Emerging marine biotoxins

In this guide

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10. Emerging marine biotoxins were identified by evaluating assessments by other authorities including EFSA, Cefas, Food Safety Authority Ireland (FSAI), French Agency for Food, Environmental and Occupational Health and Safety (ANSES) and the French Research Institute for Exploitation of the Sea (IFREMER). A literature search was also conducted to identify any potential emerging marine biotoxins since the publication of these reports. The marine biotoxin groups identified were brevetoxin (BTX), palytoxin (PITX), tetrodotoxin (TTX), novel azaspiracid (AZA) and DA analogues, PTX, cyanobacterial toxins and toxins within the CI family including spirolide (SPX), gymnodimine (GYM), pteriatoxin (PtTX) and PnTX. PTX (TOX/2023/58) and PnTX (TOX/2023/37) have been discussed separately and have not been included in this statement.

11. For the majority of the biotoxins identified limited information or data was available on their toxicology, any human case reports or their occurrence in UK and/or EU waters.

12. Animal toxicological data and where available human case reports have identified five of the emerging biotoxins as neurotoxins, i.e. BTX, TTX, PITX, SPX and GYM. Data from the literature suggested the BTX, TTX and PITX groups interfere with the sodium/potassium voltage gated ion channels resulting in the depolarisation of membranes in excitable and non-excitable cells and contraction of muscle cells (EFSA, 2009b; 2010b; 2017). Hence symptoms of acute exposure to BTX, TTX and PITX in humans overlap with an array of neuromuscular and cardiorespiratory effects. Regarding the remaining CI neurotoxin groups, SPX and GYM, the evidence points to both inhibiting the muscarinic and nicotinic acetylcholine receptors in the central and peripheral nervous system and the neuromuscular junction (EFSA, 2010a). No human case reports could be identified for SPX and GYM exposure. Animal data however characterised acute toxicity of CIs by the rapid onset of systemic neurotoxicity and death. No long-term studies on CIs were available.

13. Of the cyanotoxins, MCs are the most investigated group. Current literature suggested MCs are actively transported into cells by specific organic anion transport proteins (OATPs) and due to the high number of OATPs in the liver, MCs are primarily hepatotoxic; however, distribution to other organs and tissues also occurs. MCs bind to certain protein phosphatases that are involved in a range of regulatory pathways, e.g., those responsible for cytoskeletal structures, cell replication, stress response and DNA repair (Testai et al., 2016; WHO, 2020; 2022). In humans, acute illness following consumption of drinking water contaminated with cyanobacteria typically causes gastroenteritis (Percival and Williams, 2023). Limited toxicological data was available for other cyanotoxins, i.e., anatoxins (ATX), cylindrospermopsin (CYN) and β-methylamino-L-alanine (BMAA). BMAA and ATX demonstrated neurotoxic effects whilst CYN demonstrated cytotoxicity (WHO, 2020). The mechanisms of ATX, BMAA and CYN toxicity are not well understood, and one limitation is a lack of available standards/purified toxins; therefore, only poorly characterised extracts have been used in experimental studies to date.

14. Human intoxications and deaths have been reported for TTX, PITX and MCs; however, only intoxications were reported for BTX, and no human cases have been reported for ATX, BMAA, CYN or any CIs to date. It must be noted that for some cases of human intoxication, the involvement of PITX remains unconfirmed as it was unclear whether the incident could solely be attributed to PITX due to incomplete or missing toxin identification/quantification data (Cefas, 2014). Furthermore, the fatalities from MC exposure occurred not due to consumption of contaminated food or water but after mistreated water was used

in renal dialysis (WHO, 2020).

15. No toxicological data, occurrence data or reports of human intoxications were available for PtTX, novel AZA and DA analogues.

16. Little information was available on whether cooking may break down or alter the concentrations of these marine biotoxins. Data was only available for MC and TTX, regarding the former, the data was inconsistent with reports of increases, decreases and no changes after cooking. For TTX the limited information available showed TTX was heat stable and did not decompose during cooking (Islam et al., 2011; Bane et al., 2014; Turner et al., 2015; FAO/WHO, 2016). Literature has shown that cooking can reduce the concentrations of STX and DA through boiling or steaming due to partial leaching into the cooking liquid (EFSA, 2009a; 2009c). However, there is no other information on how cooking effects BTX, PITX, SPX and GYM or other cyanotoxins.

17. Occurrence data for the emerging biotoxins was limited as they are not regulated or included in current routine monitoring programmes. The only recent EU monitoring program was conducted by the French Research Institute for Exploitation of the Sea (IFREMER) over a five-year period (2018-2022) (Amzil et al., 2023). The results from the monitoring programme showed that unregulated lipophilic toxins, i.e. PTXs, PnTX, GYMs, BTXs and MCs, could be identified and quantified in various species of shellfish every year. This program was the first to find MC, GYM and BTX groups in shellfish. Members of the PITXs were not detected in shellfish, but were detected in other seafood organisms, e.g., sea urchins, fish, gastropods and crustaceans.

18. Limited occurrence data on the emerging marine biotoxins was also available in academic publications. Of note was a recent report of a cyanobacterial bloom in Lough Neagh in Northern Ireland (DAERA., 2024). Species known to produce MCs such as *Microcystis aeruginosa* were identified and ten MC-group toxins were measured in the water with congeners MC-LR and MC-RR present at high concentrations in some algal mats (1,137–18,493 µg/L) (Reid et al., 2024). Vareli et al. (2012) also reported levels ranging from 45-142 µg MC-LR/kg fresh weight in saltwater mussels from Greece. ATX and CYN have only been detected in fish but only outside Europe while BMAA were reported in shellfish from France, Sweden and Greece (Testai et al., 2016; Amzil et al., 2023). SPXs have been identified in shellfish in Norway, Spain, Italy (EFSA., 2010a) and specifically 13-desmethyl spirolide C and 20-methyl spirolide G have been reported in shellfish from Great Britain (Alexander et al, 2024). PITX has been reported in mussels and sea urchins from other European countries, including

Greece, Italy and Spain (EFSA, 2009b). TTXs and their analogues unlike the other emerging biotoxins have been reported frequently in gastropods and bivalves from European waters, such as France, Spain, Italy, Greece, the Netherlands, Ireland and the UK (EFSA, 2017; Gerssen et al., 2018; Bacciocchi et al., 2019; Blanco et al., 2019; Bordin et al., 2021; Dhanji-Rapkova et al., 2020; Hort et al., 2020).

19. Due to the limited toxicological information, no HBGVs have been established for BTX and CIs; however, the EU Community Reference Laboratory for marine biotoxins (CRLMB)/EU Regulatory Reference Laboratory (EURL) has proposed a guidance level of 400 µg sum of SPXs/kg shellfish meat (CRLMB, 2005; Pigozzi et al., 2008). Acute reference doses have been derived for PITX and TTXs of 0.2 µg/kg bw (sum of PITX and ostreocin-D) and 0.25 µg/kg bw respectively (EFSA, 2009b; 2017). The World Health Organisation (WHO) proposed a provisional tolerable daily intake (TDI) for MC of 0.04 µg/kg bw (WHO., 2020; 2022); however, the database for other cyanotoxins on repeated, long-term oral exposures was limited and not sufficient to derive a TDI without high levels of uncertainty. No chronic HBGVs or guidance levels have been set either in the EU or other countries for the emerging marine biotoxins discussed here except SPX and MC.