044	N/A	No Acqui...	N/A	N/A
31					191210_SCRml_QC...	202.1806 / 0.31	0.34	0.31	N/A	3970		[M+H]+	(201.17388)	202.181		202.1802	N/A	No Acqui...	N/A	N/A
32					191210_SCRml_QC...	327.0771 / 0.31	0.10	0.31	N/A	656		[M+H]+	(326.07032)	327.077		327.0789	N/A	No Acqui...	N/A	N/A
33					191210_SCRml_QC...	133.0857 / 0.77...	0.66	0.77	N/A	511		[M+CH3OH+...	(100.05280)	133.086		133.0888	N/A	No Acqui...	N/A	N/A
34					191210_SCRml_QC...	84.9592 / 0.34	0.05	0.34	N/A	751		[M+H]+	(83.95246)	84.959		84.9584	N/A	No Acqui...	N/A	N/A
35					191210_SCRml_QC...	371.3158 / 0.34	0.11	0.34	N/A	492		[M+H]+	(370.30903)	371.316		371.3147	N/A	Spiromes...	34.3	N/A

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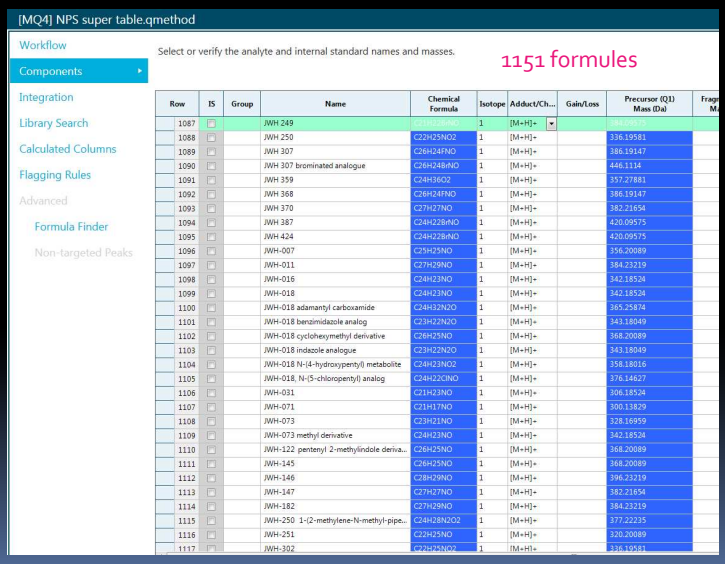
Intro | Actualité | Belgique | Défi analytique | Cas Lg 1 | Cas Lg 2 | Conclusion

Screening « non ciblé – ciblé »



Row	IS	Group	Name	Chemical Formula	Isotope	Adduct/Ch...	Gain/Loss	Precursor (Q1) Mass (Da)
1087			JWH 249	C23H25NO	1	[M+H]+		332.20089
1088			JWH 250	C22H25NO2	1	[M+H]+		336.19581
1089			JWH 307	C26H24FNO	1	[M+H]+		386.19147
1090			JWH 307 brominated analogue	C26H24BrNO	1	[M+H]+		446.1114
1091			JWH 359	C24H36O2	1	[M+H]+		357.27881
1092			JWH 368	C26H24FNO	1	[M+H]+		386.19147
1093			JWH 370	C27H27NO	1	[M+H]+		382.21654
1094			JWH 387	C24H22BrNO	1	[M+H]+		420.09575
1095			JWH 424	C24H22BrNO	1	[M+H]+		420.09575
1096			JWH-007	C25H25NO	1	[M+H]+		356.20089
1097			JWH-011	C27H29NO	1	[M+H]+		384.23219
1098			JWH-016	C24H23NO	1	[M+H]+		342.18524
1099			JWH-018	C24H23NO	1	[M+H]+		342.18524
1100			JWH-018 adamantyl carboxamide	C24H32N2O	1	[M+H]+		365.25874
1101			JWH-018 benzimidazole analog	C23H22N2O	1	[M+H]+		343.18049
1102			JWH-018 cyclohexymethyl derivative	C26H25NO	1	[M+H]+		368.20089
1103			JWH-018 indazole analogue	C23H22N2O	1	[M+H]+		343.18049
1104			JWH-018 N-(4-hydroxypentyl) metabolite	C24H23NO2	1	[M+H]+		358.18016
1105			JWH-018, N-(5-chloropentyl) analog	C24H22ClNO	1	[M+H]+		376.14627
1106			JWH-031	C21H23NO	1	[M+H]+		306.18524
1107			JWH-071	C21H17NO	1	[M+H]+		300.13829
1108			JWH-073	C23H21NO	1	[M+H]+		328.16959
1109			JWH-073 methyl derivative	C24H23NO	1	[M+H]+		342.18524
1110			JWH-122 pentenyl 2-methylindole deriva...	C26H25NO	1	[M+H]+		368.20089
1111			JWH-145	C26H25NO	1	[M+H]+		368.20089
1112			JWH-146	C28H29NO	1	[M+H]+		396.23219
1113			JWH-147	C27H27NO	1	[M+H]+		382.21654
1114			JWH-182	C27H29NO	1	[M+H]+		384.23219
1115			JWH-250 1-(2-methylene-N-methyl-pipe...	C24H28N2O2	1	[M+H]+		377.22235
1116			JWH-251	C22H25NO	1	[M+H]+		320.20089
1117			JWH-302	C22H25NO2	1	[M+H]+		336.19581

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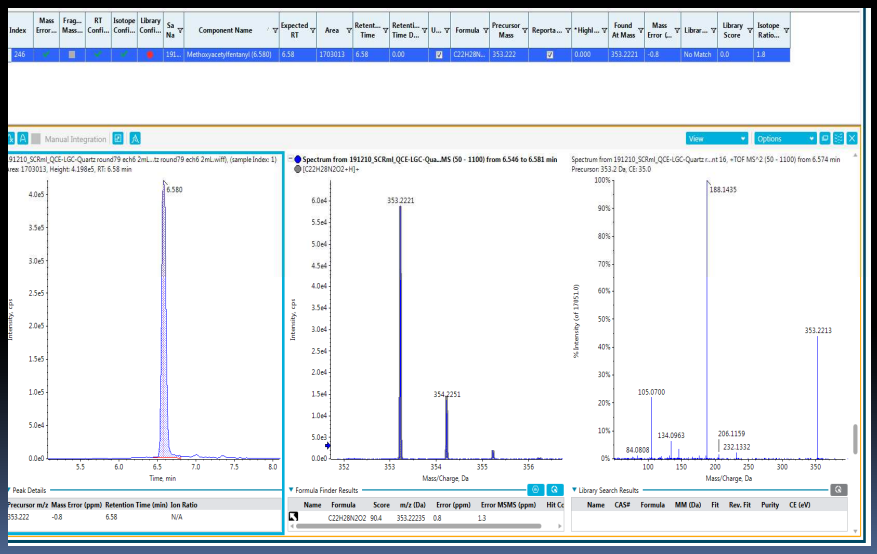
Screening « non ciblé – ciblé »



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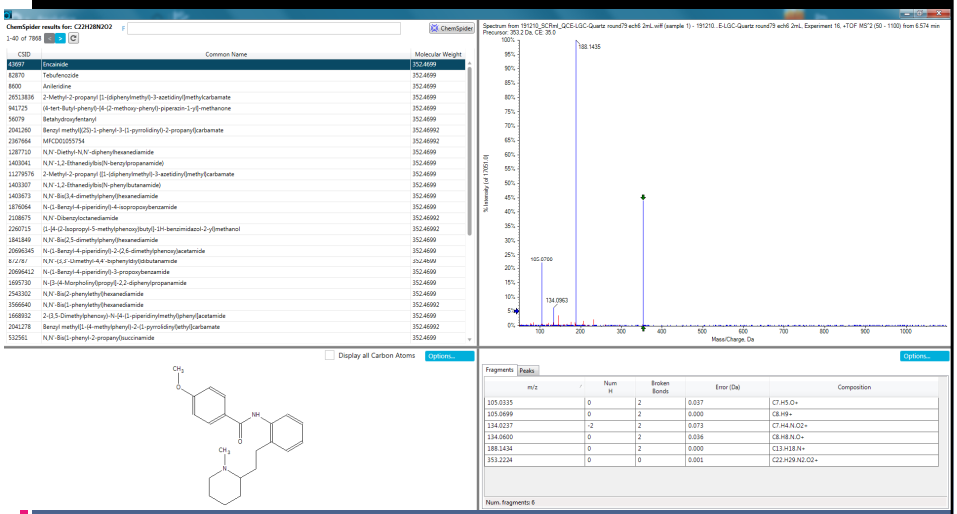
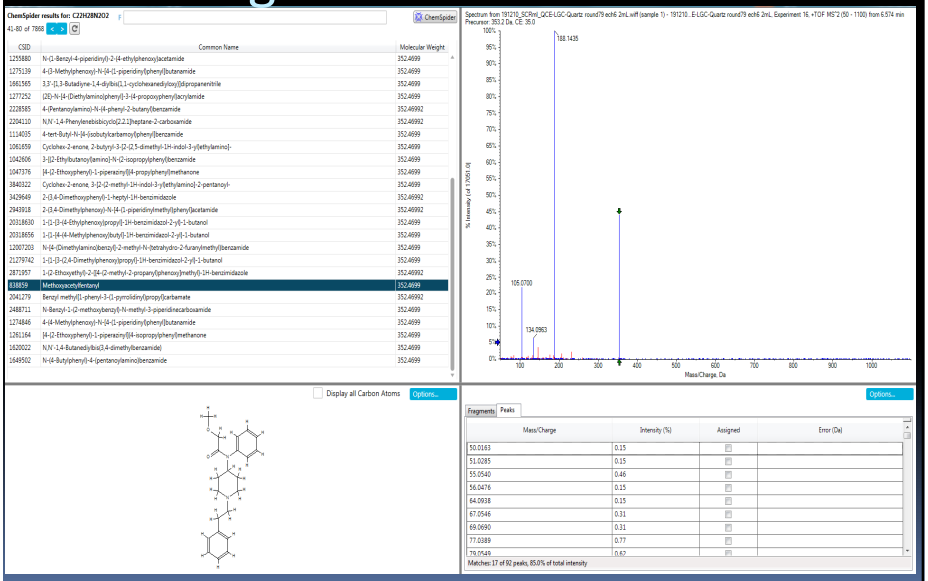
Screening « non ciblé – ciblé »



Screening « non ciblé – ciblé »



Concentrations retrouvées

Publication	NPS	[sanguine]	Contexte
Adamovicz et al. 2017	UR-144	0.15 à 17 µg/L (Med: 1.6)	Intoxication (39 cas)
Adamovicz et al. 2016	3-MMC	<1-1600 (Med: 18.5)	Tout confondu (95 cas)
Backberg et al. 2015	Butyrfentanyl 4-fluorobutyrfentanyl	0.6 et 0.9 µg/L 15 µg/L	Intoxication (4 cas) Intoxication (1 cas)
Helander et al 2015	Diphenidine Methoxphenidine	2 à 262 µg/L 187 à 409 µg/L	Intoxication (14 cas) Intoxication (3 cas)
Helander et al. 2016	Acetylfentanyl 4-Methoxybutyrfentanyl Furanylfentanyl	0.6 à 51.6 µg/L (Med: 14.8) 1.3 et 3.1 µg/L 4.4 et 148 µg/L	Intoxication (7 cas, 1 décès) Intoxication (2 cas) Intoxication (2 cas)
Schep et al. 2015	BB-22 AM2233 PB-22/5F-PB-22 JWH-122	0.097 µg/L 148 µg/L 80 µg/L 10 µg/L	1 seul patient, intoxication multiple
Shanks et al. 2016	5F-AMB	0.3 µg/L	Décès
Karinen et al. 2017	MPA	1.9 à 286 µg/L (Med: 24)	Usage (18 cas)
	MXE	2.7 à 490 µg/L (Med:26)	Usage (15 cas)
	4-FA	4.7 à 580 µg/L (Med : 34)	Usage (16 cas)
	5-IT	13 à 590 µg/L (Med: 225)	Intoxication (8 cas)
	4-MTA	430 à 2080 µg/L (Med : 1170)	Intoxication (6 cas)
	Bromo-Dragonfly	4.7 µg/L	Décès (1 cas)
	2-FMA	6.9 µg/L	Décès (1 cas)
	25C-NBOMe/25I-NBOMe	0.60 / 0.41 et 3 µg/L	Décès (2 cas et 1 cas)

Evaluation de la LOD: méthode

- 35 NPS testés:
  - Phencyclidine
  - Cathinone
  - Méphédrone
  - DOB
  - PMA
  - PMMA
  - 2-Aminoindane
  - NM-2-AI
  - MDAI
  - 5-EAPB
  - 5-MAPB
  - 5-APB
  - PMMA
  - 5-OH-DMT
  - N,N-DMT
  - 5-MeO-DMT
  - 25B-NBOMe
  - 2-CH
  - 2-CB
  - 2-CI
  - mCPP
  - Mescaline
  - 2C-T-7
  - 2C-T-2
  - 2-(3,4-DMP)EA
  - 4-MTA
  - BDB
  - Estazolam
  - DMA
  - HMA
  - HMMA
  - MDDMA
  - N-propylamphetamine
  - N-ethylamphetamine
- Sang enrichi: 0.5 – 1 – 2.5 – 5 – 10 – 20 µg/L

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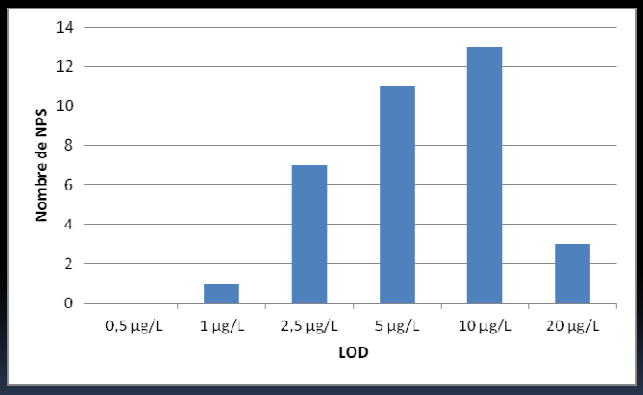
Evaluation de la LOD: résultats

- Extraction « screening »



- Extraction « Phree » et cocop: LOD ↑

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- Introduction/rappels
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- Actualité en Belgique
- Défi analytique
- Cas liégeois n°1: MDAI-EAPB
- Cas liégeois n°2: 2-AI
- Conclusion

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Death following consumption of MDAI and 5-EAPB

Marine Deville[a,*], Nathalie Dubois[a], Ewa Cieckiewicz[b], Pascal De Tullio[c], Eric Lemaire[d], Corinne Charlier[a]

56th Annual Meeting of TIAFT

GHENT

Addictive days and Toxic nights

TIAFT 26-30th August 2018

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Case Report

- **Contexte**

Toxicomane décédé (28 ans)

Poudres non identifiées
Matériel utilisé pour sniffer

Lorazépam, prazépam, zopiclone,amoxicilline, bisoprolol

- **Examen externe**

- Epistaxis
- Pas de lésion corporelle
- Prélèvement de sang et d'urine

- **→Cause toxique hautement suspectée**

Materiel & Méthodes

- **Screening**

Sang/Urine (traitée ou non par glucuronidase)	1 mL
Standard Interne (prazepam)	100 µL
Na_2CO_3 1M	500 µL
Diéthyl Ether/ Dichlorométhane/Hexane/ alcool n-amylique (50/30/20/0.5:v/v) → Agitation → Centrifugation → Evaporation	5 mL
Phase Mobile	100 µL

HPLC-DAD (*Waters*)
Alliance 2695 + PDA 2996
Colonne: Symmetry C8, 5 µm, 250 X 4,6 mm *(Waters)*
Phase Mobile A : Tampon Phosphate pH 3,8 43,5 mM
Phase Mobile B: Acétonitrile

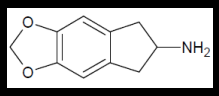
UPLC-TOF-MS (*Sciex*)
Eksigent LC 100 XL + TripleTOF 4600
Colonne: Kinetex 2.6 C18, 100 Å, 50 x 3.00 mm *(Phenomenex)*
Phase Mobile A : 10mM Ammonium formate
Phase Mobile B: ACN/MeOH (50/50)

- Poudres: dilution → HPLC-DAD & UPLC-TOF-MS

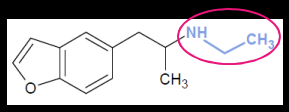
Résultats

- **Poudres**

5,6-MethyleneDioxy-2-AminoIndane
MDAI : 68 %

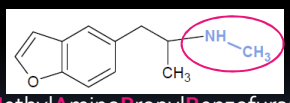


EthylAminoPropylBenzofuran
EAPB : 87 %



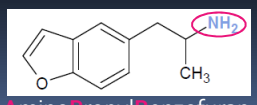
- **Echantillons Biologiques**

	Sang (mg/L)	Urine (mg/L)	Cas 1 [1]	Cas 2 [1]
MDAI	2,09	69,4	26,3	3,3
EAPB	6,45	14,8	-	-
MAPB	0,089	1,00	-	-
APB	0,546	4,88	-	0,34



MAPB

MethylAminoPropylBenzofuran



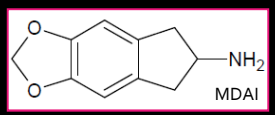
APB

AminoPropylBenzofuran

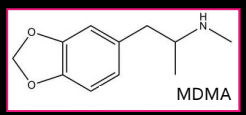
[1] Corkery JM., et al., MDAI toxicity: a brief overview and update, Hum Psychopharmacol Clin Exp (2013)**28**; 345-355

MDAI - EAPB

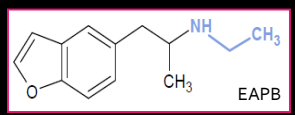
- **MDAI** (5,6-MethyleneDioxy-2-AminoIndane)
  - Insufflation, ingestion orale
  - Euphorie, empathie
  - Confusion, anxiété, dépression, attaques de panique, tachycardie,…
  - Insuffisance rénale/hépatique, syndrome de détresse respiratoire aigü, hypertension pulmonaire , troubles valvulaires aortiques, rhabdomyolyse, …



MDAI



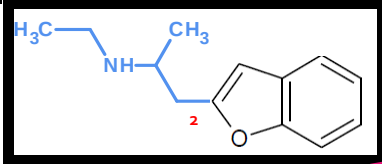
MDMA

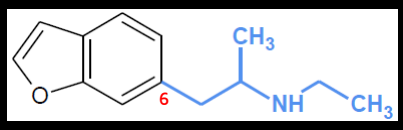


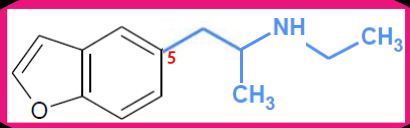
EAPB

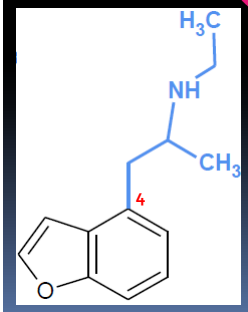
- **EAPB** (EthylAminoPropylBenzofuran)
  - Très peu de données scientifiques
  - Insufflation, ingestion oral (parachutie)
  - Stimulant, empathogène, appréciation de la musique - effet plus faible que la MDMA mais plus fort que l'APB
  - Tachycardie, tension dans les machoires, insomnie → convulsions, arrêt cardiaque (APB)

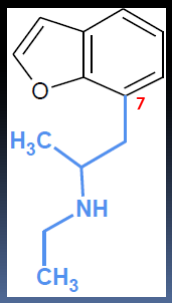
EAPB: distinction des isomères







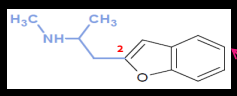


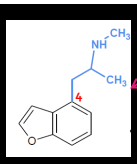


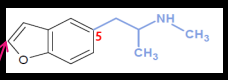
Résonance Magnétique Nucléaire

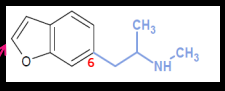
MAPB: distinction des isomères

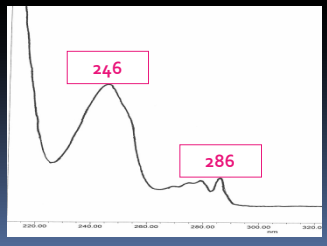
	Temps de rétention	
Isomer	HPLC – DAD	UPLC – TOF-MS
2-MAPB	10,32	5,48
4-MAPB	9,81	5,27
5-MAPB	9,58	5,16
6-MAPB	9,53	5,16
7-MAPB	9,46	5,17







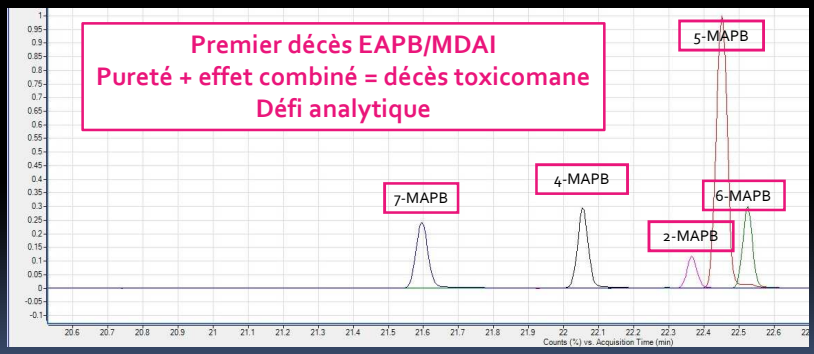




MAPB distinction des isomères

GC-MS-MS (EI) [2]:

- Dérivation: Heptafluorobutiamide (HFBA) : 75°C – 30 min
- HP-5MS 30m x 0,25 mm; gradient



[2] Stanczuk A., et al., Identification of APB phenyl ring positional isomers in Internet purchased products, Durg Test Analysis(2013)5; 270-276

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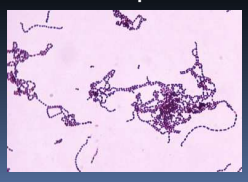
Case report

- Homme de 24 ans
- 3ème visite aux urgences pour symptômes ORL en aggravation depuis une semaine, traité par paracétamol, ibuprofène et oxymétazoline
- Sudation profuse, érythème généralisé, tachycardie sinusale
- Œdème paupière droite, poignet et coude gauches, jambe douloureuse.
- Soins intensifs: intubation et antibiothérapie
- Choc septique, CIVD, défaillance multiviscérale
- Chemsex → Screening NPS



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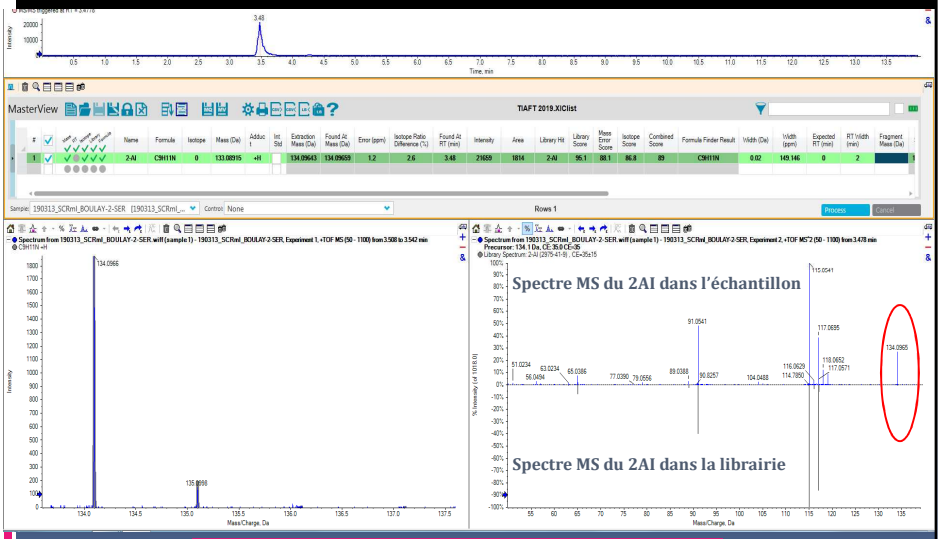
Intro | Actualité | Belgique | Défi analytique | Cas Lg 1 | Cas Lg 2 | Conclusion

Résultat du Screening



→ Commande du standard de référence

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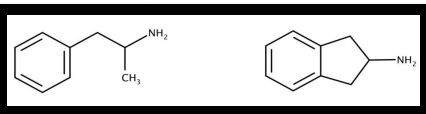
2-Aminoindane



- Ingestion/insufflation nasale
- Inhibition sélective du transporteur de la noradrénaline et libération de dopamine et noradrénaline dans la synapse
- Effets légers > effets stimulants physiques et mentaux comparables à la MDMA
- Antidouleur, vigilance, euphorie
- 4 rapports de cas:
  - Détecté en 2011 au UK, pas de détails
  - Décès méthadone (807 µg/L) + 2-AI (101 µg/L) + médicaments
  - Détecté lors d'une overdose au MT-45
  - Détecté dans des urines poolées d'urinoir de nightclub londonien

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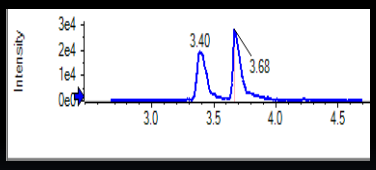
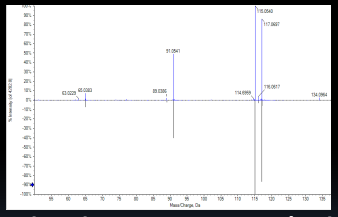
Substance de référence

- Injection sur la TOF: Δt = 0,3 min → effet matrice?
- Echantillon du patient enrichi avec le 2-AI





- Réception du standard 2.5 mois après la commande
- Volume d'échantillon reçu

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Méthode LC-MSMS

UHPLC-MS-MS (*Waters*) UPLC Acquity + Quattro Premier

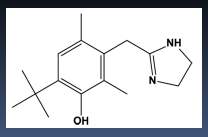
- Colonne: BEH C18, 1.7 µm, 50 X 2.1 mm (*Waters*)
- Phase Mobile A : eau + 0.1% acide formique
- Phase Mobile B: méthanol + 0.1% acide formique
- Mode Gradient : 15 min

Résultats:

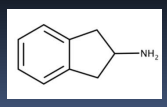
- Δt = 0,1 min
- Ion Ratio 133.9 > 116.9 / 133.9 > 115.1 Standard : 6.62 ≠ Sample : 2.37
- Même interférence dans 6 échantillons testés sur 900. Origine?

Ion ratios indispensable

Oxymétazoline (Nesivine®)



2-AI



- Validation: 10 matrices blanches / composés fréquemment rencontrés

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Conclusions

- La consommation de NPS est anecdotique comparé aux drogues « classiques »
- Une technique sensible ET spécifique est indispensable

TIAFT 2020
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