Risk ranking results

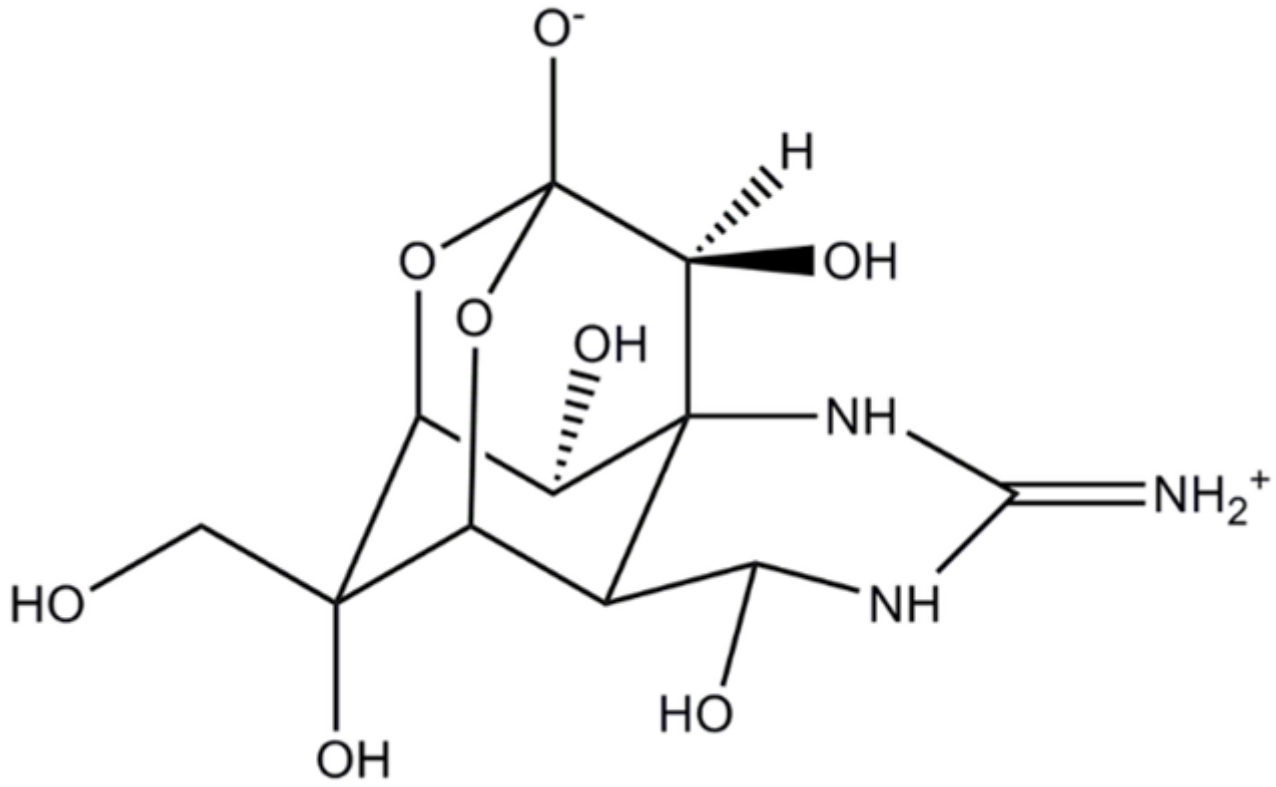
In this guide

33. The risk rankings, following the decision tree in Figure 1, for the emerging marine biotoxins are presented in Tables 1–6. A narrative is supplied

alongside the risk ranking to clearly depict the underlying considerations which led to the numerical scores applied to each biotoxin.

Table 1. Tetrodotoxin (TTX).

Category	No.	Score	Narrative
Monitoring	4	Limited monitoring	TTX is not routinely monitored; however, the French Research Institute for Exploitation of the Sea (IFREMER) conducted a five-year monitoring program for unregulated marine biotoxins between 2018 and 2022 which included TTX.
Human case reports	5	Documented cases of human intoxications and fatalities	Documented cases of human intoxications and fatalities (EFSA, 2017). Death, caused by respiratory failure and cardiac collapse.
Toxicity	5	Causes severe neurotoxic effects with low LD50	TTX is neurotoxic (LD50 oral administration 232 µg/kg bw and intragastric administration 532 µg/kg bw in mice).
Occurrence	5	Frequently detected in UK waters	Detected at 0.0003–0.541 mg/kg in gastropods and bivalves in France, Spain, Italy, Greece, Netherlands, Ireland and UK.
Total:	19	Summary:	For TTX all categories score high, and no specific category is driving the total score.



The figure shows the chemical structure of tetrodotoxin shown in black line and text.

Figure 1. Chemical structure of TTX (Lago et al., 2015).

Table 2. Palytoxin (PITX).

Category	No.	Score	Narrative
Monitoring	5	No monitoring	There is currently no monitoring of PITX in the UK or EU.

Human case reports	5	Documented cases of human intoxications and fatalities	Documented cases of human intoxications and fatalities (EFSA, 2009b; CEFAS, 2014; FSAI, 2016; Otero and Silva, 2022). Symptoms include myalgia and weakness, possibly accompanied by fever, nausea and vomiting, and rhabdomyolysis, characterised by injury to skeletal muscle, muscle breakdown and leakage of myocytes into plasma. Renal failure and disseminated intravascular coagulation. Skin, eye and respiratory irritation. Death.
Toxicity	5	Causes severe neurotoxic effects with low LD50	PITX is neurotoxic (LD50 oral administration 510–767 µg/kg bw in mice and 40 µg/kg bw in rat).
Occurrence	2	Detected in Northern EU waters	Detected at 300–625 µg/kg in shellfish meat. Detected in France, Greece, Italy and Spain.
Total:	17	Summary:	For PITX all categories except occurrence scored high. Only the detection of PITX in northern EU, rather than the UK, prevents the maximum score.

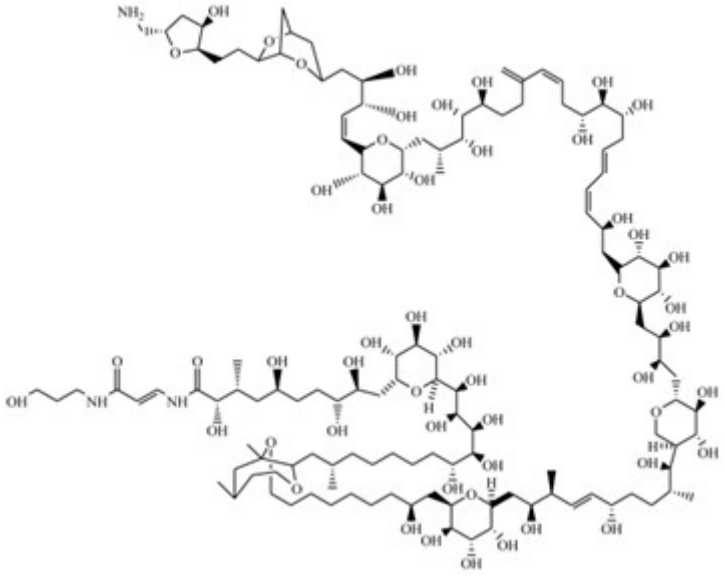


Figure 2 is a Chemical structure of PITX shown in black line and text on a white background.

Figure 2. Chemical structure of PITX (Ramos and Vasconcelos., 2010).

Table 3. Brevetoxin (BTX).

Category	No.	Score	Narrative
Monitoring	4	Limited monitoring	BTX is not routinely monitored; however, the IFREMER conducted a five-year monitoring program of unregulated marine biotoxins between 2018 and 2022 which included BTX.
Human case reports	3	Documented cases of human intoxications	A few hundred intoxications reported (EFSA, 2010b; CEFAS, 2014; ANSES, 2021). Symptoms include nausea, vomiting, diarrhoea, paraesthesia, cramps, bronchoconstriction, paralysis, seizure and coma. No human fatalities or persistent symptoms reported.

Toxicity	4	Causes severe neurotoxic effects with relatively high LD50	BTX is neurotoxic (LD50 oral administration 520–6600 µg/kg bw in mice). BTX was ranked one lower than other neurotoxins (TTX, SPX, and PITX) as the LD50 range for BTX is several folds higher than other neurotoxins.
Occurrence	2	Detected in Northern EU waters	Recent report of BTX-2 and BTX-3 detected in mussels in France (82–345 µg/kg).
Total:	13	Summary:	For BTX no maximum scores for categories were given. The severe neurotoxic effects and lack of monitoring drive the score. However, occurrence data on BTX in northern EU was available, as well as reports of human intoxications but no deaths, overall, lowering the total score.

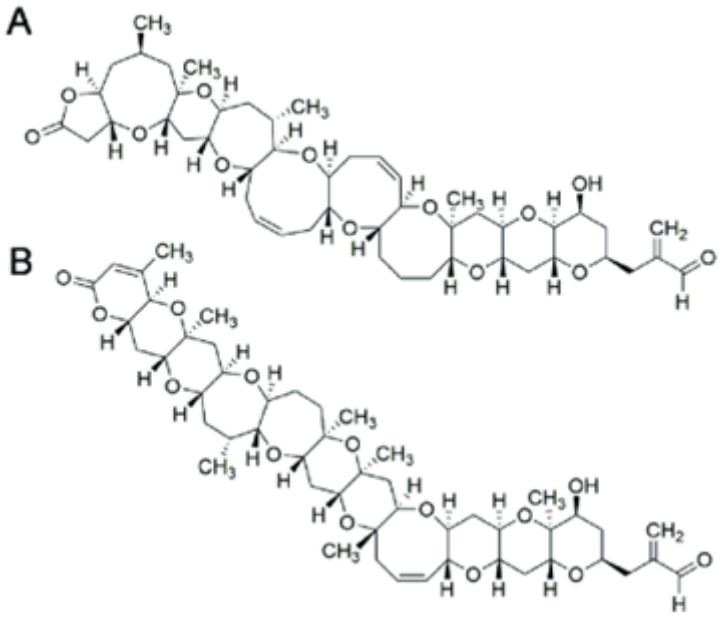


Figure 3 shows a Chemical structure of BTX1 (A) and BTX2 (B) shown in black line and text on a white background.

Figure 3. Chemical structure of BTX1 (A) and BTX2 (B) (Vilariño et al., 2018).

Cyanotoxins

34. Cyanotoxins are a diverse group spanning a variety of chemical structures produced by different species and genera of cyanobacteria. MCs are the only class of cyanotoxins with information available for all categories of the risk ranking process (Figure 4). An attempt was made to risk rank other classes of cyanotoxins but due to insufficient data this was not possible.

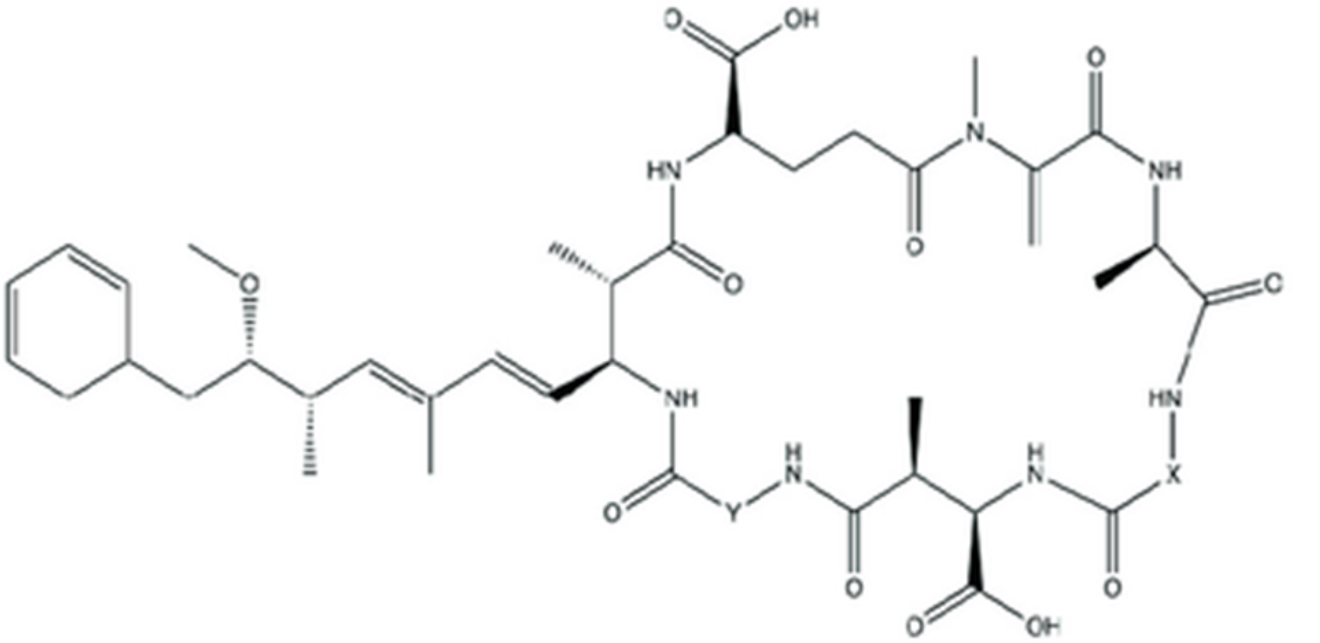


Figure 4 shows the general structure of MCs, shown in black line and text on a white background.

Figure 4. General structure of MCs where X and Y are variable amino acids at positions 2 and 4 respectively (adapted from Lad et al., 2022).

Table 4. Microcystin (MC).

Category	No.	Score	Narrative
Monitoring	4	Limited monitoring	MC is not routinely monitored; however, the IFREMER conducted a five-year monitoring program of unregulated marine biotoxins between 2018 and 2022 which included MC.

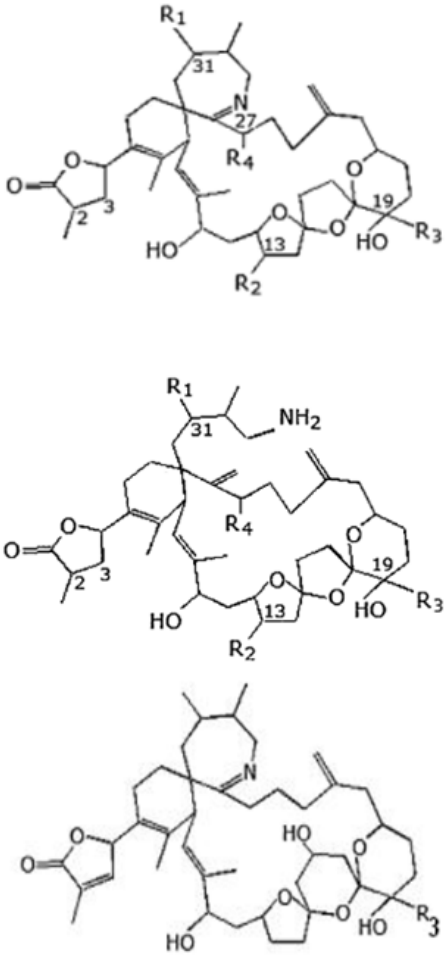
Human case reports	5	Documented cases of human intoxications and fatalities	Fatalities due to MC exposure have been reported (Testai, 2016; WHO, 2020). Symptoms include gastroenteritis, intrahepatic haemorrhage and death.
Toxicity	3	Causes gastro-intestinal effects with low to moderate LD50	MC most commonly causes gastroenteritis but also hepatotoxicity (MC-LR LD50 oral administration 5–10.9 mg/kg bw in mice and in rats > 5 mg/kg bw).
Occurrence	3	Rarely detected in UK waters	Detected in Northern Ireland (Lough Neagh) and France. Reported at 45–142 µg MC-LR/kg fresh weight in saltwater mussels from Greece.
Total:	15	Summary:	Reported fatalities from MC exposure, the lack of monitoring and detection in the UK albeit rare all drive the score. Only its lesser toxicity lowers the score.

Cyclic imines (CIs)

Table 5. Spirolides (SPX).

Category	No.	Score	Narrative
Monitoring	4	Limited monitoring	SPX is not routinely monitored; however, the IFREMER conducted a five-year monitoring program of unregulated marine biotoxins between 2018 and 2022 which included SPX.

Human case reports	1	No documented cases	No documented cases of human intoxications for SPX.
Toxicity	5	Causes severe neurotoxic effects with low LD50	SPX is neurotoxic (LD50 oral administration 53–1000 µg/kg bw in mice).
Occurrence	4	Occasionally detected in UK waters	Found in shellfish in France, Norway, Spain and Italy. A recent report (Alexander et al., 2024) found SPX-1 and 20-Me-SPX G in bivalve molluscs across the UK at maximum concentrations of 13.4 µg/kg and 51.4 µg/kg respectively.
Total:	13	Summary:	For SPX the main driver is neurotoxicity followed by occasional occurrence in the UK but a lack of routine monitoring. The absence of human case reports lowers the score substantially.



Spirolide (SPX)	R_1	R_2	R_3	R_4	$\Delta^{2,3}$	MW
SPX A	H	CH_3	CH_3	H	$\Delta^{2,3}$	691
SPX B	H	CH_3	CH_3	H		693
SPX C	CH_3	CH_3	CH_3	H	$\Delta^{2,3}$	705
SPX D	CH_3	CH_3	CH_3	H		707
13-desmethyl SPX C	CH_3	H	CH_3	H	$\Delta^{2,3}$	691
13,19-didesmethyl SPX C	CH_3	H	H	H	$\Delta^{2,3}$	677
13-desmethyl SPX D	CH_3	H	CH_3	H		693
27-hydroxy 13,19-didesmethyl SPX C	CH_3	H	H	CH_3	$\Delta^{2,3}$	691
SPX E	H	CH_3	CH_3	H	$\Delta^{2,3}$	709
SPX F	H	CH_3	CH_3	H		711
SPX G			H			691
20-methyl SPX G			CH_3			705

MW: molecular weight; $\Delta^{2,3}$: Double bond between C2-C3

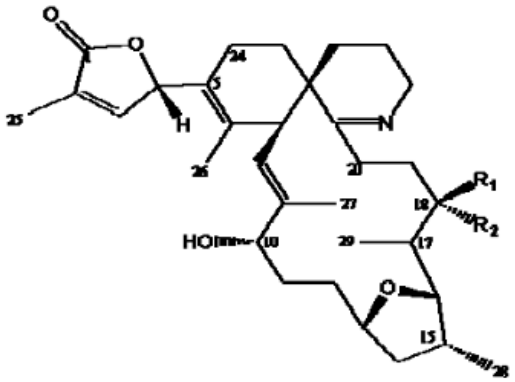
Figure 5 shows the chemical structure of SPXs shown in black line and text on a white background.

Figure 5. Chemical structure of SPXs (EFSA.,2010a).

Table 6. Gymnodimine (GYM).

Category	No.	Score	Narrative
Monitoring	4	Limited monitoring	GYM is not routinely monitored; however, the IFREMER conducted a five-year monitoring program of unregulated marine biotoxins between 2018 and 2022 which included GYM.

Human case reports	1	No documented cases	No documented cases of human intoxications for GYM .
Toxicity	4	Causes severe neurotoxic effects with relatively high LD50	GYM is neurotoxic (GYM-A LD50 oral administration 755–4057 µg/kg bw in mice). GYM is ranked one lower than other neurotoxins (TTX, SPX, and PITX) as the LD50 range for GYM-A is several folds higher than the other neurotoxins.
Occurrence	2	Detected in Northern EU waters	Recent reports of GYM-A detected in shellfish from France in IFREMER.
Total:	11	Summary:	For GYM the main drivers of the score are the lack of monitoring and its severe neurotoxic effects. The absence of human case reports and its detection in the EU but absence in the UK lowers the overall score.



Gymnodimine (GYM)	R_1	R_2	MW
GYM A	H	- [(a)]	507
GYM B	H	OH	523
GYM C	OH	H	523

(a): Double bond between C17-C18; MW: molecular weight

Figure 6 shows a chemical structures of GYMs shown in black line and text on a white background.

Figure 6. Chemical structures of GYMs (EFSA., 2010a).