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COMMENTARY

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Commentary on Bade *et al.*: Threat of nitazenes and other potent synthetic opioids—Is Europe prepared? Time to respond and to learn

Preparedness to respond to increased access and use of new and potent synthetic opioids requires developing action-oriented monitoring systems capable of combining multiple data sources, performing analytical triangulation, and the generation of timely alerts.

Bade *et al.* [1] make an important contribution to the potential use of wastewater analysis for monitoring the presence of nitazenes. They state that this approach may be useful for capturing early signals of the presence of these substances (and potentially other highly potent opioids) on a population level, especially when combined with other data sources and systems. Given the high potency of nitazenes, the low expected use dose, the still small number of regular users in most countries and the dilution of a wastewater treatment plant due to the size of the catchment area, the presence of nitazenes may be challenging to detect if relying primarily on wastewater analysis.

Over reliance on one data source increases the risk of missing local outbreaks of poisonings [1, 2]. Reports from Germany, France, Ireland and the Netherlands illustrate that the detection of new synthetic opioids has been confirmed using triangulation of multiple data sets [3–6]. The European Union Early Warning System (EWS) on new psychoactive substances (NPS) is Europe's flagship mechanism for detecting NPS, such as nitazenes, and it draws on multiple information sources. Alongside the EWS, the European Union Drugs Agency (EUDA) monitoring framework provides a robust analysis by analysing seizure data, data from drug-related death mortality registries as well as the European web survey on drugs (EWSD), along with city level sources, such as wastewater analysis, analysis of syringe residues, samples collected by drug-checking services and acute toxicity presentations to hospitals [7].

Since 2019, the EU EWS has reported the emergence of 23 different nitazenes detected in at least 21 European countries [8, 9]. The quantities of nitazenes seized in 2023 tripled compared to 2022, and the number of tablets seized containing nitazenes doubled in 2024 compared to 2023 [8]. These include nitazenes found in counterfeit medicines. Syringe residue analysis identified nitazenes in Tallinn, Estonia (34% in 2023 and 35% in 2024), in Riga, Latvia (74% and 33%); and in Klaipeda, Lithuania (4% in 2024). The type of nitazenes found were: isotonitazene, metonitazene, protonitazene, N-Desethyletonitazene, protonitazepyne, etonitazepyne. Most syringes contained at least one other drug, a signal of potentially common polysubstance use. In 2023 and 2024, drug-checking services sporadically detected nitazenes in samples brought on-line and given by the buyers to the services for content confirmation. In the 2024 European web survey on drugs, participants in Germany, Austria, Latvia, Sweden and Spain reported having used nitazenes in the past 12 months [10].

The European Drug Emergencies Network hospital in Riga, Latvia, reported 21 presentations in 2023 and 2024. The median age was 37, 17 of 21 were males. The most commonly identified nitazenes were etonitazene, metonitazene and etodesnitazene. The most common substances reported alongside nitazenes were benzodiazepines, cannabis and cocaine. Hospitals in Munich, Germany (in 2021), and Utrecht, the Netherlands (in 2024), reported one case each of nitazenes in acute drug toxicity presentations.

Nitazenes drove the increase in drug-related deaths in Latvia and Estonia in 2022 to 2023 [11], and were implicated in 101 of 154 (66%) of the cases in Latvia in 2023, decreasing to 33 of 76 (43%) in 2024. In Estonia, although numbers peaked in 2023, (61 of 119 cases, 52%), nitazenes were still implicated in 42 of 100 cases (42%) in 2024. Norway (June 2023–August 2024) and Sweden (January 2023–September 2024) reported, respectively, 34 and 30 deaths associated with nitazenes [8].

These examples of different methods employed to detect nitazene use illustrate the value of multi-layered monitoring systems and signal detection tools that combine population and individual level data and that can integrate analysis received directly from people using drugs. Improvement of the toxicology capacity—including more and better *post-mortem*, drug-checking, wastewater analysis and analytical confirmations from forensic and clinical laboratories is crucial to ensure our preparedness for potent—and quickly appearing—new drugs [12]. As highlighted, wastewater and toxicology data need to be triangulated with drug seizure data, information about the availability, purity and prices of drugs from different sources (e.g. bought over the internet or in the streets) [8]. However, a key challenge remains to triangulate these sparse signals, whether from wastewater or other sources and identify ways of transforming them into policy recommendations and evidence-based and innovative actions in Europe and beyond [13–15].

To conclude, timely, granular and actionable information based on a set of key national-level epidemiological indicators, EWS and city-level data collection methods are allowing policy makers to respond rapidly to drug-related problems. Developing integrated approaches is one of the key pillars for preparedness policies, alongside ensuring evidence-based, resilient and agile drug prevention, treatment, and harm reduction services and sustainable funding streams.

KEYWORDS

deaths, European Union, nitazenes, preparedness, synthetic opioids, toxicity

AUTHOR CONTRIBUTIONS

Isabelle Giraudon: Conceptualization; data curation; formal analysis; writing—original draft; writing—review and editing. **Ana Gallegos:** Data curation; validation; writing—review and editing. **Senad Handanagić:** Formal analysis; validation; writing—review and editing. **Jane Mounteney:** Conceptualization; formal analysis; validation; writing—review and editing.

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DECLARATION OF INTERESTS

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Isabelle Giraudon
Ana Gallegos
Senad Handanagić
Jane Mounteney

Substance Use, Harms and Responses Unit, European Union Drugs Agency (EUDA), Lisbon, Portugal

Correspondence
Isabelle Giraudon, Substance use, harms and responses unit, European Union Drugs Agency (EUDA), Lisbon, Portugal.
Email: isabelle.giraudon@euda.europa.eu

ORCID

Isabelle Giraudon https://orcid.org/0000-0003-4365-1404
Senad Handanagić https://orcid.org/0000-0001-8212-1153

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