



# Workstream 5

## NPS Top lists and national technical folders

### *French Top list elaboration*

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*Observatoire français des drogues et des toxicomanies (OFDT)*

Co-funded by  
the European Union



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**Date:** 26/11/2015

## Purposes

Building of the national top lists was at first a necessary phase of I-Trend project, as determining the scope of research within different WS (technical folders, forum monitoring, shops monitoring).

It also was a useful information for decision makers and surveillance systems at a national level (prevention, standard sharing among laboratories, example to use in general population surveys...).

The process of Top list elaboration does not replace risk assessment, as the point is not to select the most dangerous substances but the ones that are thought to know the larger diffusion.

## Method

### 1<sup>st</sup> step

The first Top list was elaborated around June 2013.

On the first round, only easily available sources have been used to assess potential diffusion of substances:

- Seizures from police and customs, although they may be partly biased;
- SINTES (EWS and substances collected from users) although not exhaustive and probably biased

Data related to harm weren't available at this time due to the fact that the agency that is in charge of toxicovigilance for psychoactive substances (addicto-vigilance) doesn't have a consolidated basis of cases signalled by its network.

Popularity of substances of forum has been used too as an expert advice because forum monitoring method was still under construction at this time within WS1 of the I-Trend project and couldn't produce quantitative indicators yet.

Then expert's advice has been requested to finalize each national Top list.

Expert from toxicovigilance found it difficult not to use potential harm criteria and to enter into a NPS definition that was not based on legal status.

Finally no specific method of aggregation of different sources was carried out but a reasoned process.

Table 1: Data sources used for round 1 of NPS Top list selection

Type of Data	Source	Toxicological analysis	Quantitative unit for ranking	Period
Seizures	Scientific Police	Y	Nb of cases	
	Custom services	Y	Nb of cases	
Substances collected from users	French EWS SINTES	Y	Nb of cases	
Substances online popularity	Forums monitoring	N		
Experts consultation	- Law enforcement laboratory customs		1	
	- police		1	
	- Toxicovigilance		2	
	- French CDC		1	
	- University hospital laboratory		1	

Source: I-Trend, OFDT

Table 2: first French Top 10, 2013

Substances	Legal status	Scheduling date
AM-2201	n	
UR-144	n	
MDPV	Scheduled	27 July 2012
4-MEC	Scheduled	27 July 2012
25-I NBOME	n	
5-MEO-DALT	n	
6-APB	n	
5-APB	n	
Ethylphenidate	n	
Methoxetamine	Scheduled	5 August 2013

Source: I-Trend, OFDT

It did not appear possible for legal reasons to purchase scheduled substances. We were not covered by our governmental supervisor Unit to purchase online illicit substances. So only non-scheduled substances have been purchased (7 substances out of 10)

## 2<sup>nd</sup> step

In 2014, more sources were available, notably the ones originated from I-Trend project itself. Three sources have been added:

- Online Forum monitoring developed within I-TREND Project;
- Online survey in NPS users also developed With I-TREND Project;
- Toxicovigilance data from National Agency for Medicines and health products safety (ANSM)

Table 3: Data sources used for round 2 of NPS Top list selection

Type of Data	Source	Toxicological analysis	Quantitative unit for ranking	Period
Toxicovigilance	National Agency for Medicines and Health Products Safety (ANSM)	Y	Nb of cases	Jan-Sept 2014
Seizures	Scientific Police	Y	Nb of cases	Jan-Sept 2014
	Custom services	Y	Nb of cases	Jan-Sept 2014
Substances collected from users	French EWS SINTES	Y	Nb of cases	Jan-Sept 2014
Substances online popularity	Forums monitoring	N	Average nb. of daily views	Jan-May 2014
Users answers	Online surveys Last used NPS in 12 month users	N	Prevalence (%) of use among respondents	June-Oct 2014

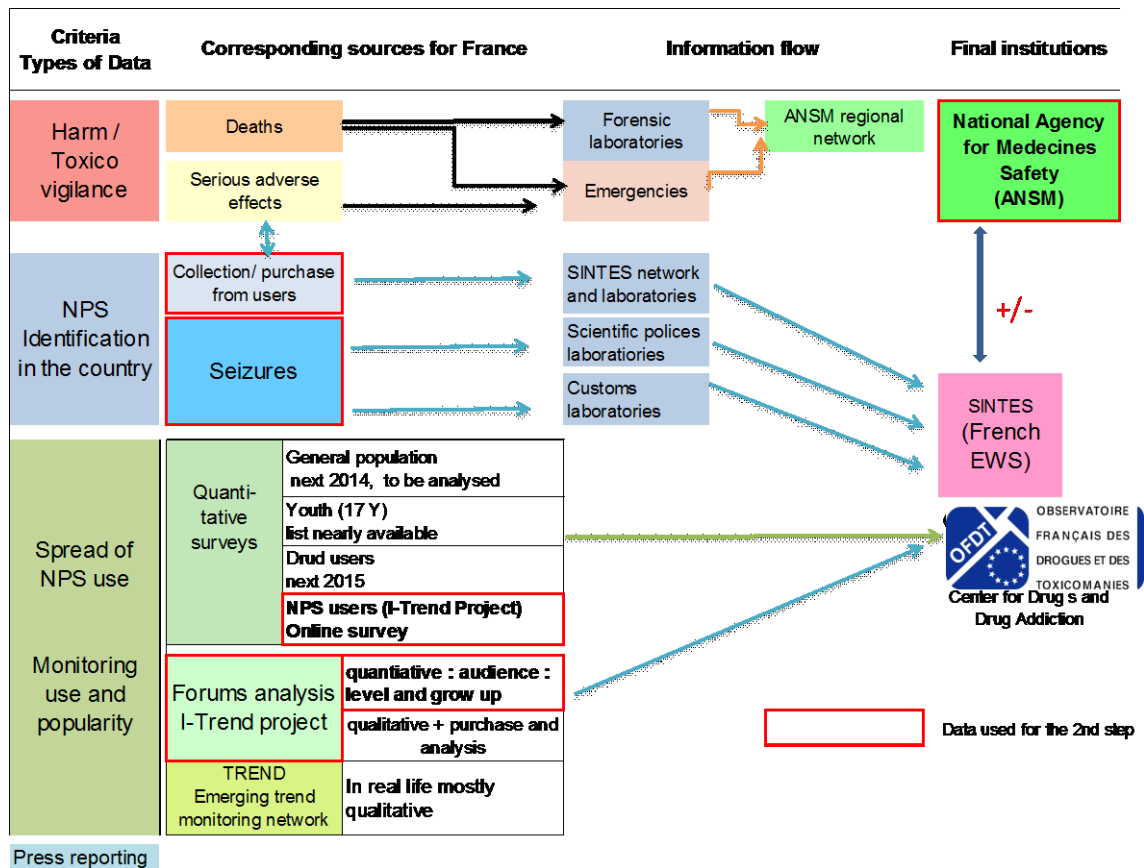
Source: I-Trend, OFDT

Finally, six sources have been used (Table 3, Chart 1).

- Data collected from Forum monitoring are quantitative. They are based on a part of I-Trend project that consisted first to identify relevant forums and in selected forums, to select all discussion thread related to each substances, and to monitor over different time period the number of new view for those thread. Number of new view related to one compound are added and allow the calculation of an average number of daily (new) view over a specified period.
- The online survey provided two lists: NPS used within the last year, and last used NPS. It was decided to keep the latest, thought to give a more recent overview of respondent preference.
- Data from TREND scheme (emerging Trend monitoring system which focuses on population with high prevalence of drug use) didn't enter the process due to a not strong enough methodology for popularity assessment adapted to NPS. Most of NPS circulate in festive events under classical drugs names and most of party goers show a poor knowledge of NPS.

As tools (online forum popularity of NPS monitoring and online survey) were still in an elaboration phase as well as data exchange with ANSM is not as smooth as with police and customs services, periods covered by data are not the same for all sources. This weakness of the method should be surrounded when the process become a routine one.

Chart 1: French information system on NPS, and data sources for NPS prioritization



Source: I-Trend, OFDT

Table 4: List of NPS captured by each available source

National Agency for Medicines and Health Products Safety Not ordered	Seizures Scientific Police	Nb of cases	Seizures customs services	Nb of cases	French EWS SINTES mostly on new substances	Nb of cases	Forums monitoring	average number of daily views	Last used NPS (online survey)	%
25C-NBOMe	Methoxetamine	6	x-MEC	79	Methoxetamine	10	3-MMC	164	Methoxetamine	15,1
25I-NBOMe	5F-AKB-48	5	4-FA	78	3-MMC	9	Methylone	95	Ethylphenidate	7,3
2C-B-FLY	ALPHA-PVP	4	DMT	69	2C-B	3	Ethylphenidate	94	2C-B	5,2
2C-C	2C-E	2	Methylone	63	2C-P	3	4-MEC	90	2C-P	4,3
2C-D	4-MEC	2	3-MMC	60	25C-NBOMe	2	Methoxetamine	85	3-MMC	3,9
2C-E	MDPV	2	x-EAPB	44	4-MEC	2	BK-2CB	70	25I-NBOMe	3,4
2C-I	THJ 018	2	4-MEC	17	ALPHA-PVP	2	MDPV	67	2C-D	3,0
2C-P	THJ 2201	2	Ethylphenidate	14	DOC	2	Synthacaine	65	2C-E	3,0
2C-T-7	25C-NBOMe	1	MPA	14	Ethylphenidate	2	MPA	60	4-MEC	3,0
3,4-CTMP	25H-NBOMe	1	JWH-073	12	MDPV	2	Mephedrone	60	4-MMC	3,0
3-MMC	2C-D	1	2C-B	10	25B-NBOMe	1	6-APB	52	25C-NBOMe	2,6
4,4'DMAR	2C-P	1	Éthylcathinone	10	25H-NBOMe	1	AMT	48	2C-I	1,7
4-ACO-DIPT	AB FUBINACA	1	Harmine	10	2C-E	1	25I-NBOMe	47	5-MAPB	1,7
4-FMA	AM-2201 JWH-122	1	x-MAPB	10	4,4'DMAR	1	LSZ	46	DOC	1,7
4-HO-DET	BB-22 or QUCHIC	1	ALPHA-PVP	9	5-APB	1	Pentedrone	43	LSZ	1,7
4-HO-MET	DMT	1	MAM-2201	9	5F-AKB-48	1	Diphenidine	41	Methylone	1,7
4-HO-MIPT	JWH018	1	MDPV	9	5-MAPB	1	5-EAPB	41	MPA	1,7
4-MEC	m-CPP	1	Pentedrone	9	5-MEO-DALT	1	Branded Product	37	25B-NBOMe	1,3
4-MMC	STS-135	1	5F-AKB-48	7	ALPHA-PBP	1	5-MAPB	36	AM-2201	1,3
5-APB	UR-144	1	DOC	7	DMT	1			BK-2CB	1,3
5-EAPB	x-phénéthylamine	1	x-APDB	7	Étizolam	1			DOB	1,3
5F-AKB-48			x-FA	7	FLUBROMAZEPAL	1			x-JWH	1,3
5-MAPB			25C-NBOMe	6	JWH-073	1			2C-T-7	0,9
6-APB			4-MMC	6	LSA	1			4-AcO-DMT	0,9
ALPHA-PVP			Éthylone	6	METHYLONE	1			4-MeO-DMT	0,9
AM-2201			JWH-073	6	MPA	1			5-APB	0,9
AMT			JWH-081	6	PHENIBUT	1			5-MeO-MIPT	0,9
DMT			25I-NBOMe	5	PMMA	1			5F-AKB-48	0,9
DOC			bk-MPA	5	PRIMIDONE	1			6-APB	0,9
ETHYLPHENIDATE			JWH-210	5	x-APB	1				
Hawaïen Baby			x-APB	5						
Woodrose					x-EAPB	1				
MBDB			4-MA	4	x-MEO-PCP	1				
MDAI			Étizolam	4	2-MEO-KETAMIN	1				
MDEA			m-CPP	4						

Source: I-Trend, OFDT

Next issue was to obtain one aggregated list from the six chosen sources.

Actually, the main elements available to rank substances are:

- The number of sources that capture the substance;
- The weight of each substance in each source that allow us to rank the substances within each list. Actually, substances could be weighed within all the lists, except in the one reflecting serious health events (Toxicovigilance).

A desirable process would be to weigh lists according to reliability of the source as able to represent which substances are the most commonly used or according to the importance of what they measure. For example, it seems reasonable to give importance to the list referring to health issues (toxicovigilance).

Giving a higher weigh to list based on toxico-analysis has be discussed too and it was decided to test a classification based only on sources with toxicological evidence.

In this session we don't have sufficient element to weigh lists.

To test different approaches for building the final top list, 3 top lists have been built with 4 ranking methods:

1. Ranking according to the number of sources that catch the substances (Table 6, 1)
2. A second method tried to take into account both indicators (rank and number of sources) by calculation a ratio:  
 $R = \text{average rank of the substance} / \text{number of sources where the substance appears.}$   
 The smaller ratio are in the top of the list.  
 To do so, substances have been first ranked within NPS lists from each sources (Table 5)  
 Substances captured in the toxicovigilance source were all given the rank 1 (we had no data to weigh substances of that list), considering that we couldn't drop this source and that it was important to give importance to it.  
 This method has been applied only for substances that had been captured in at least two sources.  
 The average rank, then the ratio, have been calculated for each substances.
3. Ranking according to the number of sources with toxico-analysis evidence that capture the substances.
4. 3 + 2

Table 5: Substances ranked for each source

National Agency for Medicines	Scientific Police	Custom services	French EWS SINTES	Forums monitoring	Last used NPS )	
Toxicovigilance	Seizures	Seizures	Substances colleted from users	Substances online popularity	Users answers to online survey	
TA / Not ranked	TA /Ranked	TA /Ranked	TA /Ranked	NoTA / Ranked	NoTA / Ranked	
25C-NBOMe	1 Methoxetamine	1 x-MEC	1 Methoxetamine	1 3-MMC	1 Methoxetamine	1
25I-NBOMe	1 5F-AKB-48	2 4-FA	2 3-MMC	2 Methylone	2 Ethylphenidate	2
2C-C	1 ALPHA-PVP	3 DMT	3 2C-B	3 Ethylphenidate	3 2C-B	3
2C-D	1 2C-E	4 Methylone	4 2C-P	3 4-MEC	4 2C-P	4
2C-E	1 4-MEC	4 3-MMC	5 25C-NBOMe	5 Methoxetamine	5 3-MMC	5
2C-I	1 MDPV	4 x-EAPB	6 4-MEC	5 BK-2CB	6 25I-NBOMe	6
2C-P	1 THJ 018	4 4-MEC	7 ALPHA-PVP	5 MDPV	7 2C-D	7
3-MMC	1 THJ 2201	4 Ethylphenidate	8 DOC	5 Synthacaine	8 2C-E	7
4-MEC	1 25C-NBOMe	9 MPA	8 Ethylphenidate	5 MPA	9 4-MEC	7
6-APB	1 25H-NBOMe	9 JWH-073	10 MDPV	5 Mephedrone	9 4-MMC	7
ALPHA-PVP	1 2C-D	9 2C-B	10 25B-NBOMe	11 6-APB	11 25C-NBOMe	8
Ethylphenidate	1 2C-P	9 Éthylcathinone	12 25H-NBOMe	11 AMT	12 2C-I	9
MDPV	1 AB FUBINACA	9 Harmine	13 2C-E	11 25I-NBOMe	13 5-MAPB	9
Methoxetamine	1 AM-2201 JWH-122	9 x-MAPB	13 4,4'DMAR	11 LSZ	14 DOC	9
METHYLONE	1 BB-22 or QUCHIC	9 ALPHA-PVP	13 5-APB	11 Pentadrone	15 LSZ	9
DMT	1 DMT	16 MAM-2201	16 5F-AKB-48	11 Diphenidine	16 Methylone	9
DOC	1 JWH018	16 MDPV	16 5-MAPB	11 5-EAPB	17 MPA	9
MPA	1 m-CPP	16 Pentadrone	16 5-MEO-DALT	11 5-MAPB	19 25B-NBOMe	10
AMT	1 STS-135	16 5F-AKB-48	16 ALPHA-PBP	11	AM-2201	10
4,4'DMAR	1 UR-144	16 DOC	20 DMT	11	BK-2CB	10
4-MMC	1 x-phénéthylamine	x-APDB	21 Étizolam	11	DOB	10
5-APB	1	x-FA	22 FLUBROMAZEPA	11	x-JWH	10
5-EAPB	1	25C-NBOMe	23 JWH-073	11	2C-T-7	11
Hawaïen Baby Woodrose	1	4-MMC	24 METHYLONE	11	4-AcO-DMT	11
MBDB	1	Éthylone	24 MPA	11	4-MeO-DMT	11
MDAI	1	JWH-073	26 PHENIBUT	11	5-APB	11
MDEA	1	JWH-081	26 PMMA	11	5-MeO-MIPT	11
Morning Glory	1	25I-NBOMe	26 PRIMIDONE	11	5F-AKB-48	11
PMMA	1	bk-MPA	29 TRAMADOL	11	6-APB	11
STS-135	1	JWH-210	30 x-APB	11		
Tiletamine	1	x-APB	30 x-EAPB	11		
2C-B-FLY	1	4-MA	30 x-MEO-PCP	11		
2C-T-7	1	Étizolam	33 2-MEO-KETAMIN	11		

Source: I-Trend, OFDT

Table 6: Classifications obtained by the aggregation method 1 to 4

1		2		3		4	
NPS	Nb of sources	NPS	average rank/ nb sources	NPS	nb of sources with TA	NPS	average rank/ nb sources with TA
4-MEC	6	Methoxetamine	0,4	4-MEC	4	Methoxetamine	0,3
METHYLONE	5	3-MMC	0,6	DMT	4	3-MMC	0,9
Ethylphenidate	5	Ethylphenidate	0,8	ALPHA-PVP	4	4-MEC	1,1
25C-NBOMe	5	4-MEC	0,8	25C-NBOMe	4	ALPHA-PVP	1,4
2C-P	5	METHYLONE	1,1	MDPV	4	Ethylphenidate	1,6
MDPV	5	MDPV	1,3	2C-P	4	MDPV	1,6
3-MMC	5	ALPHA-PVP	1,4	5F-AKB-48	4	METHYLONE	1,8
MPA	5	2C-E	1,4	Ethylphenidate	3	2C-E	1,8
Methoxetamine	5	MPA	1,5	METHYLONE	3	5F-AKB-48	1,9
2C-E	4	2C-B	1,8	MPA	3	DMT	1,9
ALPHA-PVP	4	25C-NBOMe	1,8	2C-E	3	MPA	2,2
5-MAPB	4	5F-AKB-48	1,9	3-MMC	3	25C-NBOMe	2,4
DMT	4	2C-D	1,9	Methoxetamine	3	2C-D	2,5
25I-NBOMe	4	DMT	1,9	DOC	3	DOC	2,9
5F-AKB-48	4	2C-P	2,1	x-EAPB	2	2C-P	3,0
DOC	4	DOC	2,2	JWH-073	2	4,4'DMAR	3,0
2C-D	3	5-MAPB	2,5	25I-NBOMe	2	5-APB	3,0
5-APB	3	2C-I	2,5	4,4'DMAR	2	PMMA	3,0
2C-B	3	6-APB	2,6	STS-135	2	5-MAPB	3,0
4-MMC	3	5-APB	2,6	4-MMC	2	2C-B	3,3
6-APB	3	25I-NBOMe	2,9	25H-NBOMe	2	x-EAPB	4,3
5-EAPB	2	PMMA	3,0	5-APB	2	STS-135	4,3
2C-C	2	4,4'DMAR	3,0	Étizolam	2	25H-NBOMe	5,0
2C-T-7	2	2C-T-7	3,0	2C-C	2	4-MMC	6,3
25H-NBOMe	2	AMT	3,3	PMMA	2	25I-NBOMe	6,8
BK-2CB	2	4-MMC	3,6	5-MAPB	2	2C-C	8,8
JWH-073	2	BK-2CB	4,0	x-APB	2	JWH-073	9,3
25B-NBOMe	2	x-EAPB	4,3	AB FUBINACA	2	x-APB	10,3
LSZ	2	STS-135	4,3	2C-D	2	Étizolam	11,0
4,4'DMAR	2	5-EAPB	4,5	2C-B	2	AB FUBINACA	11,0

Source: I-Trend, OFDT

These different classifications methods give very closed results, if we don't care about classification within the top list, which seems a reasonable position according roughness of data sources and of the aggregating process. We chose the final Top list considering the ranks of each compound in the four classification. The top list encompasses first and second blocs in the following list. We consider that we can't define any rank within each block. The list is completed by other substances that seems important to consider too. It seems important to enlarge the list because of the time variability of users' preferences and the still roughness of the data.



*French Top list 2014*

Top List	Legal status	Scheduling date
The First Top		
Methoxetamine	Scheduled	5 August 2013
3-MMC	Scheduled	27 July 2012
4-MEC	Scheduled	27 July 2012
Ethylphenidate	In process	
The second Top		
ALPHA-PVP	Scheduled	27 July 2012
MDPV	Scheduled	27 July 2012
METHYLONE	Scheduled	27 July 2012
2C-E	N	
MPA	N	
5F-AKB-48	In process	
25C-NBOMe	N	

Source: I-Trend, OFDT

A third group should remain in the scope, considering that it's difficult to only consider 10 substances.

DMT
2C-D
2C-P
DOC
2C-B
5-MAPB
5-APB
2C-I
6-APB

It has been discussed whether the classification would consider groups of molecules instead of sole molecules. It's worth noting that the classification could have been different. At first, some toxicological laboratories don't make difference between two molecules like 5-APB or 6-APB for example and note x-APB. These analysis are not taken into account in a molecular classification. But even completely identified, series like 2C-X one would have been more weighted, as well as maybe the X-NBOMe series with a grouped approach.

The question seems even more important in France, as regards to synthetic cannabinoids, that are rather absent of the top list, but seems the more used NPS in general population survey. That's why, for these latter, the quality and relevance of used sources have to be questioned. The health serious events are still in France not very well reported; users of synthetic cannabinoid among general population probably didn't answer the online survey; and seizures aren't really a random process.

## Comparison between the lists

Table 7: Comparison between 2013 and 21014 Top list

2013 Top list	2014 Top list
AM-2201	Methoxetamine
UR-144	3-MMC
MDPV	4-MEC
4-MEC	Ethylphenidate
25-I NBOME	ALPHA-PVP
5-MEO-DALT	MDPV
6-APB	METHYLONE
5-APB	2C-E
Ethylphenidate	MPA
Methoxetamine	5F-AKB-48
	25C-NBOMe

Source: I-Trend, OFDT

If we consider the ten first (eleven for Top list 2), we only have 4 common NPS: MDPV, 4-MEC, ethylphenidate, methoxetamine. If we extend the list, more NPS are common: 25C-NBOMe, 25I-NBOMe, 2C-E, methylone.

Table 8: Comparison between 2013 and 21014 enlarged Top list

Enlarged 1st Top list	Enlarged 2nd Top list
AM-2201	Methoxetamine
UR-144	3-MMC
MDPV	4-MEC
4-MEC	Ethylphenidate
25-I NBOME	ALPHA-PVP
5-MEO-DALT	MDPV
6-APB	METHYLONE
5-APB	2C-E
Ethylphenidate	MPA
Methoxetamine	5F-AKB-48
MAM-2201	25C-NBOMe
JWH -073	DMT
JWH -081	2C-D
JWH -122	2C-P
JWH-250	DOC
JWH-210	2C-B
2-FMC	5-MAPB
3-FMC	5-APB
4-FMC	2C-I
Ethcathinone	6-APB
4-FMP	4,4'DMAR
3-FMP	PMMA
2-FMP	25I-NBOMe
2 C-E	2C-T-7
2C-C-NBOME	4-MMC
4-ACO-DMT	x-EAPB
Benzofury	STS-135

Source: I-Trend, OFDT

One of the major difference between the two lists is related to the synthetic cannabinoid that were really present in the first selection but not represented by only one molecule in the second and were even more numerous in the extended selection of candidates to Top 10.

The fact that that are absent of the second top list, can be linked to several points:

- They were less present in customs seizure list on 2014 than on 2013
- But also, they are often sold as plant mix and less labelled by users with their molecular name, and so less quoted in the survey; It is possible too that the survey drawn mostly drugs users and not general population users, likely to have just use cannabis and cannabinoid.
- The issue is the same on forums popularity.

It is noteworthy to point out the fact that the second Top list includes several scheduled substances among the most circulating NPS, the first of all having been classified during the I-Trend project in 2013, suggesting in France scheduling didn't change users preferences.

It is therefore, difficult to determine which changes are related:

- to methods that changed between the two rounds, being more sophisticated for the second one. For the first top list no weigh was used to class the substances. The process has been more qualitatively reasoned than quantitative. The fact that we considered that synthetic cannabinoid were certainly more largely used than other played a role in first top list.
- to sources, that were more numerous for the second round, that lead to a lower importance of the seizures sources on the second round. Notably, one source related to users declaration was used in the second round and the source related to substances online popularity was used on a more rigorous way one the second round than on the first.
- to evolution of users interest or use : some substances were drawing users interest on 2013, but were not largely used in 2013

Several other rounds would be needed to stabilize and strengthen the process in order to be able to identify real changes in NPS use.

## Conclusion

- 10 substances in the list aren't sufficient. It seems that excepted 1 to 5 substances, the range of used substances is much larger (results from WS5, but also WS1 and WS 3). We could propose several top lists made of small groups with a nearly equal probability to be used in each little group (no classification inside groups).
- It appears than our selection process promotes more substances sold under molecular names than under branded name. We have to overcome that issue (maybe two top lists).

About the Top list elaboration:

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- It appears than our selection process promotes more substances sold under molecular names than under branded name. We have to overcome that issue (maybe two top lists).

Whatever we do, gathering needed information depends on political decision and willing.

It has to be clear in all countries that one centre is officially in charge of gathering data and producing an overview on the general situation.

The data collection need a cooperation between national data producer's entities and the ability of the entity to manage their data. The budget cuts in all administrations make it less and less easy (forensic data, OFDT staff...).

Addictovigilance system that covers in France toxicovigilance on psychoactive substances needs means and willing to build a unique database and to share its data.

We have to be clear by presenting the data on the fact that they do not aim to "prioritize for scheduling" but "to give an overview on the most spread substances".