8. Risk Assessment

The allowance levels currently valid for phycotoxins are based mainly on data derived from poisoning incidents. However, these data are seldom accurate and complete, and mainly restricted to acute toxicity. In some cases, the allowance level is also adapted to the limitations of the detection method. For risk assessment purposes, human intake levels of (shell)fish should be standardized.

8.1 Risk Assessment for Paralytic Shellfish Poisoning (PSP)

Currently the toxicological risk evaluation for PSP toxins can only be based on acute toxicity data. Sub-chronic and chronic data for animals as well as humans are not available. Lowest doses causing mild symptoms of PSP in humans vary between 120 and 304 µg/person and lowest doses associated with severe intoxications/fatalities vary between 456 and 576 µg STX/person. In order to protect more susceptible persons (children, elderly, unhealthy) usually an uncertainty factor of 10 is applied for calculation of TDI values for contaminants, based on human data. However, for PSP the calculations are complicated by the following factors: at what levels should the effects be considered as “adverse”, and what level is the actual NOAEL and LOAEL? On the other hand, since the data on PSP represent many individuals, displaying large differences in susceptibility, an uncertainty factor of 10 may not be needed (Aune, 2001). Most countries apply a tolerance level of 80 µg STX eq/100 g mussel meat. If the consumption of shellfish is estimated to be between 100 and 300 g/meal, a margin of safety of about < 1 to 3.8 toward mild symptoms is present and, more important, a margin of safety of only 1.9 to 7.2 toward serious intoxications or death. These margins are quite small or there is no margin at all.

However, it is neither practical nor realistic to establish a very low tolerance level because the mouse bioassay is currently the most widely used method to determine PSP toxins and the present detection limit of this assay is approximately 40 ng PSP (STX eq)/100 g shellfish. Once more sensitive (and reliable) analytical chemical methods are available, the toxicity figures of STX and derivatives after acute and (sub)chronic exposure should be re-evaluated.

8.2 Risk Assessment for Diarrhoeic Shellfish Poisoning (DSP)

The various toxins in the DSP complex can be divided into three groups namely okadaic acid and the structurally related DTXs, the PTXs and the YTXs.

An EU Working Group on Toxicology of DSP and AZP has recommended allowance levels for these three groups of DSP toxins (EU/SANCO, 2001).

OA and DTXs

In animal experiments, cancer promoting and genotoxic effects of OA and DTXs are seen at relatively high doses and long exposure periods compared with the levels causing diarrhoea in humans shortly after consumption of contaminated shellfish. Consequently it is unlikely that a substantial risk of cancer exists in consumers of shellfish due to these toxins. Therefore, human risk assessment is based on a N(L)OAEL from animal or human data with the use of an uncertainty factor. Human data are preferred when available.

Taking into account all human exposure figures, it can be concluded that the lowest levels causing diarrhoeic effects in humans vary from 32 to 55 µg OA and/or DTX1. These figures have been
derived from Japanese and Norwegian human data. The effects seem to be restricted to diarrhoea, vomiting, headache and general discomfort. No serious and irreversible adverse health effects have been seen at these levels (EU/SANCO, 2001). Current European Regulations allow maximum levels of OA, DTXs and PTXs together of 160 µg OA eq/kg edible tissue. If the consumption of shellfish is estimated to be between 100 and 300 g/meal, there is a margin of safety of about < 1 to 3.4 toward the diarrhoeic effects. These margins are quite small or there is no margin at all. EU/SANCO (2001) stated that, if the level of OA and DTXs in shellfish is not higher than 16 µg/100 g shellfish meat, there is no appreciable health risk at a consumption of 100 g mussel meat/day.

**PTXs**

Concerning the PTXs, human toxicity data are not available. Therefore a safe level for humans is based on animal toxicity data. For toxins in the PTX group, data on animal toxicity are only available for PTX2. Effects such as tumour induction and tumour promoting are not known. The LOAEL for PTX2 by oral administration to mice was reported to be 0.25 mg/kg bw based on diarrhoeic effects and effects on the liver. The NOAEL should be estimated by applying a factor of 10 to the LOAEL. To extrapolate the animal data to human risks, a factor of 100 is applied. Thus, by applying an uncertainty factor of 1000, a safe level of 0.25 µg/kg bw can be calculated for humans ~ 15 µg for an adult weighing 60 kg. EU/SANCO (2001) has recommended an allowance level of 15 µg/100 g shellfish meat. However, if the consumption of shellfish is estimated to be between 100 and 300 g per meal, the allowance level has to be between 5 and 15 µg/100 g edible shellfish tissue.

For PTX2 seco acid (PTX2-SA), human exposure data are available from a pipi shellfish poisoning event (56 cases of hospitalisation) in New South Wales (Australia) in December 1997 (ANZFA, 2001). According to Quilliam et al. (2000), PTX2-SA may have contributed to the gastrointestinal symptoms, vomiting or diarrhoea in humans (Aune, 2001). Burgess and Shaw (2001) reported that the patients consumed approximately 500 g of pipis containing 300 µg PTX2-SA/kg (~150 µg PTX-2SA/person ~2.5 µg/kg bw for a 60 kg weighing person). A safe level for humans of 0.025 µg/kg bw for PTX2-SA can be calculated by applying an uncertainty factor of 100 (10 for intraspecies differences and 10 for extrapolation from LOAEL to NOAEL) (~1.5 µg/person weighing 60 kg). This means that for PTX2-SA, the allowance level has to be between 0.5 and 1.5 µg/100 g edible tissue at consumption between 100 and 300 g per meal.

**YTXs**

For the YTXs, no human data are available. Therefore, a safe level in humans is based on animal data. The NOAEL in mice by acute oral administration was estimated to be 1.0 mg/kg bw based on cardiac effects. A safe level for humans towards acute toxic effects of YTX is calculated to be 10 µg/kg bw by applying an uncertainty factor of 100. For an adult weighing 60 kg, this would mean a safe level of 600 µg YTX. In view of the lack of data on repeated administration and a high uncertainty factor recommended by WHO for a substance that injures cardiac muscles, the calculated safe level for humans given above could be lowered by a factor 6 to 100 µg (EU/SANCO, 2001). EU/SANCO (2001) recommended an allowance level of 100 µg YTXs/100 g shellfish meat. However, if the consumption of shellfish is estimated to be between 100 and 300 g per meal, the allowance level has to be between 33 and 100 µg/100 g edible shellfish tissue.
8.3 Risk Assessment for Amnesic Shellfish Poisoning (ASP)

The generally applied guideline value of 20 mg DA/kg mussels is derived from an ASP incident in Canada (Prince Edward Island) and is taken on by several other countries. The guideline level of 20 mg DA/kg is equal to an intake of 0.03 to 0.1 mg DA/kg bw per person with a body weight of 60 kg assuming that consumption of mussels is between 100 and 300 g/meal. The epidemiological data used to derive the guideline value, revealed mild gastrointestinal effects in humans at 1 mg DA/kg bw. Afterwards the guideline value was supported by acute studies in animals. However, when doses required to cause overt toxicity in animal species were compared, mice and rats appeared to be relatively insensitive compared with monkeys and oral dosing required more toxin (more than 10 times in rodents) to achieve the same effects as i.p. dosing. Rats showed overt effects of DA poisoning at single oral doses of about 80 mg/kg bw, whereas monkeys showed vomiting, gagging and yawning already at 1 mg/kg bw. A single oral dose of 0.75 mg DA/kg bw in monkeys did not induce overt effects. This apparent decreased sensitivity in rodents may be the result of their inability to vomit and/or the finding that the plasma half-lifetime of DA in the rat is about 6 times less than that in the monkey. Comparing the guideline value of 20 mg DA/kg of mussel tissue (~ 0.1 mg/kg bw for humans assuming a consumption of 300 g mussels per meal) with the no-effect dose (0.75 mg/kg bw) in acute oral studies in monkeys, a factor smaller than 10 is between these figures. There is no knowledge of the effects of long-term exposure to low levels of DA. However, short-term animal studies with repeated exposure do not point to altered DA clearance from serum or greater neurotoxic responses than after single exposures.

Reasonable good dose-response data were determined for 10 persons involved in the Canadian incident (elderly people, aged from 60 to 84 years). According to these data the NOAEL is 0.2-0.3 mg DA/kg bw, while the LOAEL was 0.9-2.0 mg DA/kg bw and serious intoxications were recorded at 1.9 to 4.2 mg DA/kg bw. Interestingly, the intake estimates showed surprisingly large consumption of blue mussels, 120 to 400 g mussel meat per person per meal (Aune, 2001). This means that there is a factor two between the NOAEL and the regulatory limit of 20 mg DA/kg mussel meat which is equivalent to 0.1 mg/kg bw for a 60 kg weighing person with a mussel meat consumption of 300 g per meal. Between the LOAEL and the regulatory limit there is a margin of 9 to 20 and between the level of serious effects and the regulatory limit there is a margin of 19 to 42.

8.4 Risk Assessment for Neurologic Shellfish Poisoning (NSP)

Based on the lack of sufficient data on toxicity and the analytical difficulties in determining brevetoxin exposure, risk assessment is not possible. Current risk management (in states on coasts of the Gulf of Mexico) is based on shellfish bed closures at 5 000 $G. breve$ cells/litre with reopening based on determination of PbTx in shellfish at <80 µg/100 g.

8.5 Risk Assessment for Azaspiracid Shellfish Poisoning (AZP)

EU/SANCO (2001) stated that based on poisoning incidents in Ireland, levels of AZAs causing human intoxication were calculated to be between 6.7 and 24.9 µg. These figures included a reduction in AZA content due to heating of the mussels. New data on heat stability revealed that this reduction of the toxin content due to heating was not justified. Therefore the recalculated range of the lowest observed adverse effect level (LOAEL) appeared to be between 23 and 86 µg per person assuming a maximum consumption of 100 g shellfish per meal. EU/SANCO (2001) applied a safety factor of three to convert the LOAEL to a NAOEL. Based on an intake level of a maximum of 100 g shellfish meat/meal, and the lowest LOAEL divided by three, EU/SANCO (2001) stated that an allowance level of 8 µg AZAs/100 g of shellfish should result in no
appreciable risk for human health. To allow for detection by the mouse bioassay a level of 16 µg/100 g was proposed. However at a shellfish consumption of 300 g per meal, a person will consume already an amount of AZAs equal to the LOAEL in humans.

Ofuji et al. (1999b) reported a level for total AZAs in raw mussel meat in poisoning incidents of 1.4 µg/g of meat. At a consumption of 100 to 300 g per meal this means an intake of 140 to 420 µg AZAs/person. As these figures represent an effect level (LOAEL) usually a factor 10 is used for calculation of a NOAEL. This means that the NOAEL is 14 to 42 µg per person assuming a consumption of 100 to 300 g shellfish meat/meal. As a consequence the allowance level in shellfish meat has to be 14 µg/100 g. It has to be noted that no factor of 10 was applied to the NOAEL for intraspecies differences (variation in the human population).

8.6 Risk Assessment for Ciguatera Fish Poisoning (CFP)

The available animal data on ciguatoxin are not suitable for risk assessment. Therefore, human data derived from poisoning incidents should be used.

Mild CFP symptoms in some persons can be already expected after consuming fish containing the main Pacific ciguatoxin (P-CTX-1) at a level of 0.1 µg/kg. The main Caribbean ciguatoxin (C-CTX-1) is less polar and 10-fold less toxic than P-CTX-1. Assuming a fish consumption of 500 g per meal and a human body weight of 50 kg, this corresponds to 0.001 µg/kg bw (=LOAEL). These figures are derived from a large serving of the least toxic fish causing effects in some people. A level of 0.01 µg/kg bw, which is ten times the level causing mild symptoms in some persons, would be expected to be toxic in most people. By applying an uncertainty factor of 10 (for intraspecies differences) to the lowest level causing mild symptoms in humans (=LOAEL), a “safe” level of 0.01 µg/kg of fish flesh can be calculated (Lehane, 2000; Lehane and Lewis, 2000). It has to be noted that the usual application of an uncertainty factor of 10 to the LOAEL for calculation of a NOAEL was not performed.

8.7 Concluding remarks

At present the risk assessment of phycotoxins has not been performed in a straightforward way. Risk management and risk assessment have been mixed in the process complicating the procedure. In general, there is a lack of toxicological data particularly on repeated exposure. Epidemiological data mainly existed of poisoning incidents with their inherent limitations. This all cumulated in provisional risk assessments of certain phycotoxins which were not always logic and consistent. For some phycotoxins, even the lack of minimal data has prohibited risk assessment.

If adequate scientific (toxicological, epidemiological and occurrence) data are available, a risk assessment can be performed by applying generally accepted safety or uncertainty factors. An adequate set of animal data will allow the derivation of a no-observed adverse effect level (NOAEL). A safe level for humans can be calculated by applying an uncertainty factor of 100 (10 for interspecies differences and 10 for intraspecies differences) to the NOAEL. If an adequate set of human data is available, a safe level for all humans can be calculated by applying an uncertainty factor of 10 (for intraspecies differences) to the NOAEL, derived from those human data.
9. Conclusions and Recommendations

9.1 Conclusions

Consumption of a variety of shellfish and fish causes an increasing number of human intoxications around the world. Diagnosis depends mainly on recognition of specific signs and symptoms and on identification of marine toxins present in remains of the seafood involved. Indicators for effects and exposure are usually not available due to inadequate analytical methods for the sometimes complex algal toxin mixtures. The effects of algal toxins are generally observed as acute intoxications. Health effects of episodic exposure and chronic exposure to low levels of algal toxins are hardly known. The latter effects may go unreported by the affected individual(s) or may be misdiagnosed by physicians.

Monitoring seafood for toxicity is essential to manage the risks. However, there are several limitations in monitoring for toxicity such as the variation in toxin content between individual shellfish, different detection and even extraction methods for the various toxins requiring a decision which toxins one is testing for, and the frequency of sampling to ensure that toxicity does not rise to dangerous levels in temporal or spatial gap between sampling times or locations. Furthermore, the growing harvest of non-traditional shellfish (such as moon snails, whelks, barnacles, etc.) may increase human health problems and management responsibilities.

Monitoring for toxic plankton may possibly overcome some of these problems. However, plankton populations are patchy and ephemeral, it is difficult to make a quantitative correlation between numbers of toxic plankton and levels of toxins in seafood and the amount of toxin per cell can vary widely. Data on the occurrence of toxic algal species may indicate which toxins may be expected during periods of algal blooms and which seafood products should be considered for analytical monitoring. A problem is that certain algal species, which have never occurred in a certain area, may suddenly appear and then rapidly cause problems. The plankton observations are used to focus toxicity testing, but are not in themselves used for regulatory decisions. Moreover, most monitoring and regulatory programmes often are not adequate to meet the expanding threat of new harmful algal blooms. As a result, when new outbreaks occur, the response is often uncoordinated and slow. Harmful algal blooms cannot be predicted and there is little information on bloom initiation.

Toxic blooms are mostly detected by visual confirmation (water discolouration and fish kills), illness to shellfish consumers and/or human respiratory irritation with actual toxicity verified through time-consuming mouse bioassays and chemical analyses in shellfish samples. This “after-the-fact” strategy is the consequence of the extremely difficult prediction of the occurrence and magnitude of a bloom. To prevent human intoxication, monitoring programmes relying on enumeration and microscopic identification of harmful taxa in water samples generally suffice. However microscopic based monitoring requires a high level of taxonomic skill, usually takes considerable time, and can be highly variable among personnel.

One of the most serious problems is the lack of information on the biology of harmful algae. For example, little is known about the abundance, distribution, population dynamics and physiology of most of the harmful species, both in local waters and elsewhere. Long-term, routine monitoring of phytoplankton and the environment is essential to obtain data necessary to determine even the most elementary ecology of harmful species. Moreover, because bloom dynamics are complex, the factors that determine bloom dynamics of a species in one geographic area may not affect that
species in another area, even though the areas are not widely separated. Therefore alternative evaluation systems for predicting bloom occurrences are highly desirable.

In establishing regulatory criteria and limits for marine toxins, various factors play a role such as the availability of survey data, the availability of toxicological data, the distribution of the toxins throughout sampled lots and the stability in the samples, the availability of analytical methods and regulations already in force in several countries. With respect to toxicity, until now only data on the acute oral toxicity both in experimental animals and humans are available for the majority of the marine toxins. However, repeated exposure to lower sublethal dose levels may be a common feature.

Concerning detection methods, there is a general, worldwide need for rapid, reliable and sensitive methods to determine marine toxins in (shell)fish. The present mouse bioassay is not sensitive enough, shows a considerable variation, is time consuming, is vulnerable to interferences and is unethical in terms of animal welfare. Quilliam (1998b) argues for LC-MS as a universal detection method for all marine toxins. This technique has a low limit of detection, high selectivity and the ability to deal with the structural diversity and labile nature of the toxins. In addition, separation of complex mixtures, accurate and precise quantitation, automation and high throughput, legal acceptability for confirmation and structural information of new toxins are possible with this method. Another new approach that seems promising is the development of biosensors with which multiple toxins can be determined simultaneously.

The development and introduction of adequate and efficient analytical methods can be accelerated by providing information in a fast and proper way, for instance by setting up an Internet accessible database. The database should include parameters such as (chemical) names, physical/chemical properties, classification(s), toxic effect(s), sources, habitat, regulatory limits and literature references.

### 9.1.1 Conclusions related to Paralytic Shellfish Poisoning (PSP)

The tolerance levels set for PSP toxins thus far are largely pragmatic decisions based on intoxication events, and although there are many reported cases of human intoxications due to shellfish toxins, it is difficult to obtain reliable human toxicity data. For example, variations in observed toxicity of PSP toxins to humans may be due not only to variable sensitivity between people, but also to the composition of individual toxins in the samples. Toxin profiles can vary according to the species of shellfish consumed and the area of harvest. In addition, toxic doses are often estimated from left-over toxic seafood. This is not necessarily representative of the ingested food because PSP toxins may be unevenly distributed throughout lots and within individual shellfish, and not all PSP toxins are stable.

It is possible to measure PSP compounds by a number of analytical-chemical methods but they all have some limitations, and they often cannot easily be operated because of the lack of reference materials, although recently some progress has been made in this area. In 2003, certified standards of STX, neoSTX, dc-STX, GNTX 1-4, GNTX 2/3 and GNTX 5 are commercially available. However, they are expensive and mainly available from one source. Yet, their availability significantly improves the quality of the data that are obtained by LC-methodology. The efforts undertaken by the European Commission's SMT Programme have led to shellfish reference materials with certified mass fractions of some of the toxicologically most significant PSP toxins. Despite these positive developments, the analytical situation remains difficult and the lack of pure PSP compounds in sufficient quantities for repeated dose toxicity studies is a limiting factor in the development of reliable risk assessment.
9.1.2 Conclusions related to Diarrhoeic Shellfish Poisoning (DSP)

The variety in biological activities of the DSP toxins may cause some problems. Although PTXs and YTXs are acutely toxic to mice after i.p. injection, their oral toxicity to humans is unknown. Therefore, more toxicological data on PTXs and YTXs have to become available. Furthermore OA and DTX possess tumour promoting activity and OA shows also genotoxic and immunotoxic activity. These effects raise questions as to the human health risks of (sub)chronic exposure to low levels of these compounds. A pressing problem is the lack of sufficient quantities of DSP toxins to perform (sub)chronic animal toxicity studies.

Although mammalian bioassays for DSP toxicity are applied worldwide, there are large differences in performance of, for instance, the mouse bioassay (toxicity endpoint is animal death; no consensus on appropriate observation time) among different countries, resulting in differences in specificity and detectability. A major problem is the fact that the mouse bioassay detects all DSP components and probably also other toxins. However, it is not possible to distinguish between the various toxins whereas specific legal limits for the toxin groups have been established (for instance in the EU). On the other hand, the rat bioassay detects only OA and DTXs because the endpoints in this assay are soft stool, diarrhoea and feed refusal which effects are known to be caused by OA and DTXs only (and AZAs).

Chemical methods (LC) are useful for identification and quantification of selected diarrhoeic toxins (usually OA or DTXs). Recently an LC method for the detection of YTXs was developed, but until now no method for PTXs is available except an LC-MS method; however its performance is not yet satisfactory. Chemical methods are applied as a regulatory tool primarily for confirmation of the results obtained in a bioassay.

None of the many approaches to determine DSP toxins in shellfish has been evaluated in a formal collaborative study according to ISO/IUPAC/AOAC so that the performance characteristics are not fully known. The further development, evaluation and comparison of the various techniques would become significantly easier if reliable reference standards and reference materials (such as lyophilized mussel samples with certified contents of several DSP toxins) could be developed and made available to the scientific community.

9.1.3 Conclusions related to Amnesic Shellfish Poisoning (ASP)

Compared to the paralytic and diarrhoeic shellfish poisons, problems with amnesic shellfish poisons seem to be of a lesser magnitude. Only one confirmed outbreak of ASP causing severe illness in exposed people was reported worldwide, specifically in Prince Edward Island, Canada in 1987. After the first outbreak in Canada, human illnesses (mild and short lived) were only observed in one outbreak, specifically after consumption of contaminated razor clams (from the West Coast of the United States). However, health authorities were not able to confirm that the illnesses were caused by DA. In two outbreaks, the death of cormorants and/or brown pelicans due to the consumption of contaminated anchovies or mackerel was reported indicating that herbivorous fish can act as vectors for DA. In the last few years (1999 to 2002), DA was detected also in shellfish from some European countries.

Methods of analysis for DA are rather straightforward and less complex than those for paralytic and diarrhoeic shellfish poisons. One chemical method for DA in mussels (LC with UV detection) has been successfully validated in a formal collaborative study, whereas another (improved) method is currently subject to a collaborative study. Certified reference materials and calibrants are readily available.
9.1.4 Conclusions related to Neurologic Shellfish Poisoning (NSP)

When humans are exposed to brevetoxins, different exposure routes are possible; the oral route via consumption of contaminated shellfish, the inhalatory route via exposure to aerosolised brevetoxins, and the dermal route via direct contact with contaminated seawater. The effects of the various exposure routes on humans are difficult to assess because toxicity data for brevetoxins are limited. Some acute studies in mice and data from poisoning cases in humans and (marine) mammals are available but acute dermal and inhalation studies are lacking, as well as oral, dermal and inhalation studies with repeated exposure of laboratory animals. Therefore reliable hazard assessment is not possible.

Pure toxins and toxin metabolites would be needed to be able to carry out toxicity studies. In addition, analytical reference materials would be needed to further develop and improve the analytical methodology and to allow analytical quality assurance of monitoring laboratories. Currently the various obstacles on the way to reliable assessment of brevetoxin occurrence and exposure further hamper risk assessment and thus the establishment of meaningful regulations.

Despite these problems, regulations for NSP toxins in shellfish are in force in a few countries, specifically the USA, Italy and New Zealand based on the mouse bioassay. The action level is 20 MU/100 g shellfish flesh (~80 μg PbTx-2/100 g shellfish flesh).

9.1.5 Conclusions related to Azaspiracid Shellfish Poisoning (AZP)

One cause for concern is the lung tumours found in mice after repeated doses of 20 μg AZA/kg bw and higher. This finding should be confirmed in experiments with larger numbers of mice and longer exposure periods (Ito et al., 2002).

The current allowance level has to be revised as new data become available. However, the lack of supply of pure toxins is a serious obstacle to all kinds of studies. The production of pure toxins, in turn, depends on the availability of large amounts of toxic mussels. Development of rapid detection methods such as LC-FLD, ELISA and functional assays should be explored.

9.1.6 Conclusions related to Ciguatera Fish Poisoning (CFP)

Ciguatera poisoning mainly occurs in tropical regions throughout the world and is sporadic in Europe, particularly in the Northern European countries. Therefore, a regular analytical check on the presence of ciguatoxins in imported large predatory fish from endemic areas is considered adequate in countries which are not an endemic area for CFP.

A few specific regulations exist for ciguatoxins. A positive finding in a fish would remove that fish from sale. In some cases, restrictions are placed on the sale of fish of certain species or size from a given area, with no testing of the toxin. The larger a fish is, the older it probably is, and the more toxin it has probably accumulated. Reef carnivores considered being regular ciguatoxin carriers are often banned from sale as a matter of principle. The hazard is linked to the accumulation in the food chain of a toxin, which is impossible to link with any algal bloom. Cell counting of plankton will not predict when a fish has accumulated ciguatoxins or not (Boutrif and Bessey, 2001).
9.2 Recommendations

Based on the preceding conclusions, the following recommendations are presented:

1. Data on bloom development with respect to hydrographic and climatic conditions, and nutritional status of the water column are needed.

2. Toxicity studies on effects after repeated exposure to marine toxins should be performed.

3. Chemical analytical techniques capable of separating, identifying and quantifying individual marine toxins should be further developed.

4. As alternatives to rodent assays, assays have to be developed to be used when uncharacterized bloom events occur. Emphasis on the use of in vitro techniques where blooms have been characterized should reduce the use of test systems with live animals.

5. To facilitate fast application of adequate analytical methods for marine biotoxins, a database should be developed including basic data on marine biotoxins such as chemical structures, physical/chemical properties and analytical methods.

6. Both for the submission of toxicity data and for the development and validation of analytical techniques, the production of pure toxin standards and certified reference material are required.

7. Formal risk assessments of the marine biotoxins should be performed by recognized international bodies – such as the Joint FAO/WHO Committee on Food Additives (JECFA) and the European Food Safety Authority (EFSA) – and should be based on sound scientific data of toxicity and exposure. In the absence of sufficient data, an expert consultation could be considered in order to explore the possibilities for adequate risk assessment which should be the basis for meaningful regulations.
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