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**Belackova, V, Pazitny, M, Drapalova, E, Martinez, M, van der Gouwe, D, Begley, EK, Kidawa, M, Tomkova, A and Kmetonynova, D**

**Assessing the impact of laws controlling the online availability of 25I-NBOMe, AH-7921, MDPV and MXE – outcomes of a semi-automated e-shop monitoring**

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### Article

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7 **Assessing the impact of laws controlling the online availability of**  
8 **25I-NBOMe, AH-7921, MDPV and MXE – outcomes of a semi-automated**  
9 **e-shop monitoring**10  
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17 Institute, Liverpool John Moores University, Liverpool, UK, and <sup>6</sup>National Bureau for Drug Prevention – Ministry of Health, Warsaw, Poland18 **Abstract**19  
20 *Aims:* The indicator of availability has been used in the risk assessment (RA) of new psychoactive  
21 substances (NPS). This paper aims to examine the pre- and post-control availability of 25I-  
22 NBOMe, AH-7921, MDPV and MXE, which were assessed by the EMCDDA. *Methods:* Data were  
23 collected by a semi-automated software tool (I-TREND SASF) on e-shops in national languages  
24 (Czech, French, Dutch, Polish and English) that offered shipping of these compounds into the  
25 respective countries; frequency analysis was used. *Findings:* The number of e-shops selling  
26 these substances decreased between III/2014 and XII/2015 (except for AH-7921). Both increases  
27 and decreases were found on the country-level for all the compounds (except for an overall  
28 decrease for MXE). In one instance an NPS disappeared from this market in 2015 (25I-NBOMe in  
29 NL); 25I-NBOMe and AH-7921 in France and AH-7921 in Poland appeared for the first time in  
30 2015. The shops listing AH-7921, 25I-NBOMe and MDPV in XII/2015 ranked higher in terms of  
31 “popularity” than in III/2014. The IP addresses were more likely to be outside the EU in 2015  
32 than in 2014. *Conclusions:* We found no evidence that national-level compound bans  
33 contributed to the changes in online NPS markets. Indicators of the accessibility, availability,  
34 popularity, and IP origin should be considered in RA. Data triangulation with street markets and  
35 the darknet is needed as well as more research into the “displacement” and “replacement”  
36 effects of control laws.37  
38  
39 **Introduction**40  
41 The availability of psychoactive substances and analysis of  
42 drug market activity are important indicators that help to  
43 understand the supply of illicit drugs and to design policies to  
44 reduce it (EMCDDA & Europol, 2007). Drug seizures,  
45 together with information on drug prices, purity at the street  
46 level, and the composition of seized samples (mainly sourced  
47 from the police and customs) can provide a multi-dimensional  
48 view of drug availability as a whole, especially if combined  
49 with user-sourced drug sample analysis as in the case of the  
50 Dutch Drug Information and Monitoring System (further  
51 DIMS) (Brunt & Niesink, 2011). Data on drug availability is  
52 routinely collected e.g. within the REITOX (Réseau Européen  
53 d’Information sur les Drogues et les Toxicomanies) network.54  
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81 **Keywords**82 New psychoactive substances, risk  
83 assessment, online shops, availability,  
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100 Nevertheless, in countries where there is no systematic  
101 collection of data and/or drug samples from drug users and  
102 drug sellers, the police-sourced information on drug markets  
103 might be representative of law enforcement activity rather  
104 than of the behaviour of illicit market players (Blumstein,  
105 1993; Caulkins, 2007; Tonry, 1995).106  
107  
108 **Monitoring the online market in psychoactive**  
109 **substances**110  
111 Increasing use of the internet by both drug users and sellers  
112 has opened up a new space for more accurate monitoring of a  
113 specific drug market segment – the online indexed (surface)  
114 market in psychoactive substances. Web monitoring activities  
115 are considered vital in order to gain a better understanding of  
116 the phenomena of new psychoactive substances (NPS)  
117 (Corazza et al., 2013, 2012a,b). Specifically, the monitoring  
118 of online markets, unlike information about drug supply on  
119 “traditional” drug markets, offers a picture of all the  
120 psychoactive substances being offered in real time, and of  
121 their characteristics.

121 A vast number of outlets have appeared on the surface web  
 122 (publicly available online web pages), selling (mostly) NPS  
 123 that are not controlled, also sold as “legal highs”, “bath  
 124 salts”, or “research chemicals” (Newcombe, 2009;  
 125 Vardakou, Pistos, & Spiliopoulou, 2011). Online markets  
 126 selling NPS have been subjected to several research enquiries.  
 127 Schmidt and colleagues evaluated the accessibility of “legal  
 128 highs” via the internet by UK-based retailers and found 39  
 129 unique websites with 1308 products (Schmidt et al., 2011).  
 130 Meyers and colleagues conducted research on the availability  
 131 of “bath salts” in online shops on the surface web (we refer  
 132 to them further as *e-shops*); 31 websites were found globally  
 133 (Meyers et al., 2015). Some e-shops also exist in a grey area  
 134 by restricting purchase options to trusted members via  
 135 password-protected platforms (Martinez, Kmetonyova, &  
 136 Belackova, 2016). Unlike smart shops or head shops (Ryall  
 137 & Butler, 2011), online retailers can service user populations  
 138 across regions and countries.

139 For the sale of illegal psychoactive substances, online  
 140 markets on the so-called “darknet” provide access to a  
 141 variety of illicit goods (Barratt, 2012; Barratt & Aldridge,  
 142 2016; Van Hout & Bingham, 2013, 2014). These online  
 143 spaces can only be accessed through IP-anonymising soft-  
 144 ware, and those that operate as marketplaces use a  
 145 decentralised electronic currency (the bitcoin) which is  
 146 difficult to track (Nakamoto, 2008; Soska & Christin,  
 147 2015). One of the most renowned darknet market places for  
 148 illicit goods was Silk Road, which opened in 2011 and closed  
 149 by the end of 2014, following a police intervention (Barratt,  
 150 Ferris, & Winstock, 2014). NPS can also be found in these  
 151 markets, although to a much smaller extent than illegal goods  
 152 (Barratt et al., 2014; Van Buskirk, Naicker, Roxburgh, Bruno,  
 153 & Burns, 2016).

### 154 155 Monitoring of NPS availability at the European level

156 The standardised attempts to assess online availability at the  
 157 European level began as unstructured searches through  
 158 popular search engines for the purpose of the risk assessment  
 159 (RA) of several NPS, such as 2C-T-2, 2C-T-7 or GHB  
 160 (EMCDDA, 2002, 2004).

161 Since 2006, the EMCDDA has been conducting multilin-  
 162 gual surveys called “snapshots” in which six specific NPS-  
 163 related search strings are entered into three web search  
 164 engines in each country, with the URLs of the e-shops that are  
 165 identified being collected along with information about the  
 166 site and the products for sale (Hillebrand, Olszewski, &  
 167 Sedefov, 2010). For instance, the 2011 snapshot was carried  
 168 out in 18 languages and found 631 e-shops offering NPS for  
 169 sale (EMCDDA, 2012).

170 The EMCDDA snapshot methodology has been used, for  
 171 example, to show a decrease in the availability and price of  
 172 AMT over a six-month period (Wood & Dargan, 2014), to  
 173 demonstrate the greater availability of a controlled substance  
 174 than those that are not controlled (Nizar, Dargan, & Wood,  
 175 2015) and to perform international comparisons of NPS prices  
 176 (Vermette-Marcotte, Dargan, Archer, Gosselin, & Wood,  
 177 2014). Since 2011, the outcomes of the snapshot survey have  
 178 been included in the RA of NPS conducted by the EMCDDA  
 179 (2009).  
 180

### 181 RA and the availability of NPS

182 RA is a structural evidence-based activity aiming to object-  
 183 ively collect relevant information about the potential risks  
 184 posed by psychoactive substances and to assess risk quanti-  
 185 tatively (Caulkins, Reuter, & Coulson, 2011), providing a  
 186 background for informed decisions by policy makers, regu-  
 187 latory bodies, and stakeholders in drug services (Drapalova,  
 188 Grund, & Belackova, 2016; Fitch et al., 2003; Mounteney,  
 189 2009; Rhodes, Stimson, Fitch, Ball, & Renton, 1999).

190 Globally, the risks of newly emerged substances are  
 191 assessed by the Expert Committee on Drug Dependence of  
 192 the World Health Organisation (WHO, 2010). On a European  
 193 level, RAs are performed by the Scientific Committee of the  
 194 European Monitoring Centre for Drugs and Drug Addiction  
 195 (EMCDDA, 2009). Since 1998, the EMCDDA has performed  
 196 19 RAs, of which 17 have suggested control measures at the  
 197 European level.

198 The RA process collects data to assess the amount and  
 199 probability of harm in several dimensions, including bio-  
 200 logical, psychological, social, and economic harms to  
 201 individuals, groups and societies. The data about the avail-  
 202 ability of NPS is primarily assessed within the category of  
 203 “Public health risks” where it concerns the availability and  
 204 quality of a new psychoactive substance on the market (purity,  
 205 adulterants, etc.) and the populations and settings where it is  
 206 obtained and used. Secondly, the availability of NPS is  
 207 considered under “Options for control and possible conse-  
 208 quences of the control measures”, where, additionally, the  
 209 prices of NPS are assessed alongside the potential impact of  
 210 NPS control (EMCDDA, 2009).

211 In the process of providing information about the risks in a  
 212 timely manner for evidence-based policy decisions, RA  
 213 procedures are challenged by the large number of newly  
 214 emerging substances and by their rapid turnover (Drapalova  
 215 et al., 2016; Winstock & Ramsey, 2010). It is thus crucial to  
 216 obtain real-time data in order for RA procedures to be  
 217 accurate and to correspond to the situation on the NPS  
 218 market.  
 219

### 220 Aims

221 This paper assesses the online availability of four NPS that  
 222 were subjected to RA by the EMCDDA in the period from  
 223 January 28th, 2014 to April 28th, 2014 (Mounteney &  
 224 Griffiths, 2014). These were 25I-NBOME (EMCDDA,  
 225 2014c), AH-7921 (EMCDDA, 2014d), MDPV (EMCDDA,  
 226 2014a) and methoxetamine (EMCDDA, 2014b), further  
 227 referred to as MXE As an outcome of the RA, EU member  
 228 states were required to control these compounds before  
 229 October 2nd, 2015 (EC, 2015).  
 230

231 Table 1 shows when the countries in this analysis, the  
 232 I-TREND project partners – the Czech Republic (CZ), France  
 233 (FR), the Netherlands (NL), Poland (PL) and the United  
 234 Kingdom (the UK) – adopted control of the four NPS.  
 235 It shows that all the countries banned the four compounds  
 236 by the required time, and that several countries had banned  
 237 some of the compounds even prior to the council decision  
 238 (FR and the UK had banned them all except for AH-7921;  
 239 MDPV had been controlled in all the I-TREND countries  
 240 except for NL).

Table 1. Control of the four NPS in project partner countries.

|           | Czech Republic  | France           | Netherlands | Poland          | United Kingdom   |
|-----------|-----------------|------------------|-------------|-----------------|------------------|
| 25I-NBOMe | 1.10.2015       | <b>24.9.2013</b> | 1.7.2015    | 1.7.2015        | <b>10.6.2013</b> |
| AH-7921   | 1.10.2015       | <b>24.9.2013</b> | 1.7.2015    | 1.7.2015        | 1.1.2015         |
| MXE       | 1.10.2015       | <b>5.8.2013</b>  | 1.7.2015    | 1.7.2015        | <b>5.4.2012</b>  |
| MDPV      | <b>6.4.2011</b> | <b>27.7.2012</b> | 1.7.2015    | <b>8.6.2011</b> | <b>16.4.2010</b> |

This paper aims to evaluate the impact of both the EU-level decision and national-level control measures on the indicators of online accessibility and availability of the four NPS, on the country of origin of their IP addresses, and on the “popularity” ranking of these e-shops. The paper also discusses the relevance of these different indicators to RA procedures.

## Methodology

A semi-automated shop-finder software (I-TREND SASF), developed within the I-TREND project and adopted to the five project partner languages (CZ, FR, PL, NL and UK), searched the surface web for the four compound names (25I-NBOMe, AH-7921, MDPV and MXE) shortly before their RA by the EMCDDA (March 22nd, 2014) and 21 months later (December 29th, 2015); the latter date was almost two months after the control measures were supposed to have been adopted by all EU member states.

### Data collection using the I-TREND semi-automatic shop-finder (I-TREND SASF)

I-TREND SASF performs online searches based on the EMCDDA snapshot methodology – see the background section and EMCDDA (2009) – with the modification that it stores only a limited number of outcomes ( $n = 100$  in this study) for each search engine and set of key words. The advantage over the snapshot methodology is that I-TREND SASF can search the internet periodically or at any “ad hoc” moment while building upon human-assisted categorisation from its previous searches. This means that once a search outcome (a web page) has been approved by the administrator as an actual e-shop (rather than a discussion board or another web page irrelevant to the purpose of the search), it is classified as such in any further searches (and irrelevant outcomes are excluded in any further searches too). This makes the use of I-TREND SASF time-saving in comparison to the EMCDDA snapshot. Further on, several characteristics of the “approved” e-shops are retrieved automatically and stored (e.g. IP address unique identifier, country code, popularity ranking). Last but not least, with the use of I-TREND SASF, it has been possible to isolate unique e-shops (i.e. to exclude any URLs which serve to display one e-shop under multiple links); only “unique” e-shops are presented in this analysis. Further information about the methodology can be found elsewhere (Martinez et al., 2016).

An ad hoc search by I-TREND SASF was conducted for the purpose of this research in III/2014 (the first point) and in XII/2015 (the second point) using the three most “popular” search engines in each I-TREND project partner country

(e.g. Google.pl, Yahoo.fr, Seznam.cz; the selection was made with the use of online ranking web pages such as alexa.com, pageranking.org and checkpagerank.net). The search phrases used in this research consisted of several terms identifying e-shops in national languages (“basket/trolley/shopping cart”, “buy” and “price”) and of the four compound names that were subject to this analysis (25I-NBOMe, AH-7921, MDPV and MXE). At each point in time, the e-shops were further checked in order to verify that the compounds of interest were available at the e-shop, were in stock, and could be shipped into the country for which the shop was identified.

## Data analysis

A frequency analysis was carried out, focussing on the changes between the two monitoring points. The first indicator that was examined was the number of outcomes (e-shops selling NPS in national languages) per substance and country (referred to as “accessibility”), together with the overall “availability” of the selected NPS in each of the countries (whether or not e-shops selling the compound were found in a country-level search).

The second indicator subjected to analysis was the publicly available country code of the e-shop’s IP address, which indicates the country in which the online shop was technically hosted (the location of the “server”); the physical location of the vendor might be different, however.

The third indicator was the global ranking of the e-shop according to www.alexa.com, which represented the site’s “popularity”. Alexa.com was chosen because it listed more characteristics of the webpages we identified as e-shops selling NPS than other ranking systems; another benefit was that it displayed separate results for sub-domains (e.g. nsd.webshop.com and nps.webshop.com rather than just webshop.com). The rank was calculated by Alexa.com using a combination of the average number of daily visitors to the site and page views on the site over three-month periods, based on the records from internet users with the Alexa device installed (Kamerer, 2013). The most popular online sites (Facebook, Google) rank close to 1; the top 1% of popular pages ranks < 2,000,000. I-TREND SAFS automatically downloaded the rank of each of the approved e-shops, if available. For the purpose of this analysis, the rank values of the web pages identified by I-TREND SAFS were divided into five categories based on the percentile distribution of the entire sample rank in 2014 (VERY HIGH – below 100, HIGH – 100th to 2 mil, MIDDLE – 2 to 5 mil, LOW – 5 to 10 mil, and VERY LOW – more than 10 mil). A high rank not only suggests that the page is popular, but also implies a higher likelihood that the web page will be displayed as a search outcome.

## Findings

At the first monitoring point (III/2014), 66 e-shops identified for the project partner countries were selling at least one of the four NPS subjected to RA. At the second point (XII/2015), 33 e-shops were selling one or more of the four compounds (half of the shops found at the first monitoring point). These were all active unique e-shops (all parallel or duplicate shops, e.g. the same shop under multiple URLs, had been removed).

A total of nine of these e-shops were identified in both III/2014 and XII/2015. This means that 57 e-shops that had been selling the four compounds at the first monitoring point were “dead”, meaning they ceased to exist ( $n=43$ ), were no longer selling any products ( $n=11$ ), were not offering any of the four substances, or appeared in the 101st or a further search outcome at the second monitoring point ( $n=6$ ). It also shows that 24 new e-shops selling these compounds appeared at the second monitoring point. Out of the 66 outcomes in III/2014 and 33 in XII/2015, several were identified within search outcomes for more than one I-TREND country (four in 2014, seven in 2015).

As a result of the decrease in the overall number of shops selling the four compounds, their accessibility was thus lowered significantly within the five EU countries in XII/2015. Interestingly, as will be discussed further, several compounds were identified in country-specific searches at the second point that were not originally available at the first point. This suggests that in some cases, the availability of these compounds actually increased.

### Fluctuations in availability and accessibility

The highest number of e-shops across both monitoring points that was selling at least one of the compounds (accessibility across countries) was found in the UK ( $n=43$  in III/2014,  $n=17$  in XII/2015); however, this was also the largest decrease in the number of relevant e-shops that occurred (–61%). The second largest number of e-shops was found for PL ( $n=17$  in III/2014,  $n=13$  in XII/2015), with a somehow smaller rate of decrease (–24%) compared to the UK. A remarkably lower number of e-shops selling the four NPS of interest was found in the searches in FR ( $n=4$  in III/2014,  $n=6$  in XII/2015), in NL ( $n=5$  in III/2014,  $n=4$  in XII/2015), and in CZ ( $n=3$  in III/2014,  $n=4$  in XII/2015). An overview of the e-shops per country is provided in Figure 1.

When accessibility per compound is looked at, the most widely-marketed NPS in our sample was MXE, with 44 e-shops selling the compound in III/2014 and 20 in XII/2015 (on a per-country basis, it was the most widely-marketed compound in the UK, PL, FR and CZ in III/2014 and in the UK, FR, PL and NL in XII/2015), followed by MDPV (the most widely-marketed in NL and FR in III/2014 and in CZ and NL in XII/2015), followed by 25I-NBOMe and followed by AH-7921; see Table 2.

Across all the countries, the number of e-shops selling MXE decreased over the monitoring period. There was also a noticeable decrease in the number of e-shops selling the other

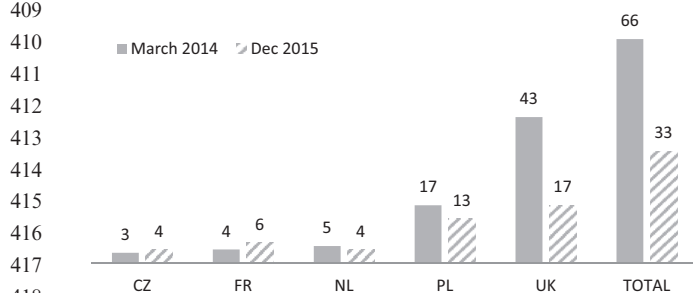


Figure 1. Number of e-shops per country listing at least one compound assessed in 2014 and 2015.

compounds, and yet this varied between the individual countries and compounds (both increases and decreases occurred). This finding is discussed in detail below.

Over the monitoring period, the number of shops selling MDPV decreased in some countries (FR, NL, the UK) and increased in others (CZ, PL). Online searches during XII/2015 found that 25I-NBOMe was no longer stocked in NL, and the number of UK e-shops selling it had decreased. No change in the number of shops selling 25I-NBOMe was detected either in the PL search or in CZ (where it never appeared).

AH-7921 was the least widely-marketed substance of the four. While AH-7921 never appeared in the CZ and NL searches, it was identified in the PL and FR search in XII/2015 for the first time. Additionally, the number of e-shops selling the compound in the UK ( $n=6$ ) remained consistent at the two monitoring points.

This shows that despite overall decreases in accessibility, in some cases the availability of the compounds per country increased (AH-7921 in FR and PL, 25I-NBOMe in FR) or remained the same (all the compounds that were available per country in III/2014 remained so in XII/2015, except for 25I-NBOMe in NL, which was no longer available in XII/2015).

### Country of e-shop domain origin (IP address)

In terms of the e-shops' IP addresses identified in III/2014, most of them were located in a US domain ( $n=20$ , 30% of all

Table 2. Number of shops listing particular NPS per I-TREND project country.

|                        | CZ | FR         | NL     | PL         | UK        | Total <sup>d</sup> |
|------------------------|----|------------|--------|------------|-----------|--------------------|
| 25I-NBOMe <sup>b</sup> |    |            |        |            |           |                    |
| 03–2014                | 0  | 0          | 2      | 3          | 15        | <b>20</b>          |
| 12–2015                | 0  | 1          | 0      | 3          | 5         | <b>9</b>           |
| TREND <sup>a</sup>     | 0  | First time | Remove | No change  | –         | –                  |
| AH-7921                |    |            |        |            |           |                    |
| 03–2014                | 0  | 0          | 0      | 0          | 6         | <b>6</b>           |
| 12–2015                | 0  | 1          | 0      | 1          | 6         | <b>6</b>           |
| TREND <sup>a</sup>     | 0  | First time | 0      | First time | No change | <b>No change</b>   |
| MDPV                   |    |            |        |            |           |                    |
| 03–2014                | 2  | 4          | 5      | 4          | 22        | <b>31</b>          |
| 12–2015                | 4  | 2          | 3      | 5          | 5         | <b>12</b>          |
| TREND <sup>a</sup>     | +  | –          | –      | +          | –         | –                  |
| MXE <sup>c</sup>       |    |            |        |            |           |                    |
| 03–2014                | 3  | 4          | 4      | 14         | 25        | <b>44</b>          |
| 12–2015                | 1  | 3          | 3      | 8          | 10        | <b>20</b>          |
| TREND <sup>a</sup>     | –  | –          | –      | –          | –         | –                  |
| Total                  |    |            |        |            |           |                    |
| 03–2014                | 3  | 4          | 5      | 17         | 43        | <b>66</b>          |
| 12–2015                | 4  | 6          | 4      | 13         | 17        | <b>33</b>          |
| TREND <sup>a</sup>     | +  | +          | –      | –          | –         | –                  |

<sup>a</sup>Changes in accessibility per country and compound are marked as – decrease, + increase or “no change”. Changes in availability per country and compound are marked as “First time”, “remove”; there is no sign for “no change” in availability. Where a compound wasn't available in either of the periods, it is marked as “0”.

<sup>b</sup>An additional shop (UK) that was listing the substance was identified by the tool in 2015, but was found to be out of order, and thus is excluded from the figures.

<sup>c</sup>Out of stock in two additional shops (PL, UK) in 2015 and two other shops listing the substance were identified (UK, NL), but were found to be out of order in 2015, and thus they were excluded from the figures.

<sup>d</sup>The totals are lower than the sum in both the columns and rows, as several e-shops were identified in more than one country and were selling more than one compound.

shops), a Dutch domain ( $n = 11$ , 17%) or a domain in another EU country ( $n = 12$ , 18%); see Figure 2. That said, the majority of the IP addresses selling NPS compounds in III/2014 were based in EU countries ( $n = 38$ , 58%). This was a higher share than in XII/2015 ( $n = 16$ , 49%). During the second monitoring period, the ratio of e-shop domains located in the US increased notably ( $n = 15$ , 45%); see Figure 2.

### E-shop popularity

An Alexa Global Ranking was available for 66% of the shops identified in III/2014 ( $n = 44$ ) and 58% of the shops identified in XII/2015 ( $n = 19$ ), i.e. they were visited by internet users with the Alexa device installed on their browsers; the results below are discussed for those e-shops only (see Figure 3).

In III/2014, more than a quarter of the e-shops selling the NPS of our interest ranked among the very high (7%,  $n = 3$ ) or high (18%,  $n = 8$ ) distributions, i.e. 25% of the shops ranked “high” or above; in XII/2015, a similar proportion of the e-shops ranked among the most popular (“high” = 26%,  $n = 5$ ). Nevertheless, a greater proportion of e-shops selling the four compounds at the second monitoring point were ranked “low” or “very low” (36% in III/2014, 52% in XII/2015). While the ranking of the most numerous e-shops selling MXE decreased between III/2014 and XII/2015 (from 33% to 27%

ranking “high” or above), for the e-shops selling all other compounds it increased (from 24% to 29% “high” or above in MDPV, 38% to 48% in AH-7921, and 3% to 48% in 25I-NBOMe). It should be pointed out, though, that the shops with the highest ranking proportions overall were those selling AH-7921 and 25I-NBOMe in XII/2015; the shops selling AH-7921 in III/2014 also had the highest ranking among all the shops in that period.

### Discussion

We assessed the indicators of online availability for four NPS (25I-NBOMe, AH-7921, MDPV and MXE) that were subjected to RA by the scientific committee of the EMCDDA and suggested for control by EU member states. We retrieved data before their European-level RA (March 22nd, 2014) and two months after their control had become mandatory (December 29th, 2015); several compounds were, however, already controlled prior to the first monitoring point in some I-TREND project countries (all of them in FR, all except AH-7921 in the UK, and MDPV in CZ and PL).

### Developments in accessibility and availability and impact of control

Essentially, the overall number of e-shops selling these substances identified on the surface web decreased substantially for the I-TREND project countries (decrease in “accessibility”); this also applied on a per country basis, except for France, where there were more shops identified in III/2015 than in XII/2014. Decreases in the number of e-shops offering MXE were observed across all four country searches; the number of e-shops selling 25I-NBOMe also decreased in the UK and the number of MDPV selling shops decreased in FR, NL and the UK.

On the other hand, there was only one instance in which an individual compound completely disappeared from the market during the second monitoring point (25I-NBOMe in NL). In three cases, substances were found in national language searches in XII/2015 (25I-NBOMe in FR and AH-7921 in FR

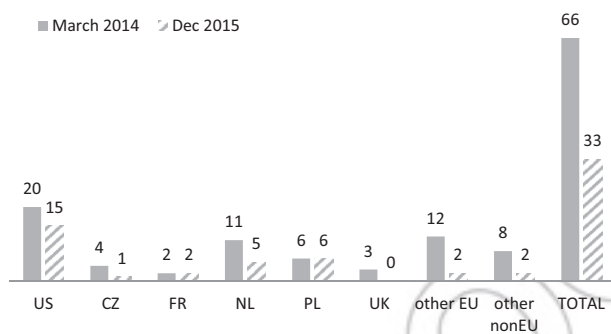


Figure 2. IP address of e-shops selling the compound in March 2014 and December 2015.

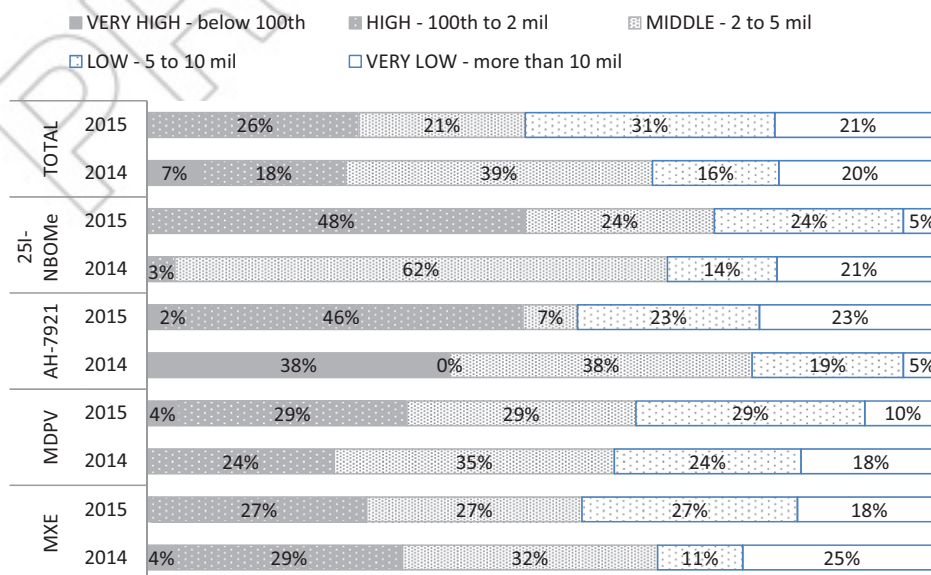


Figure 3. Alexa global ranking of the e-shops selling the four compounds in 2014 and 2015 (only e-shops where the ranking was available).

601 and PL), but they did not originally appear there in III/2014  
602 (an increase in “availability”). In two cases, the number of e-  
603 shops offering a particular compound in a given country  
604 increased (MDPV in CZ and PL). All four compounds could  
605 be found in the UK throughout both points; the number of  
606 shops offering AH-7921 in the UK and 25I-NBOMe in PL did  
607 not change during the monitoring period.

608 First, this indicates that the responses of online vendors to  
609 control measures varied across the five countries; this is  
610 expressed in the outcome of online searches of the internet  
611 using selected key words in the five national languages. It  
612 also suggests that despite decreases in accessibility (the  
613 number of e-shops listing or selling a particular compound),  
614 the availability of some compounds per country could  
615 increase (FR, PL) or remain the same (PL, UK).  
616 Additionally, the relative “popularity” evidently increased  
617 for the e-shops listing all compounds except for MXE,  
618 suggesting that those shops had become more heavily  
619 accessed by internet users in XII/2015.

620 When looking at the impact of country-level bans on the  
621 accessibility and availability of the four compounds, they  
622 appear to be rather limited. The number of e-shops identified  
623 through country-level searches decreased by more than half in  
624 the UK (from  $n=43$  to  $n=17$ ) in XII/2015. The UK had  
625 previously legislated against all three compounds where the  
626 decrease occurred (prior to the first monitoring point),  
627 whereas the decrease in the number of e-shops selling the  
628 compounds in countries where legislation was introduced in  
629 between the monitoring points was much lower (from  $n=17$   
630 to  $n=14$  in PL) or increased slightly (from  $n=3$  to  $n=4$  in  
631 CZ).

632 When one looks at the trends per compound, the only  
633 country where a substance disappeared from the national-  
634 level searches after it was banned was NL (in the case of 25I-  
635 NBOMe). In this respect, NL stands out of the sample,  
636 similarly to the way it does with policies and their outcomes  
637 in other drugs (MacCoun & Reuter, 1997; Reinerman, Cohen,  
638 & Kaal, 2004).

639 In fact, 25I-NMOBe and AH-7921 were newly offered on  
640 the FR online market in XII/2015 despite the fact that they  
641 had already been banned in 2013, prior to the monitoring  
642 beginning. The number of e-shops selling MDPV increased  
643 between III/2014 and XII/2015 for CZ and PL, where MDPV  
644 was already banned in 2011. Remarkably, in PL, one  
645 compound appeared in online searches only after it was  
646 banned (AH-7921). From this we can conclude that in some  
647 countries, the compounds were made available online despite  
648 being made illegal.

649 The results here give reason to believe that the shift to non-  
650 European IP addresses (from the EU countries to the US and  
651 non-EU countries), although it has no influence on availabil-  
652 ity or accessibility to users, can be seen as an outcome of the  
653 broader control measures on the European or international  
654 level. In this respect, it is noteworthy that 116 NPS were put  
655 under control in China, a likely producing country of NPS  
656 (Van Buskirk et al., 2016), on October 1st, 2015. It is  
657 plausible to assume that this has contributed to an overall  
658 decrease in the number of e-shops offering the four  
659 compounds in this analysis, and possibly to a greater extent  
660 than the individual bans in destination countries.

## 661 Displacement to other markets and replacement of 662 compounds

663 In order to assess the full impact of regulation on the  
664 availability of the four compounds, further inquiry is needed  
665 in terms of finding out whether the substances that were less  
666 widely marketed online increasingly appeared on the  
667 “darknet” after they were controlled or on other street-  
668 level illegal markets in Europe, referred to as “displacement  
669 effect” (Aldridge & Decary-Hetu, 2016) and whether substi-  
670 tutes for them emerged (“replacement effect”). Evidence on  
671 “displacement” and “replacement” can offer insights into  
672 unintended consequences of NPS control laws, described  
673 previously in relation to drug prohibition (Benson, 2009;  
674 MacCoun, 1993; Thornton, 2007).

675 When it comes to the “displacement” of the four  
676 substances on the darknet, an assessment made by the  
677 Cyprus National Focal Point suggests that only two sub-  
678 stances (25I-NBOMe and MXE) were sold in the period  
679 between June and October 2015, the former to a greater extent  
680 than the latter (EMCDDA, 2015b); the sale of 25I-NBOMe on  
681 the darknet had already been reported in 2013 (Caldicott,  
682 Bright, & Barratt, 2013). Both 25I-NBOMe and MXE, at the  
683 same time, happened to experience a large decrease in the  
684 number of outlets selling them on the surface web (see Table  
685 3), and 25I-NBOMe ceased to be sold by NL e-shops after the  
686 ban. MDPV, however, was not found in darknet market places  
687 at all (it had been banned in most countries prior to the first  
688 monitoring point, and the number of shops offering it had  
689 decreased almost threefold by the second point). This suggests  
690 that some compounds continued to be sold on the darknet  
691 after the ban and others never appeared there.

692 MDPV was largely seen on street markets and among  
693 injecting drug users in Europe in 2010 and 2011, prior to  
694 several country-level bans, and has somehow persisted since  
695 (EMCDDA, 2015a; Rácz et al., 2015). There is insufficient  
696 evidence to reach a clear conclusion on the occurrence of  
697 MDPV on street markets within the I-TREND project partner  
698 countries. In the Netherlands, MDPV has been a topic of  
699 discussion among potential drug users in drug fora since at  
700 least 2007 (DHPForum.nl, date of reference June 16, 2016)  
701 and was first handed in for chemical analysis at the Dutch  
702 Drugs Information and Monitoring System (DIMS) in 2010,  
703 about five years before it was banned. However, some level of  
704 increased user interest was found in the Czech Republic  
705 during 2014, when MDPV was discussed among the partici-  
706 pants in Czech online fora for the first time despite the fact  
707 that it had been prohibited in 2011.

708 With respect to the “replacement effect”, i.e. the extent to  
709 which alternative new substances to these four NPS are  
710 emerging (EMCDDA, 2009), previous analysis of new  
711 synthetic cannabinoid mixtures demonstrated that the com-  
712 pounds were exchanged as a response to legislative changes  
713 (Dresen et al., 2010; Kikura-Hanajiri, Uchiyama, Kawamura,  
714 & Goda, 2014). Also, quantitative analysis of online fora has  
715 provided insights into a decrease in discussions of particular  
716 compounds on online boards after they were banned, and an  
717 increase in the discussion of other compounds, but such  
718 developments are difficult to attribute to the effect of a  
719 compound being banned (Ledberg, 2015). Notwithstanding  
720

721 that the compounds in our analysis have themselves been  
722 offered as “replacement” at some point (Corazza et al.,  
723 2012a,b).

724 Several indicators of “replacement” could be found in  
725 both the qualitative and quantitative data collected through  
726 the I-TREND project. For instance, in the Czech Republic, the  
727 participants in online discussion fora hypothesised that  
728 several compounds could be a good substitute, given that  
729 MXE was banned (Drapalova & Belackova, 2016). Among  
730 the compounds which appeared in discussions on inter-  
731 national fora as possible substitutes were MXP, MXM, 3-  
732 MeO-PCP, 4-MeO PCP, 3-MeO-PCE, Ephedrine and  
733 Diphenidine.

734 When it comes to the “replacement” effect on the supply  
735 side of the market, several of the e-shops that were active in  
736 December 2015 were offering an “analogue to MXE” being  
737 MXP ( $n=4$ ), others were offering “replacement for MXE”  
738 being deschloroketamine ( $n=2$ ), and some were offering  
739 either of the two without any reference to MXE ( $n=4$ ). Out  
740 of these e-shops that were offering either of the two  
741 “analogues”, several were offering MXE at the same time  
742 ( $n=4$ ), while others did not have MXE in stock or were not  
743 listing it at all at that time ( $n=6$ ).

744 This together suggests that while new substances are  
745 emerging on the market, attributing them to a particular  
746 compound or even its ban is a complex issue. In order to  
747 measure the full consequences of compound control, more  
748 conceptualisation and firm criteria for “replacement” need to  
749 be set up and a comprehensive research design would be  
750 needed to capture this effect.

#### 751 Limitations and methodological considerations

752 One of the limitations of attributing an effect to country-level  
753 bans is the lack of measures that could indicate the level of  
754 control enforcement in time and across the countries, which  
755 has been a limitation of many studies in the arena of drug  
756 policy (Ritter, Livingston, Chalmers, Berends, & Reuter,  
757 2016).

758 Another limitation on assessing the effectiveness of a ban  
759 on certain compounds in terms of limiting their online  
760 availability is that the e-shops in this study cannot be seen as  
761 specifically “Czech”, “Polish” or “French”, as a simple  
762 translation of the e-shop or some of its pages would make it  
763 appear in the search for a different country (or language).  
764 Also, the cross-border nature of NPS e-shops can best be  
765 demonstrated through UK searches, as many NPS users in the  
766 EU use English to make their online purchases despite it is not  
767 their native language (Drapalova & Belackova, 2016). Thus,  
768 the UK search outcomes might as well be sensitive to EU-  
769 level or international legislative developments or to individual  
770 bans in other EU countries than to the legislation in the UK.

771 A number of methodological decisions have been made  
772 around the indicators used in this analysis, and these have to  
773 be considered in future research. The number of e-shops (an  
774 indicator of “accessibility”) will depend on whether the  
775 researchers chose to consider all the search outcomes  
776 achieved using selected key words or whether they exclude  
777 some of them if they are not properly translated. Additionally,  
778 numerous e-shops chose to be displayed under a multitude of

781 URLs, in order to maximise their online visibility; the number  
782 of unique shops (presented in this paper) could be as low as  
783 67% of the total search outcomes; see (Martinez et al., 2016).  
784 Thus, the figures will differ according to whether only unique  
785 e-shops are presented or not. Additionally, when one is  
786 searching for e-shops offering particular compounds, the  
787 actual availability of these compounds should be verified  
788 directly on the e-shop web pages, alongside country-level  
789 shipping restrictions on these compounds.

790 All the steps described above were taken in this analysis,  
791 thus reducing the number of search outcomes. The rather low  
792 number of outcomes does not permit the analysis of e.g. the  
793 statistical significance of the observed trends. This “small  
794 sample” limitation is most apparent with regard to the “low-  
795 profile” compounds (25I-NBOMe, AH-7921), which yielded  
796 probably the most striking patterns of online availability,  
797 accessibility and popularity (in terms of having newly  
798 appeared in countries that had banned them or of being  
799 relatively highly ranked by Alexa).

800 Additionally, a number of technical features of online  
801 searches administered through conventional search engines  
802 (e.g. Google.com) were beyond our control. Thus, the  
803 findings have to be understood within the scope of their  
804 volatile nature.

805 Finally, it was beyond the scope of this study to test  
806 whether the product would actually arrive when ordered, or  
807 whether it would contain the compound which was adver-  
808 tised. Some of the vendors could, in fact, be a scam, and  
809 substances which appeared to be available to purchase might  
810 never reach their buyers.

#### 811 Conclusions

812 This analysis suggests that when it comes to the online market  
813 with NPS, the power of policies introducing national-level  
814 control laws is limited. In some countries, the online  
815 “availability” of selected NPS increased after control meas-  
816 ures were introduced (where the compounds were newly  
817 offered) and mostly, fluctuations in availability and accessi-  
818 bility of the e-shops with NPS in this research did not seem to  
819 be linked to national-level bans. It is possible that the  
820 national-level control laws within the EU have shifted some e-  
821 shops’ IP addresses away from the EU – which matters little  
822 to the consumers. A decrease in “accessibility” of the four  
823 compounds, as measured by the number of e-shops offering  
824 them, didn’t correspond to the national-level bans, but could  
825 have been influenced by other control laws, such as those in  
826 producing countries. Lastly, e-shops seemed to counterbal-  
827 ance their low or decreased numbers by their rather high  
828 “popularity”; this suggests that even if the number of e-shops  
829 decreases, those that remain are likely to be visited more by  
830 the consumers.

831 This analysis has pointed to the range of indicators that are  
832 feasible and meaningful for the purpose of RA procedures and  
833 in evaluating the impact of control measures (accessibility,  
834 availability and popularity). Semi-automated monitoring tools  
835 not only offer the possibility of collecting all these efficiently,  
836 but also allow timely information to be collected. It is,  
837 however, important to triangulate the monitoring of the  
838 surface e-shops with data from other sources. While it is  
839



apparent that some compounds appear on other markets too and that alternative substances to those under control are emerging, it remains a challenge to further conceptualise and measure the “displacement” and “replacement” effects. This would help to go beyond the scope of the present paper in assessing whether and to which extent emergence of new, potentially harmful compounds is associated with control laws as their “unintended effect”.

Assessing the impact of laws controlling the online availability of 25I-NBOMe, AH-7921, MDPV and MXE – outcomes of a semi-automated e-shop monitoring

## Declaration of interest

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