COLOMBO PLAN
HEALTH ALERT

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The Center for Forensic Science Research & Education

Public health and public safety officials worldwide should be aware of an emerging threat of the Benzimidazol-2-one (Orphine) class of opioids, which are causing increased mortality (death) and morbidity.

With potencies equal to or greater than the fentanyl class of opioids, these drugs can interact with other opioids to increase the risk of respiratory depression and death.

FEBRUARY 2026

Emerging Global Synthetic Opioid Threats:

Benzimidazol-2-ones – The Orphines

Following the recent core structure scheduling by China of the nitazenes (benzimidazoles), markets have seen a decline in these potent opioids in late 2025, and their replacement by a new class of synthetic opioids, the benzimidazol-2-ones, also known as the **"Orphines".** This alert describes the emergence of these potent opioids, and spotlights their detection in US and international drug markets.

- Brorphine was the first highly potent synthetic opioid of the **benzimidazol-2-one ("orphine") class**, detected in **European drug markets around 2019, and in the US in 2020**. It likely originated from **clandestine synthesis in China**, emerging as a fentanyl analog-replacement or opioid adulterant with potency similar to or slightly less than fentanyl.

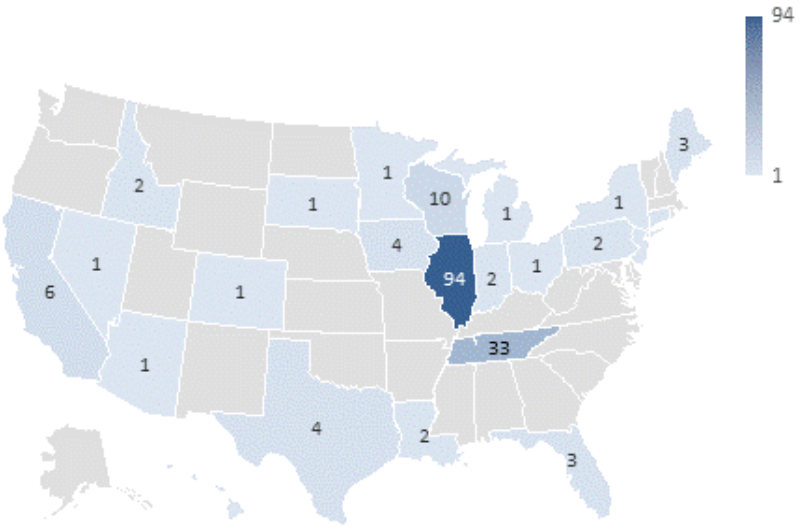
- Following initial alerts, brorphine was rapidly scheduled or emergency-controlled in multiple jurisdictions (e.g., EU, UK, US, Canada). This regulatory response appears to have accelerated structural diversification, with multiple halogenated and cyclized analogs appearing about four years after brorphine controls were put in place.

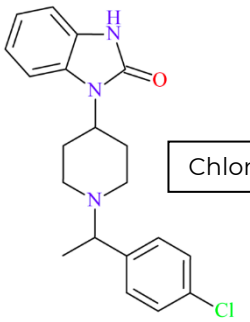
- As analytical reference standards have become more widely available, orphine analogs detected now include Chlorphine, N-Propionitrile Chlorphine (Cychlorphine), 5,6-Dichloro Desmethylchlorphine (SR-17018), Spirochlorphine (R-6890), Spirobrorphine and 5,6-Dicholoro Brorphine (SR-14968), various members of which have been reported in the UK, Europe, US, and Canada.

- Through collaboration with its partner laboratory NMS Labs, the Colombo Plan, the CFSRE and its NPS Discovery Program are working to develop methods for detecting and quantifying these new drugs, and tools to enable automated retrospective datamining of postmortem toxicology data to allow their identification as part of CFSRE's drug early warning system.

- Early data from this datamining process, obtained by scraping analytical mass spectrometric datafiles, have identified the following numbers of orphine analog cases between 2024 and 2025: 5,6-Dichloro Desmethylchlorphine (31 cases), Brorphine (81 cases); Chlorphine (8 cases); N-Propionitrile Chlorphine (84 cases); and Spirochlorphine (20 cases).

- The geographic spread of the presumptive positive cases is shown below:





Chlorophine

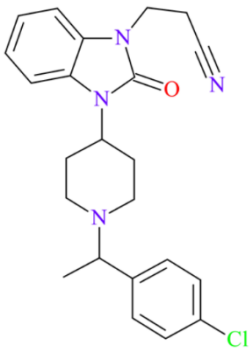
Polydrug Use and Adulteration

- The NMS Labs toxicology cases indicated that the most common adulterants and co-positivity included fentanyl, as well as other opioids and CNS depressants including nitazene analogs (e.g., metonitazene, N-pyrrolidino protonitazene, Isotonitazene, protonitazene, N-pyrrolidino metonitazene, and N-desethyl metonitazene) and illicit designer benzodiazepines (e.g., bromazolam).

- There were considerable geographic differences, with nitazene co-positivity being most common in Illinois. Methamphetamine, amphetamine, and diphenhydramine were most frequently found in Illinois, while fentanyl co-positivity was most frequently seen in Tennessee. Note that these positivity distributions reflect only jurisdictions in which NMS Labs performs testing.

Source of Synthetic Opioids:

- Following China's class-wide scheduling of fentanyl compounds in May 2019, the nitazene class of opioids originating from China, started appearing worldwide. Likewise, following China's core-structure scheduling of nitazene compounds in July 2025, the orphine class of opioids, most likely originating from China, are now appearing worldwide. In addition to already established drug classes including fentanyl, nitazene and orphine derivatives, multiple potential future classes of synthetic opioids that warrant monitoring include benzamides, acetamides, piperidines/piperazines, and cinnamylpiperazines.

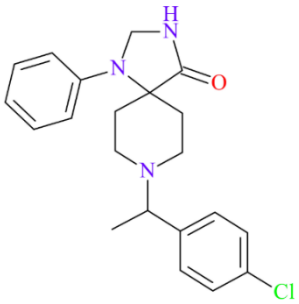


N-Propionitrile Chlorophine (Cychlorphine)

Laboratory Analysis

- While standard reference materials for many of these analogs are now commercially available and can be added to laboratory testing scopes, very few forensic toxicology laboratories currently have comprehensive testing for orphine analogs within their scopes. In cases where the presence of an opioid is suggested based on history, scene and circumstances, , but for which routine toxicology testing is negative, orphine class opioids should be considered. Please contact NPS Discovery for assistance with testing in these cases (supported by the National Institute of Justice, DOJ).

- Note that opioid and fentanyl immunoassays will not cross-react with orphine class compounds, and field test strips often used in harm reduction programs will not detect these compounds either.



Spirochlorophine (R-6890)

- Based on preliminary data for a limited number of these drugs, toxicologically significant concentrations may be in the range of <1ng/mL to 10ng/mL and may be missed during routine screening. Comprehensive interpretive data on typical postmortem concentrations are currently lacking.

- As discussed above, the orphines are frequently present in toxicology cases or in seized drug samples, along with other opioids or sedating drugs.

First Responders and Emergency Room Response

- Responses are expected to be common to other mu-opioid agonists and to produce the classic triad of opioid effects:
  - ***CNS Depression***: lethargy, stupor and coma
  - **Respiratory Depression:** Slow respiratory rate (often **<8–10/min**), with shallow breathing.
  - **Miosis** (pinpoint pupils): typically, bilateral and symmetric
- ***Treatment should be supportive:*** Treat the airway and breathing first, followed by reversal with cautious administration of an opioid antagonist (e.g. naloxone), being careful not to precipitate acute withdrawal.

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