HHS Public Access

Author manuscript

Drug Test Anal. Author manuscript; available in PMC 2021 February 01.

Published in final edited form as:

Drug Test Anal. 2020 February ; 12(2): 191–194. doi:10.1002/dta.2749.

Should NPS be included in workplace drug testing?

Alberto Salomone[1,2], **Joseph J. Palamar**[3], **Marco Vincenti**[1,2]

[1]Dipartimento di Chimica, Università di Torino, Turin, Italy

[2]Centro Regionale Antidoping e di Tossicologia "A. Bertinaria", Orbassano, Turin, Italy

[3]New York University School of Medicine, Department of Population Health, New York, NY, USA

Use of the acronym "NPS" has unquestionably become more common in recent years. Policymakers, medical personnel, toxicologists, law enforcement officials, social workers, and journalists, have gradually become familiar with the phenomenon of the New Psychoactive Substances (NPS). The initial warnings about NPS use and abuse were issued in 2009, and NPS progressively became a global issue, with over 100 countries and regions throughout the world having reported the emergence of NPS. In recent years, the consumption of NPS has proliferated at an unprecedented rate and poses a significant risk to the public health and a challenge to national and international drug policies [1]. The frequent emergence of new NPS on the black market (until recently) prevented affordable and timely analytical procedures; consequently, potential laws forbidding possession or use in specific contexts (e.g., driving) were not enforceable. In practice, NPS have not been routinely screened and they are still commonly used without legal consequences. Only recently, laboratories have begun to offer screening and confirmation analysis for NPS in the context of workplace drug testing, driving re-licensing, roadside control, and withdrawal programs [2,3]. Still, the application of these analytical methods remains somewhat sporadic and confined to highly specialized laboratories. Furthermore, these sophisticated analyses involve considerable costs, rarely affordable by clients.

A series of new factors may modify this unfavorable analytical situation for NPS screening in forthcoming years, especially in the context of *workplace drug testing* (WDT). First, several countries have banned entire classes of NPS, irrespective of their specific chemical structure [4]. Secondly, among the large variety of NPS, some are proven to have "desirable" pharmacological effects, while others are more likely to disappear because of their unpleasant side-effects [5-7]. Third, pharmacokinetic studies progressively provide information about the various NPS metabolic pathways and the target analytes to look for, in different biological matrices. Lastly, and most importantly, recent technological developments may make screening analysis for NPS more affordable and effective. For example, the modern UHPLC-MS/MS instrumentation allows the detection of large NPS panels within a single analytical run, covering different classes of target analytes due to their compatibility with unspecific (i.e., general) sample extraction procedures [8-10]. Further

prospect gaining increasing interest among forensic toxicologists is anticipated by the development of non-targeted approaches allowed by modern UHPLC-HRMS instrumentation [11-13]. Screening non-targeted analysis for NPS is also taking advantage from the significant advancement of other new technologies, such as the assays for the detection of synthetic cannabinoid receptor agonists (SCRAs) based on interactions of the compounds with CB1 and CB2 receptors [14]. The practical consequence of all these new elements is that more stable and revisable wide-ranging analytical procedures are progressively developed and made available to detect the intake of NPS and to screen biological samples for the presence of NPS without knowing their exact chemical structure. Eventually, the occurrence of false negative results is likely to decrease considerably in forthcoming years. More importantly, the cost of analysis will decrease, which is a particularly important factor in the context of WDT.

Testing in the workplace is a complex topic as it is not often directly regulated by supranational or national law. Only few countries report legislation that clearly and specifically address the issue of drug testing in the workplace. Among all countries, divergent approaches are evident, regarding the timing of testing, the location, the frequency, the subjects, and the type of specimen(s) to be tested, the panel(s) of drugs, and the guarantees concerning individual privacy and legal consequences. Random and pre-employment testing are the most common strategies adopted in WDT, generally based on urine or oral fluid analysis. While the latter would simply require a comprehensive screening of NPS parent drugs, the former is more complex as it requires knowledge and inclusion of several metabolites. It is certainly challenging to identify which legislative approach each government should adopt. Generic legislations have aimed to control both individual NPS and other have aimed to ban any group of substances with structural similarities [15,16]. Unfortunately, WDT is often neglected in many countries where a specific legislation has not been enacted. Italy is a rare case where drug tests (although not for NPS) are mandatory for certain jobs entailing safety risks to third parties, while on the other hand are prohibited under different conditions. In other European countries, employers and companies are allowed to activate a WDT program under specific circumstances (e.g., if stated in the contract) or at discretion of an occupational doctor.

In WDT, the most prevalent classes of NPS should be tested (e.g., synthetic cathinones, synthetic cannabinoids, fentanyl and its analogs), selecting the most common molecules within each class. However, analytical laboratories must constantly update their methods and keep pace with the introduction of new compounds into the black market. Nevertheless, several international alert and warning systems, as well scientific reports and publications, can certainly assist this demanding process. While the exclusion of NPS from WDT certainly appears to influence their diffusion, on the other hand, we believe that new and general directives for NPS testing are needed to prevent their use and ensure health and safety of workers. Nevertheless, these directives should respect the EU legislation on privacy and exclude unjustified intrusion into the employees' lifestyle. In this perspective, a preliminary step to foster NPS testing in the workplace context was attempted by the European Workplace Drug Testing Society. In hair-testing guidelines published in 2015, it was recommended that "WDT protocols should consider this investigation when the laboratory is offering screening and confirmation for NPS" [17]. If implemented, workplace

NPS testing would likely enjoy the dual benefit of the deterrent effect on the workforce and the phenomenon monitoring at various times and in different countries, eventually supporting the employee and providing pathways to treatment. Furthermore, an overall assessment of NPS diffusion and trends would become possible, allowing clear knowledge of their consumption within specific populations and the potential connection between their intake and, for example, occupational accidents.

Two possible scenarios are likely to account for the intake of NPS by individuals, and specifically those involved in regular (urine) testing, for instance, within the procedures for driver's license recovery or in WDT. The first scenario suggests that certain classes of drug consumers will substitute traditional cannabis products or "old" stimulants with new synthetic substances, allowing them to avoid judicial sanctions [18,19]. The replacement of "old" drugs with NPS is attractive to some users as long as these new classes of substances are not routinely screened, especially in those countries where possession and use of illegal substances is more severely punished. The second motivation often reported for NPS use is their novelty: new products have become available to the public, often stimulating curiosity to test and compare different effects and sensations.

A different but perhaps equally worrying situation is represented by the unintentional intake of NPS (as adulterants), to whom ecstasy users (for example) are at particularly high risk for unknown exposure. Forensic investigations based either on drug seizures or alternative toxicological approaches (e.g., oral fluid, hair analysis, drug checking services), have shown that tablets sold as "ecstasy" (or more recently, "Molly" in the US) can contain various substances other than MDMA, including a variety of NPS [20-27], which can cause unpredictable and often unknown adverse effects. Nevertheless, the adulteration or replacement of "traditional" drugs with NPS is not limited to ecstasy. In both North America and Europe, novel synthetic opioids (NSO) are often sold as purported heroin (and in some cases also as cocaine) to unsuspecting drug users [28-31]. In particular, fentanyl analogs have been linked to a large and rising number of overdose deaths among opiate and opioid users [32].

Nevertheless, interpretation of a positive finding would need caution, before any sanction is imposed to the tested employee. The risk of false positive results certainly represents a key issue before a decision is taken about the generalized extension of NPS testing. Some laboratories have set the limit of detection as the minimum criterion to establish use of a new drug, but this can only prove the "exposure" to a new substance. This approach has to be considered improper and preliminary, since few studies have explored criteria to differentiate 1) between occasional and regular intake, 2) between occasional intake and passive exposure, or 3) external contamination. Moreover, the mere detection of a drug in urine or hair is not useful in proving the subject as being under the drug's effect nor to assess the worker's inability to carry out his or her job. Aside from the limit of detection, which is also highly dependent on the method's sensitivity, different cut-offs based on a large population of consumers or controlled studies should be proposed. In addition, distinction between recent (i.e., possibly causing impairment at the workplace), chronic (i.e., hinting a possible addiction state), and occasional (i.e., recreational) use should be considered, with respect to both analysis results and their interpretation. In this context, an experienced toxicologist

should evaluate these cases with caution, and the scientific societies should play a fundamental role in addressing future drug laws and policies, suggesting cut-offs, specimens to be tested, and criteria to differentiate between past use, chronic use, or impairment at the workplace.

Inclusion strategies of NPS into WDT have pros and cons that should be carefully considered, and current strategies may require revision and possibly updates in forthcoming years, but it is important to engage in debate about the ultimate objectives of NPS testing and the balance between costs and benefits arising from their screening. The Italian WDT experience for traditional drugs of abuse has shown very low prevalence of positive results, possibly because the mandatory "surprise sample collection" is rarely respected while the short detection window of consumed substances in the urine matrix allows even habitual consumers to keep off from drugs just few days before control [33]. The latter example proves that even adequate analytical procedures turn out to be ineffective if the whole procedure from sample collection to data reporting is not under control. Transposing this concept into NPS testing, it is clear that systematic monitoring of the data arising from an extended WDT program would be highly recommended, together with the assessment of its effectiveness. Examples of direct and indirect parameters useful for a comprehensive evaluation of NPS testing are the reduction rate of workplace accidents and prevalence of detection of NPS use in the workforce. The obtained data would certainly assist the implementation of more general policies of social and health interest, which every government should pursue.

Summarizing, caution is certainly recommended to avoid the indiscriminate criminalization of NPS use [34,35]. Some cases may require careful result interpretation from the occupational doctor, who may also request opinions from clinical and/or forensic toxicologists, or pharmacologists, especially in cases where alleged NPS/NSO are licitly taken. The situation is well-illustrated by several synthetic opioids (e.g., fentanyl and oxycodone), which can be prescribed for clinical purposes and/or misused (e.g., because of an existing state of addiction). Another example of criticism is given by the structure-based legislation: since an extremely wide range of new molecules with similar structures can be synthetized, it is realistic to foresee that, at some point, an overlapping between the urinary metabolites of licit (i.e., medications) and illicit (i.e., unauthorized drugs) substances will occur. In this context, the recent use of medications possibly containing NPS/NSO or their metabolites will have to be disclosed before sample collection and possibly supported by a written prescription. Appropriate confirmation analysis on the collected biological sample will therefore be needed to confirm the exact chemical structure of the taken substance.

Irrespective of the necessary caution, it is increasingly evident that many of the new substances available in recent years may represent a serious threat to employee health and the maintenance of a safe workplace. We believe that prevention of drug use-related occupational accidents must be a prerogative for all governments, and this would be facilitated by an effective and comprehensive testing program. As a safeguard to all subjects involved in the process, efforts have to be addressed to identify and promote best practices for collection, analysis and interpretation of drug tests. Guidelines are already available [17,36-38] and many companies and laboratories performing the WDT worldwide are already complying with them. More is to follow, especially with regard to NPS/NSO, in order to

make everyone, from the employer to the sample collector, increasingly aware of their accountability in a decision with serious consequences.

Acknowledgments

Research from JJP reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number K01DA038800 (PI: Palamar). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. United Nations Office on Drugs and Crime 2017 http://www.unodc.org/wdr2017/en/ats.html, Accessed 27th November 2019
2. Zuba D, Adamowicz P. Analytical Methods Used for Identification and Determination of Synthetic Cathinones and Their Metabolites In: Zawilska J (eds) Synthetic Cathinones. Current Topics in Neurotoxicity, vol 12 2018 Springer
3. Marchei E, Pacifici R, Mannocchi G, Marinelli E, Busardò FP, Pichini S. New synthetic opioids in biological and non-biological matrices: A review of current analytical methods. Trends Anal Chem., 2018;102:1–15
4. New psychoactive substances in Europe: legislation and prosecution — current challenges and solutions, http://www.emcdda.europa.eu/publications/joint-publications/eurojust/nps-legislation-and-prosecution_en, Accessed 27th November 2019
5. Hondebrink L, Zwartsen A, Westerink RHS. Effect fingerprinting of new psychoactive substances (NPS): What can we learn from in vitro data? Pharmacol Ther. 2018;182:193–224 [PubMed: 29097307]
6. Assi S, Gulyamova N, Ibrahim K, Kneller P, Osselton D. Profile, effects, and toxicity of novel psychoactive substances: A systematic review of quantitative studies. Hum Psychopharmacol. 2017;32(3)
7. Gray R, Bressington D, Hughes E, Ivanecka A. A systematic review of the effects of novel psychoactive substances 'legal highs' on people with severe mental illness. J Psychiatr Ment Health Nurs. 2016;23(5):267–81 [PubMed: 27037639]
8. Favretto D, Pascali JP, Tagliaro F. New challenges and innovation in forensic toxicology: focus on the "New Psychoactive Substances". J Chromatogr A. 2013;1287:84–95 [PubMed: 23332303]
9. Couto RAS, Gonçalves LM, Carvalho F, Rodrigues JA, Rodrigues CMP, Quinaz MB. The Analytical Challenge in the Determination of Cathinones, Key-Players in the Worldwide Phenomenon of Novel Psychoactive Substances. Crit Rev Anal Chem. 2018;48(5):372–390 [PubMed: 29437467]
10. Kimble AN, DeCaprio AP. Systematic analysis of novel psychoactive substances. II. Development of a screening/confirmatory LC-QqQ-MS/MS method for 800+ compounds and metabolites in urine. Forensic Chem 2019;16:100189
11. Fu S, Stove C, Elliott S. Editorial: Advances in Analytical Methods for Drugs of Abuse Testing. Frontiers in Chem. 2019;7:1–2
12. Pasin D, Cawley A, Bidny S, Fu S. Current applications of high-resolution mass spectrometry for the analysis of new psychoactive substances: a critical review. Anal Bioanal Chem. 2017;409(25): 5821–5836 [PubMed: 28634759]
13. Klingberg J, Cawley A, Shimmon R, Fu S. Collision-Induced dissociation studies of synthetic opioids for non-targeted analysis. Frontiers in Chem. 2019;7
14. Cannaert A, Franz F, Auwarter V, Stove C. Activity-Based Detection of Consumption of Synthetic Cannabinoids in Authentic Urine Samples Using a Stable Cannabinoid Reporter System. Anal Chem. 2017;89(17):9527–9536 [PubMed: 28771321]
15. Tettey JNA, Crean C, Ifeagwu SC, Raithelhuber M. Emergence, Diversity, and Control of New Psychoactive Substances: A Global Perspective In: Handbook of Experimental Pharmacology. 2018 Springer, Berlin, Heidelberg

16. Bao Y, Meng S, Shi J, Lu L. Control of fentanyl-related substances in China. Lancet Psychiatry. 2019;6(7):e15 [PubMed: 31230685]
17. Salomone A, Tsanaclis L, Agius R, Kintz P, Baumgartner MR. European guidelines for workplace drug and alcohol testing in hair. Drug Test Anal. 2016;8(10):996–1004. [PubMed: 27402378]
18. Perrone D, Helgesen RD, Fischer RG. United States drug prohibition and legal highs: How drug testing may lead cannabis users to Spice. DRUG-EDUC PREV POLIC 2012;20(3):216–224
19. Soussan C, Kjellgren A. The users of Novel Psychoactive Substances: Online survey about their characteristics, attitudes and motivations. Int J Drug Policy. 2016;32:77–84 [PubMed: 27184218]
20. Evans-Brown M, Sedefov R. Responding to New Psychoactive Substances in the European Union: Early Warning, Risk Assessment, and Control Measures. Handb Exp Pharmacol. 2018;252:3–49. [PubMed: 30194542]
21. Krotulski AJ, Mohr ALA, Fogarty MF, Logan BK. The Detection of Novel Stimulants in Oral Fluid from Users Reporting Ecstasy, Molly and MDMA Ingestion. J. Anal Toxicol. 2018;42(8): 544–553 [PubMed: 30371847]
22. Palamar JJ, Salomone A, Vincenti M, Cleland CM. Detection of "bath salts" and other novel psychoactive substances in hair samples of ecstasy/MDMA/"Molly" users. Drug Alcohol Depend. 2016;161:200–5. [PubMed: 26883685]
23. Palamar JJ, Salomone A, Gerace E, Di Corcia D, Vincenti M, Cleland CM. Hair testing to assess both known and unknown use of drugs amongst ecstasy users in the electronic dance music scene. Int J Drug Policy 2017;48:91–98. [PubMed: 28810159]
24. Brunt TM, Nagy C, Bücheli A, et al. Drug testing in Europe: monitoring results of the Trans European Drug Information (TEDI) project. Drug Test. Analysis 2017;9:188–198
25. Oliver CF, Palamar JJ, Salomone A, Simmons SJ, Philogene-Khalid HL, Stokes-McCloskey N, Rawls SM. Synthetic cathinone adulteration of illegal drugs. Psychopharm 2019;236(3):869–879
26. Martins D, Barratt MJ, Pires CV, et al. The detection and prevention of unintentional consumption of DOx and 25x-NBOMe at Portugal's Boom Festival, Hum. Psychopharmacol. Clin. Exp. 2017;32, e2608
27. Gerace E, Seganti F, Luciano C, Lombardo T, Di Corcia D, Teifel H, Vincenti M, Salomone A. On-site identification of psychoactive drugs by portable Raman spectroscopy during drug-checking service in electronic music events. Drug Alcohol Rev. 2019;38(1):50–56. [PubMed: 30614092]
28. Ciccarone D Fentanyl in the US heroin supply: A rapidly changing risk environment. Int J Drug Policy. 2017;46:107–111 [PubMed: 28735776]
29. Misailidi N, Papoutsis I, Nikolaou P, Dona A, Spiliopoulou C, Athanaselis S. Fentanyls continue to replace heroin in the drug arena: the cases of ocfentanil and carfentanil. Forensic Toxicol. 2018;36(1):12–32 [PubMed: 29367860]
30. Salomone A, Palamar JJ, Bigiarini R, Gerace E, Di Corcia D, Vincenti M. Detection of fentanyl analogs and synthetic opioids in real hair samples. J. Anal Toxicol. 2018, doi 10.1093/jat/bky093
31. Palamar JJ, Salomone A, Bigiarini R, Vincenti M, Acosta P, Tofighi B. Testing hair for fentanyl exposure: a method to inform harm reduction behavior among individuals who use heroin. Am J Drug Alcohol Abuse. 2019;45(1):90–96 [PubMed: 30601034]
32. Gerace E, Salomone A, Vincenti M. Analytical approaches in fatal intoxication cases involving new synthetic opioids. Curr Pharm Biotechnol. 2018; doi: 10.2174/1389201019666180405162734
33. Rosso GL, Montomoli C, Morini L, Candura SM. Seven years of workplace drug testing in Italy: A systematic review and meta-analysis. Drug Test Anal. 2017;9(6):844–852. [PubMed: 28304140]
34. Potter GR, Chatwin C. Not particularly special: critiquing 'NPS' as a category of drugs. Drugs Educ Prev Policy, 2018;25(4):329–336
35. Barratt M, Seear K, Lancaster K. A critical examination of the definition of 'psychoactive effect' in Australian drug legislation. Int J Drug Policy 2017;40:16–25. [PubMed: 27884504]
36. Taskinen S, Beck O, Bosch T, Brcak M, Carmichael D, Fucci N, George C, Piper M, Salomone A, Schielen W, Steinmeyer S, Weinmann W. European guidelines for workplace drug testing in urine. Drug Test Anal. 2017;9(6):853–865. [PubMed: 28267298]
37. Taskinen S, Beck O, Bosch T, Brcak M, Carmichael D, Fucci N, George C, Piper M, Salomone A, Schielen W, Steinmeyer S, Weinmann W. European guidelines for workplace drug testing in oral fluid. Drug Test Anal. 2018;10(3):402–415. [PubMed: 28657673]

38. Oil and gas contractor drug and alcohol testing guidelines, http://www.ipieca.org/media/2812/drug_and_alcohol_testing_guidelines_2016_12_13_lr.pdf Accessed 27th November 2019