European Monitoring Centre
for Drugs and Drug Addiction

GUIDANCE NOTE 7

Substances of high concern

EMCDDA operating guidelines for the European Union Early Warning System on new psychoactive substances

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1. Purpose

The purpose of this document is to provide a list of substances of high concern monitored by the EMCDDA and the rationale for reporting events involving the identification of such substances. This is in order to ensure a systematic, uniform, reproducible, and, transparent approach is used throughout.

What is a substance of high concern?

A substance of high concern is any substance that is not a new psychoactive substance or controlled drug but that is toxic or otherwise hazardous and poses a high risk of acute or chronic poisoning or any other type of serious adverse event. Typically, such substances are capable of causing outbreaks of mass poisonings and thus identifications linked to the NPS market or controlled drug market are classed as events of potential high impact on public health.

The identification of a substance of high concern is subject to expedited reporting by the Reitox National Focal Points when:

- It is identified with or sold as a new psychoactive substance; or,
- it is identified with or sold as controlled drug; or
- there is reasonable probability that it is linked in some way to the NPS market or the controlled drug market.
- It is identified in biological sample taken from a serious adverse event and there is reasonable probability that exposure to the substance of high concern was linked in some way to the NPS market or controlled drug market. Note where it is known that the substance has been used therapeutically in the course of medical treatment (e.g. atropine), the identification is excluded from reporting.

→ If in doubt, report it. You can contact us at: ews@emcdda.europa.eu

The Reitox National Focal Points should submit reports involving substances of high concern using the relevant EMCDDA reporting tools and clearly highlight the relevant information.

Substances are added to the list by the EMCDDA based on reports of identifications involving serious adverse events reported either by the Member States or from any other information at the disposal of the EMCDDA (such as the scientific and medical literature).

Member States should report any additional substances that they judge to be a substance of high concern along with a brief rationale to the EMCDDA for consideration for inclusion on the list.

The guidance provided in this document will not fit every possible situation perfectly, and may need to be adapted in order to effectively respond to a specific event or situation. In such cases, the Reitox national focal points should contact the EMCDDA for advice as soon as possible.

→ You can contact us at: ews@emcdda.europa.eu

2. Scope

This Guidance Note applies to the EMCDDA and the Reitox national focal points.

3. Changes since last revision

- 4,4'-Methylenedianiline added to the list of substances of high concern

4. Responsibilities

It is the responsibility of the EMCDDA and the Reitox National focal points to ensure that this Guidance Note is adhered to.

5. Documents needed for this Guidance Note:

- EMCDDA operating guidelines for the European Union Early Warning System on new psychoactive substances
- Guidance Note 2: Types of information that should be reported by the Member States on a new psychoactive substance
- Guidance Note 3: Events of potential high impact on public health
- Guidance Note 4: Outbreaks

6. Related documents

- Regulation (EC) No 1920/2006 (as amended). http://data.europa.eu/eli/reg/2006/1920/2018-11-23
- Council Framework Decision 2004/757/JHA (as amended). http://data.europa.eu/eli/dec_framw/2004/757/2017-11-22

7. Terminology and definitions

- Guidance Note 1: Terminology and definitions

8. List of substances of high concern

List current as of 1 January 2022

- 4,4'-Methylenedianiline (MDA)
- Atropine
- Brodifacoum
- Bromadiolone
- Clenbuterol
- Difenacoum
- Glyburide (glibenclamide)
- Haloperidol
- Lead
- Scopolamine
- Strychnine
- Vitamin E acetate (when intended for inhalation/smoking, such as in an e-liquid or other dosage form)

9. Additional information

Below are some references related identifications of substances of high concern involving serious adverse events related to the NPS market and drug market.

4,4'-Methylenedianiline

HighAlert. Toxic chemical sold as MDMA in Auckland. 06 November 2020. https://highalert.org.nz/alerts-and-notifications/toxic-chemical-sold-as-mdma-in-auckland/

Tillmann HL, et al. Accidental intoxication with methylene dianiline p,p'-diaminodiphenylmethane: acute liver damage after presumed ecstasy consumption. J Toxicol Clin Toxicol. 1997;35(1):35-40. https://doi.org/10.3109/15563659709001163

Atropine

Boermans PA, et al. Quantification by HPLC-MS/MS of atropine in human serum and clinical presentation of six mild-to-moderate intoxicated atropine-adulterated-cocaine users. Ther Drug Monit. 2006;28(3):295-8. https://doi.org/10.1097/01.ftd.0000198537.41835.71

Weiner AL, et al. Anticholinergic poisoning with adulterated intranasal cocaine. Am J Emerg Med. 1998;16(5):517-20. https://doi.org/10.1016/S0735-6757(98)90007-9

Brodifacoum

CDC. Outbreak of life-threatening coagulopathy associated with synthetic cannabinoids use — Multiple States, United States, 2018. CDCHAN-00410. 25 May 2018. https://emergency.cdc.gov/han/han00410.asp

Devgun JM, et al. An outbreak of severe coagulopathy from synthetic cannabinoids tainted with long-acting anticoagulant rodenticides. Clin Toxicol (Phila). 2019. https://doi.org/10.1080/15563650.2019.1690149

Navon L, et al. The public health response to a large poisoning outbreak involving an illicit substance: synthetic cannabinoids contaminated with a long-acting anticoagulant rodenticide, Illinois, March-July, 2018. J Public Health Manag Pract. 2019. https://doi.org/10.1097/PHH.0000000000001002

Tole M, et al. Adherence to long-term follow-up of patients with life-threatening, inhaled synthetic cannabinoids-associated coagulopathy in Chicago. https://doi.org/10.1007/s00408-019-00227-2

Bromadiolone

Devgun JM, et al. An outbreak of severe coagulopathy from synthetic cannabinoids tainted with long-acting anticoagulant rodenticides. Clin Toxicol (Phila). 2019. https://doi.org/10.1080/15563650.2019.1690149

Clenbuterol

CDC. Atypical reactions associated with heroin use--five states, January-April 2005. MMWR Morb Mortal Wkly Rep. 2005 Aug 19;54(32):793-6. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5432a1.htm

Hoffman RS, et al. A descriptive study of an outbreak of clenbuterol-containing heroin. Ann Emerg Med. 2008;52(5):548-53. https://doi.10.1016/j.annemergmed.2008.04.026

Wingert WE, et al. Detection of clenbuterol in heroin users in twelve postmortem cases at the Philadelphia medical examiner's office. J Anal Toxicol. 2008 Sep;32(7):522-8. https://doi.org/10.1093/jat/32.7.522

Hieger MA, et al. A case series of clenbuterol toxicity caused by adulterated heroin. J Emerg Med. 2016;51(3):259-61. https://doi.org/10.1016/j.jemermed.2016.05.047

Gleason B, et al. Collaborative public health investigation of clenbuterol-adulterated heroin outbreak-Richmond, Virginia, March-April 2015. J Public Health Manag Pract. 2017;23(2):e8-e11. https://doi.org/10.1097/PHH.0000000000000419

Difenacoum

Devgun JM, et al. An outbreak of severe coagulopathy from synthetic cannabinoids tainted with long-acting anticoagulant rodenticides. Clin Toxicol (Phila). 2019. https://doi.org/10.1080/15563650.2019.1690149

Glyburide

Chin RL. Oral hypoglycemics sold as Valium on the streets: a case report. Ann Emerg Med. 2004;44(5):552. https://doi.org/10.1016/j.annemergmed.2004.05.026

Lung DD, et al. Confirmed glyburide poisoning from ingestion of "street Valium". J Emerg Med. 2012;43(2):276-8. https://doi.org/10.1016/j.jemermed.2011.06.019

Haloperidol

Peyraud N, et al. An epidemic of dystonic reactions in central Africa. Lancet. 2017;5(2):PE137-8. https://doi.org/10.1016/S2214-109X(16)30287-X

Fake diazepam tablets that did not contain diazepam but contained haloperidol (anti-psychotic) caused an outbreak of mass poisoning involving 930 cases of dystonia (muscles contract involuntarily, causing

repetitive or twisting movements) — Ituri, Democratic Republic of Congo, 2014–2015. Analytical confirmation from 9 urine samples from patients. Tablets in circulation were analysed and found to contain 10–20 mg of haloperidol per tablet. Tablets were imprinted with the letters 'AGOG' and containers were labelled as diazepam.

See also:

WHO. Medical product alert no. 4/2015. Adverse reactions caused by falsified diazepam in Central Africa. 2 July 2015. https://www.who.int/medicines/publications/drugalerts/Alert4_2015DiazepamEN.pdf

Swoboda H, et al. Misrepresented haloperidol as a cause of dystonia: A case series. Clin Tox (Philadelphia). 2016;54(8):695.

Mis-selling of haloperidol as Klonopin (clonazepam) or Valium (diazepam) caused an outbreak involving 7 cases of dystonia — Illinois, United States, No date. No analytical confirmation. Visual confirmation from 1 tablet (MYLAN 327; haloperidol 5 mg) provided by a patient.

Lead

Ghane T, et al. Lead poisoning outbreak among opium users in the Islamic Republic of Iran, 2016-2017. Bull World Health Organ. 2018;96(3):165-72. https://doi.org/10.2471/BLT.17.196287

Soltaninejad K, et al. Lead poisoning in opium abuser in Iran: A systematic review. Int J Prev Med. 2018 Jan 5;9:3. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29416839/

Scopolamine

CDC. Scopolamine poisoning among heroin users--New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996. MMWR Morb Mortal Wkly Rep. 1996 Jun 7;45(22):457-60. http://www.cdc.gov/mmwr/preview/mmwrhtml/00042596.htm

Hamilton RJ, et al. A descriptive study of an epidemic of poisoning caused by heroin adulterated with scopolamine. J Toxicol Clin Toxicol. 2000;38(6):597-608. https://doi.org/10.1081/CLT-100102008

Vallersnes OM, et al. Epidemic of poisoning caused by scopolamine disguised as Rohypnol tablets. Clin Toxicol (Phila). 2009;47(9):889-93. https://doi.org/ 10.3109/15563650903333804.

Strychnine

O'Callaghan WG, et al. Unusual strychnine poisoning and its treatment: report of eight cases. BMJ. 1982;285(6340):478. https://doi.org/10.1136/bmj.285.6340.478

Vitamin E acetate

Blount BC, et al. Evaluation of bronchoalveolar lavage fluid from patients in an outbreak of e-cigarette, or vaping, product use–associated lung injury — 10 States, United States, August–October 2019. MMWR Wkly Rep. 2019. 2019;68(45):1040–1. https:// doi.org/10.15585/mmwr.mm6845e2

FDA. Lung illnesses associated with use of vaping products. Information for the public, FDA actions, and recommendations. 5 December 2019. https://www.fda.gov/news-events/public-health-focus/lung-illnesses-associated-use-vaping-products

10. Changes since last version

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