C. Tributyltin and triphenyltin compounds

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Abstract:

Tributyltin and triphenyltin (TBT and TPT) are biocides that have been used to prevent fouling of boats, to preserve wood, kill molluscs, and for other purposes. Due to observed effects on oysters and snails, their use in boat paints has been banned in many nations. However, use on ships and some uses other than as antifouling paints continue. These uses, the relative persistence of these compounds, their tendency to bioaccumulate, and their toxicity cause lingering concerns about risks to humans and nonhuman organisms. This paper outlines an integrated assessment of TBT and TPT. Based on prior human health and ecological assessments, it suggests that an integrated assessment that recognized common pathways of transport, fate and exposure, and on common modes of action would be more efficient and complete than additional independent assessments. In addition, the presentation of risks in an integrated manner could lead to better decisions by defining the various benefits of any management action.

1. Background

Tributyltin (TBT) and triphenyltin (TPT) compounds are used widely for various purposes owing to their strong biocidal activity toward a range of aquatic organisms such as bacteria, fungi, algae, molluscs, and crustaceans. Some examples of their use have been as antifouling paints for boats and cooling towers to prevent adhesion of aquatic organisms, as wood preservatives, as slimicides in industrial processes, as molluscicides to prevent schistosomiasis, and**,** in the case of TPT, as a fungicide. However, the finding that TBT was damaging oyster production in France in the 1970s made people recognize the negative aspects of use of these compounds in the aquatic environment (Alzieu 1981). More recently, the discovery that TBT and TPT at very low concentrations (1 ng/L in water) causes "imposex," the induction of a penis in females of certain snails, suggested that TBT and TPT are endocrine disruptors (IPCS, 1999 a & b).

TBT and TPT were chosen as a case study of integrated assessment for two reasons. First, their use as antifoulants was restricted in many nations based solely on risks to nonhuman organisms. Hence, these compounds make an unusual case for integration in that the ecological risks have dominated recent regulatory actions. Second, the possibility that there may have been significant risks to humans has remained unresolved. Many reports show that marine mammals and human fish eaters have accumulated these compounds in their bodies. This exposure and the various adverse effects observed in laboratory animals, raise concerns of risks to humans and other vertebrates as well as invertebrates. The potential for bioaccumulation and the complex toxicity profiles of these compounds suggest that a holistic approach to assessment is needed.

This case study is limited to tributyltin and triphenyltin compounds and their metabolites. One metabolite, dibutyltin is also used in as a stabilizer for polyvinyl chloride polymers, and is suspected to be more toxic in some ways than tributyltin. Some other organotins, such as trimethyltin (TMT) or triethyltin (TET) compounds are known to cause principally neurotoxic effects. However they are not covered in this case study, because their use patterns and toxicity profiles differ greatly from TBT and TPT.

2. Problem Formulation

2.1 Impetus for the assessment

Concerns for TBT and TPT arose from observations of deformities and reproductive failure in oysters, and certain gastropods. These observations combined with complex toxicity profile in rodents and aquatic organisms raised concern not only for effects on molluscs, but also for the possibility of effects caused from unknown, but common background mechanisms. Observations of immune suppression and developmental and reproductive toxicity in rodents at low levels of exposure (around or less than 1 mg/kg body weight) give some support on this concern.

Nonhuman organisms can serve as sentinels for certain effects that have not been identified in humans. Opportunistic infections and mortalities of some marine mammals appear to be related to immune suppression possibly caused by exposure to multiple agents, such as organotin compounds and polychlorinated biphenyls (PCBs). Some human populations who eat a lot of fish also accumulate organotin compounds and PCBs.

2.2 Assessment questions

Environment managers in various nations have asked whether the organotin compounds posed risks to human health or environmental quality that might justify further restricting their use. Evidence shows that current partial restrictions in many countries are not effective in preventing high local pollution in some inland seas and bays where contaminants are poorly dispersed or in preventing dispersal to remote areas (Champ, 2000). This assessment question encompasses the potential restriction of global uses of TBT and TPT in antifouling paints and other uses, as well as further national or local restrictions. The question must address the global consequences of local use due to movement of treated vessels and long-range transport of the compounds.

While the issue is not addressed in this assessment due to lack of evidence, it should be noted that the release of dibutyltin compounds from polyvinyl chloride polymers, and from consumer products, as a metabolite from TBT, may also pose a risk to human health and the environment.

2.3 Assessment endpoints

The regulation of TBT was based on the observation of deformities and imposex in molluscs. Hence, the frequency of deformities must be an endpoint in any new assessment.

Reproductive effects of TBT and TPT observed both in rodents and some aquatic organisms make reduced fecundity and developmental abnormalities another potential endpoint for both humans and nonhuman organisms.

Finally, organotin compounds exhibit immunotoxic effects, making increased frequency of disease an important endpoint for both humans and nonhuman organisms.

If risks of any of these organism-level effects are estimated to be significant for nonhuman organisms, risks to higher-level endpoints should be estimated. Depending on the species and situation, these could include population production or abundance, community composition, or ecosystem production.

2.4 Conceptual models

A conceptual model of sources, fate, exposure and effects of organotins is shown in Fig.1. Sources include treatment of vessels and other marine structures with organotin antifoulants and treatment of waters with organotins to suppress molluscs. In water, the

compounds may partition to suspended solids and deposit in sediments. In addition, sediments may be contaminated by paint and paint chips from hull-maintenance operations. Organisms may be directly exposed to organotins in water and sediment. Organotins may also be bioconcentrated and then bioaccumulated through aquatic food webs. Humans may experience health effects or socioeconomic effects due to loss of livelihood and cultural practices.

The conceptual model illustrates the potential utility of integration in risk assessment. In this case, humans, seabirds and marine mammals share similar exposure scenarios, through common sources, environmental fate of chemicals and media of intake, leading to high body burdens. In addition, the effects on nonhuman organisms have consequences for humans such as the losses experienced by oyster farmers and workers.

Other potential sources of exposure, such as polyvinyl chloride tubing in waterworks or consumer products, are not dealt in this paper.

2.5 Analysis plan

An analysis plan for an assessment of the need for further regulation of organotin compounds should go beyond the focus on local effects of antifoulants on highly sensitive molluscs. It should consider the regional and global consequences of all uses and releases of organotins. It should also consider the risks from specific mechanisms of toxic action on the full range of exposed species.

Environmental sources, fate and distribution of organotin compounds must be assessed quantitatively. This requires inventorying current and historic uses, measuring the compound in environmental compartments, estimating transformation rates and partitioning parameters, and using them to generate models of human and environmental exposure. Such models are required for both local and global scales.

Additional studies should be performed to elucidate the mechanisms of toxicity behind the toxicity profile in laboratory mammals and other organisms. The implications for toxic mechanisms of the commonalities and differences in human and nonhuman organisms, especially difference in metabolism, must be taken into account. Because organotins have been found to bioaccumulate in marine organisms, it will also be important to determine how they interact (i.e., in an additive, synergistic or inhibitory manner) with other bioaccumulated marine contaminants such as mercury, PCBs and chlorinated dioxins.

3. Characterisation of Exposure

3.1 Sources and emissions

Organotin compounds are still used as antifouling agents in many developed countries for boats over 25 m in length and on all boats in developing countries where no regulations exist. Their principal use has been in anti-fouling paints, from which they are released directly to the environment by leaching during use or in paint sandblasted from hulls during maintenance.

Organotin compounds are also used as fungicides or molluscicides in some countries, either applied directly or used to treat wood for piers and other materials.

3.2 Transport and fate models

The most important common route of exposure for humans and nonhuman mammals is consumption of contaminated seafood. In addition, aquatic organisms are directly exposed to contaminants in water and sediment. Our knowledge of exposure to organotins is largely based on analyses of waters and tissues of various organisms at local, regional and global scales. However, the release, distribution, and fate of organotins from various sources have not been modeled like the persistent organochlorine compounds, although the major sources and distribution by global processes is fairly clear now.

Environmental concentrations of TBT and TPT vary depending upon how, when and where compounds are used. Up to 1.58 μg/l (sea water) and 7.1 μg/l (fresh water) of TBT, and nearly 200 ng/l of TPT (Table 1) were detected in some bay areas or marinas with many boats treated with organotin-based antifouling-paints (IPCS, 1999 a & b).

Concentrations of TBT and TPT went down to 16.4 ng/L (TBT) and 1.8 ng/L (TPT) in 1993 in Tokyo bay area (Fig.2) after a 1991 ban on use of these compounds (National Committee for CICAD, 1997). However TBT concentrations appeared not to decrease further probably because boats from countries where regulations are not tight sail in the area. Similarly, aqueous TBT concentrations in Sarah Creek, Virginia, have shown little change in the 1990s after a steep decline in the late 1980s (Hall et al. 2000). This was attributed to mobilization of TBT from sediments.

TBT and TPT are sparingly soluble in water and easily adsorbed to particulate matter in the aquatic environment. Hence they are accumulated in sediment where they are relatively persistent and are taken up by the benthic organisms such as clams. TBT and TPT are accumulated in fish and other aquatic organisms with bioconcentration factors of 10^2-10^4 (Table 1). In a global survey of organotin pollution using livers of squids, Yamada et al (1997) found high levels in coastal waters of Japan and France.

These transport and fate properties are reflected in the results of a mathematical simulation of TBT in a large freshwater lake by Traas et al (1996). They predicted that, following restriction of TBT use, aqueous concentrations would decrease rapidly, but concentrations in sediment and biota would decrease slowly.

3.3 Dose due to seafood consumption

The average intake of TBT by humans from seafood may be estimated from standard market-basket surveys. A survey conducted yearly in Japan by ca. ten local research stations estimated that the average Japanese TPT and TBT intakes in 1997 were 2.7 μg/day/ person and 2.3 μg/day/person (as chloride), respectively (Fig. 3). Keithly et al (1999) estimated TBT intake

from analyses of five to nine seafood species purchased from markets in eight cities in Asia, Australia, Europe and the USA. Based on national diets and geometric means of seafood contamination from Keithly et al. (1999), TBT doses can be estimated to range from 0.18 (United Kingdom) to 2.6 (Korea) μg/day/ person. Another study, which analyzed seafood purchased in the U.S., gave similar results (Cardwell et al. 1999a).

3.4 Internal exposure

Body burdens of organotins are highly variable, due to differences in external exposure and metabolism. The highest observed levels are in dolphins, which lack metabolic capability and accumulate high levels of organotins in their body through food chains (Iwata et al., 1997; Lee, 1996). Levels are generally lower in invertebrates and in fishes. Although data are sparse, body burdens are high enough to suggest that there could be some risk to humans and certain marine mammals (Table 1).

Body burdens of TBT in the livers of Japanese males (taken from four people by autopsy in 1997/1998) were estimated to be 84 ng/g (Table 1; Takahashi et al, 1999 a & b). Interestingly, the relatively concentrations of butyltin compounds in liver and kidney is similar to those of methyl mercury. This suggests that their distributions are less dependent on their affinity to lipid than other persistent organic pollutants such as PCBs and DDT (Tanabe et al, 1981).

TBT and TPT also accumulate in livers and kidneys of nonhuman mammals. More than 10 g/g of butyltin ions, on a wet weight basis, were detected in the livers of dolphins collected in the semi-closed Seto Inland Sea, Japan, in 1985 (Iwata et al., 1997) and in the Gulf coast of the USA in 1989 (Kannan et al., 1997). They have also been found in the blubber and adrenal glands of coastal whales (Iwata et al., 1995), in the hair of sea lions and the feathers of common cormorants (Kim et al., 1996, Guruge et al., 1996). The lack of key metabolic enzymes in some cetaceans accounts for the differences observed in human and cetacean body burdens.

3.5 Analytical tools

Integrated assessment should be based on consistent and reliable sampling, preparation and chemical analysis techniques. In addition, common statistical designs and common approaches to estimating spatial and temporal variance are needed to allow global integration of human and ecological exposure estimation and modeling. This is an important area for international and interdisciplinary harmonization.

4. Characterization of Effects

4.1 Reported effects and mode of action

The extreme toxicity of TBT to molluscs and its peculiar and highly specific effects have raised concerns about toxic effects on humans and other organisms. Although toxicological profiles of organotin compounds are complex in both aquatic organisms and laboratory mammals, integration of knowledge of the diverse effects of organotin compounds in various

organisms will shed light to possible common mechanism of some effects in humans and nonhuman organisms. Recent reports support this notion as described below.

(1) Effects on aquatic organisms:

Toxicological profiles from conventional toxicity testing of aquatic organisms with TBT and TPT are presented in Tables 2A-D. The effects levels are low, but not remarkable for a biocide. The range of acutely lethal concentrations across species (700x), is also not particularly wide. However, some of the intraspecies variances in sensitivity are quite large. In particular, acute LC_{50} values in larvae and adults of the Pacific oyster *Crassostrea gigas* are 1.6 and 1800 μg/l for TBT while chronic larval mortality occurs at 0.05 μg/l and shell deformities occur at 0.02 μg/l (IPCS 1990, EPA 1997).. The effect of TBT that has made it remarkable is imposex in gastropods, which occurs at as little as one ng/l and affects at least 150 species (deFur et al. 1999). That effects level is less than a tenth of those observed in standard chronic toxicity tests (Table 2B). While imposex appears to be a result of perturbation of estrogen formation, the mechanism of action is still not clear (Oberdorster and Cheek, 2001). Symptoms of TBT toxicity in fish include thymus reduction, decrease in numbers of lymphocytes, and inhibition of gonad development (IPCS, 1999b). These symptoms suggest that studies on mechanism of action or field studies may reveal reproductive or other effects at lower concentrations than those reported from the subchronic tests of fishes conducted to date.

(2) Effects on laboratory mammals:

TPT and TBT produce various health effects in laboratory mammals, including effects on the immune system, such as decreases in immunoglobulin concentrations, lymphopenia, and thymus or splenic atrophy in rats and mice, reproductive/developmental effects (LOAELs: lowest-observed-adverse-effect-levels are mostly in the several mg/kg range or lower), hyperplasia/adenomas on endocrine organs or decrease in white blood cells at 0.3 mg/kg bw. or lower in rat 2-year study with TPT (IPCS, 1999a, Table 2). Similar effects at similar concentrations were seen for TBT with a NOAEL (no-observed-adverse-effect-level) of 25 g/kg bw/day (IPCS, 1999b).

(3) Integration in multiple endpoints and multiple agents linked to action mechanism

Common endpoints, such as immunotoxicity found in both aquatic organisms and laboratory mammals appear to share common mechanisms of action. For example, immunotoxic action of organotins could partly be caused by cytoskelton modification in addition to perturbation of thymocyte Ca^{2+} homeostasis which may be linked to apoptosis of thymus cells caused at **5** μM level by TBT or DBT (Chow & Orrenius, 1994).

Proliferative responses of peripheral blood mononuclear cells of human and dolphins to coplanar PCBs and TBT were assayed after stimulation with different concentrations of mitogens (Nakata et al., 1998). Mitogen responses were inhibited at concentrations of 30 nM and 300 nM of TBT, in humans and marine mammals, respectively, whereas PCBs did not markedly affect the response at concentrations tested (2.7 pM -34 nM) in human cells.

Potentiation of ethoxyresorufin-o-deethylase (EROD) activity and cytotoxicity detected in rat hepatoma cells as a consequence of co-exposure to PCB and TBT is of considerable toxicological significance, given their co-accumulation in a variety of aquatic organisms (Kannan, et al, 1998).

In the case of reproductive effects, imposex in the gastropods was suggested to be related to inhibition of CYP (P450)1A1-dependent aromatase which catalyzes aromatization of androgen to estrogen (Bettin et al., 1996). However, it may also result from inhibition of other steroid-synthesizing enzymes or to direct effects on the neurohormonal system (Oberdorster and Cheek, 2001). The most sensitive reproductive effect in rats is implantation failure in early stage of pregnancy (Ema et al., 1997), which is not yet known to be related to the mechanisms suggested above.

TPT at micromolar concentrations induced calcium overload in rat pheochromocytoma cells, which caused internucleosomal DNA cleavage typical of apoptotic cell death (Viviani et al., 1995). As Ca^{2+} is involved in signal transduction in regulating various cellular activities, it could be possible that perturbation of Ca^{2+} homeostasis at the cellular level can cause a variety of effects at various concentrations depending on different critical concentrations of organotin compounds at the target organs.

Inhibition of ion transport, oxidative phosphorylation in mitochondria and cell membrane damage are suggested as other causes of organotin toxicity (Fent, 1996).

4.2 Biomarkers and indicators

Where appropriate populations of gastropods occur, the presence of masculinized female snails (imposex) may be used as a bioindicator of the presence of toxicologically significant levels of organotin compounds (Davies et al. 1987). Biochemical biomarkers of organotin exposure or effects may be developed, as mechanisms of action become better understood.

4.3 Direct and indirect effects

The deformities of oysters had economic effects on oyster farmers in France, which are likely to have had social and psychological sequella. Those effects and the observation of imposex in snails led to the restriction of TBT on small recreational and commercial craft. Those restrictions have associated costs due to the substitution of other antifouling paints, greater operating costs, and more frequent maintenance. If it is determined that organotins in seafood are significantly affecting humans and wildlife, indirect effects could result from restrictions of seafood consumption and from further restrictions on antifouling paints.

5. Risk Characterization

Risk is a function of the magnitude of exposure and the toxicity of the compounds. Risks to aquatic organisms have been characterized on the basis of aqueous concentrations. Risks to humans and piscivorous wildlife have been estimated based on concentrations in seafood and body burdens.

5.1 Combining exposure and effects: aquatic biota

Cardwell et al. (1999b) assessed risks from TBT to populations of aquatic organisms in the U.S. by comparing the distributions of acute and chronic effects benchmarks to the distributions of concentrations measured in seven harbors. They found that 25% of species in marinas were likely to experience death or decrements in growth or reproduction prior to 1989. However, by 1996, 6% of species in the sampled marinas experienced those risks. Hall et al. (2000) assessed risks from TBT to the aquatic ecosystem of the Chesapeake Bay by comparing the distributions of acute and chronic effects benchmarks to the distributions of concentrations measured at various localities in the Bay. Significant risks of chronic effects were found in several locations.

The authors of both of these assessments limited themselves to standard toxicity data and standard risk characterization methods, which are derived from methods for calculating water quality criteria. Because this practice excluded imposex and shell deformities, the assessments did not include the very effects that led to the restrictions on use of TBT. Cardwell et al. (1999b) dismissed these effects as biomarkers, which had no population-level consequences. As a result, thresholds for significant risks in the assessments (5 and 10 ng/L) were above the 1ng/L threshold for imposex (Hall et al. 2000, Cardwell et al. 1999). One might argue that the fact that imposex and shell deformities prompted a specific act of the U.S. Congress and similar responses in other countries is sufficient grounds for including those effects as endpoints. Further, the severe economic effects of oyster deformities on oyster fishermen suggest that nonstandard effects may be significant. Further, imposex does have consequences for reproduction, which have not been demonstrated in standard tests. Hence, risks to aquatic organisms are greater if the specific adverse effects of TBT are included in the assessment.

These risk characterizations focused on TBT release from boats. They did not explicitly consider other uses of TBT or other organotins. For example, the use of TBT as a molluscide to control schistosomiasis has resulted in severe effects on fish (Seinen et al. 1981). Because some fish are as sensitive as snails, such effects are to be expected (Seinen et al. 1981).

5.2 Combining exposure and effects: humans and piscivorous wildlife

Daily intake values of TPT and TBT for Japanese can be compared with the acceptable daily intake (ADI) of the World Health Organization (0.5 μg /kg bw/day) which corresponds to 25 μg /day for a Japanese person of 50 kg bw, and a guidance value evaluated by the Final Review Board of the IPCS for the CICAD on tributyltin oxide (TBTO) (0.3 μg /kg bw/day)

which corresponds to 15 μg /day per a Japanese person of 50 kg bw, to be 33.4% and 10.8%, respectively (when combined sums up to 44.2%). Since TBT and TPT exert similar toxicities to humans and organisms in the environment, combined risk from coexposure to TPT and TBT must be taken into account considering their use patterns and amount of use (IPCS, 1990; Sekizawa, 1998).

Cardwell et al. (1999) and Keithly et al. (1999) performed similar risk characterizations for people consuming fish in the North America, Asia, Australia and Europe. Using a 70 kg body weight, they found that geometric mean daily intakes of TBT were 0.9% (United Kingdom) to 12% (Korea) of the 0.3 μg TBT/kg/day tolerable dose. They analyzed a relatively small number of mostly pelagic species, which are less polluted because they live in the open ocean. In contrast, the Japanese study included various food items purchased from markets in various cities and composite foods prepared according to average food intake of recent years to estimate mean intake of various locations in the country. Since several organisms such as squids and dolphins from coastal waters of France, USA and Japan were shown to be similarly contaminated with TBT and TPT, it is probable that the apparent difference in the results between Keithly et al (1999) and the Japanese survey are primarily due to the seafood items analyzed. TBT levels causing inhibition in this study are close to those found in the marine mammals inhabiting coastal waters in Japan and North America that some populations of coastal cetaceans may be at risk of immunotoxicity.

Because of their exclusively piscivorous diet, many birds and mammals are more at risk than humans from dietary exposure to organotins. Some marine mammals, such as Dall's porpoise are devoid of CYP enzymes, which can break down TBT and DBT to MBT, and current levels of organotin body-burden are high enough to cause immune deficiency in those animals increasing their susceptibility to opportunistic infections (Tanabe, 1998; Nakata et al, 1998). In addition, organotin compounds are shown to elicit synergistic effects with PCB (Rice & Rozwell, 1998), which occur at high levels in piscivorous birds and mammals all over the world. However, these risks have not been quantified.

5.3 What is integrated?

The use of a common toxicity data set and common data on organotin concentrations in seafood to assess risks to humans and wildlife is an obvious form or integration. Such an assessment has not been performed, but the human risks are high enough to suggest a significant risk to piscivorous wildlife, particularly in ports and harbors. The 100% fish diet of these organisms and the fact that their sensitivity may be greater than laboratory mammals is cause for concern. Birds are commonly more sensitive than mammals.

The inclusion of imposex in molluscs as an endpoint effect may constitute a more subtle form of integration. While ecological risk assessors excluded this effect as not ecologically appropriate, the public and law makers appear to have made an analogy to humans and determined that development of male genitals in a female organism is adverse. That is, nonscientists performed an integration of health concerns and observed ecological effects that

bypassed conventional ecological criteria for declaring an effect to be adverse. Similarly, the deformities in oysters became endpoints in regulatory assessments both because of an implicit analogy to human deformity and because of the socioeconomic significance.

Mechanistic toxicology is another potential area for integration. The rather unusual and specific effects of organotins in molluscs suggests that a mechanistic understanding of the effects of organotins might reveal the potential for effects that are not detected in conventional mammalian or ecological toxicology.

The immunotoxic effects of organotins highlight the need for improved methods in risk assessment for that mode of action. Currently it is not feasible to predict the health consequences of a change in immune function or structure or to determine whether observed epidemics or epizootics were enhanced by immunotoxic chemicals. An integrated approach to this problem should be fruitful and efficient.

5.4 Determining causation

The concern for risks to aquatic biota from TBT originated with observations of effects on molluscs. The cause of these effects were determined by associating the effects spatially and temporally with the use of antifouling paints, by demonstrating effects in controlled laboratory exposures, and by demonstrating that effects in the field were associated with body burdens of TBT similar to those in affected organisms in the laboratory. Similarly, mortality of fish was associated with the use of TBT as a molluscicide and subsequent laboratory studies confirmed that TBT was a sufficient cause for those effects (Seinen et al. 1981). Some effects on piscivorous wildlife have been observed which, from circumstantial evidences, can be related to exposures to pollutants including organotins. A similar approach to determining causation, based on the weighing of laboratory and field derived data, should be employed when such effects are suspected.

5.5 Uncertainty and variability

Conventional ecological toxicology, and the risk assessments that rely on it, are uncertain due to the limited number of species and responses that are measured. This is illustrated by the observance of imposex and shell deformities in field populations, but not in standard tests. This suggests that other effects may be missed.

The immunotoxicity of organotins poses uncertain risks. Given current knowledge, it is not possible to predict the effects of a particular change in immune system structure or function. It is also not possible to confidently associate epidemics or epizootics with contamination by organotins or any other immunotoxic chemical.

Market basket studies in Japan show that there was about a two-fold variation in intake estimates between the national average value and that of local governments in the 1990-1993 period (Tsuda et al., 1995). Since there will be people who eat much more seafood than average,

variability in intake will contribute to variability in risks among populations, and this uncertainty in risks must be taken into consideration in protecting different populations (Sekizawa, 1998).

5.6 Presentation of results

The results of an integrated assessment of health and ecological risks should be presented in a consistent manner. That is, similar graphical, tabular and textual presentations should be used so that the current risks and consequences of action for humans and ecological receptors are clear and readily compared or combined.

6. Risk Communication

The history of TBT regulation constitutes a useful case study in risk communication. Early regulations of TPT and TBT as pesticides, in occupational settings, or in use for consumer products were based on human observations and animal studies. However, the use of TBT as antifoulants for boats and fishing nets was restricted based on demonstrated effects on nonhuman organisms without any indication that humans were at risk from this source. The affected species were invertebrates and therefore neither similar to humans nor aesthetically appealing. The public acceptance of regulatory action seems to suggest that humans are defining their interests broadly and are likely to see consequences for themselves in even the lowliest organisms, particularly if the effects are vivid. This suggests that risk communication for all chemicals should present health and ecological risks in an integrated fashion. If risk assessors do not explain the relationships in a coherent fashion, the public is likely to make its own inferences. For example, if the effects of TBT on sexual development of molluscs do not imply analogous effects in humans, those differences must be elucidated and clearly communicated.

More generally, a holistic approach to risk communication is imperative to effective risk management. It should facilitate environmental decision making by providing a consistent and coherent set of human and ecological risk estimates to help identify priorities in action. Communication of the results in a consistent and integrated manner to risk managers and stakeholders will support their understanding of assessment results and the impacts of possible management actions.

7. Risk Management

Existing environmental controls of organotin compounds as antifoulants are based mostly on incidental findings of localized effects on molluscs, particularly reproductive failure and deformity of snails and oysters. Following the lead of France, most developed countries banned or restricted the use of organotin compounds on for small boats (typically those less than 25 m in length). Their use on larger boats was continued due to the large economic benefits. TBT concentrations in Tokyo bay appeared not to decrease further after complete ban of use in Japan in 1990, probably because boats from countries where regulations are not such tight sail in the area. In many developing countries organotins are not regulated. Although monitoring has shown that local organotin levels have greatly declined as a result of regulation, unregulated

boats travel all over the world and release organotin compounds. In addition, organotin-containing paint is released during ship scraping and repainting.

In this context, regional and global scale pollution by both TBT and TPT need to be taken into account. For example, local management actions restricting use of organotin antifouling paint are less effective if boats from areas permitting such paint utilize the same area. In addition, the processes of global hydrological and meteorological circulation, which have distributed organochlorine chemicals, may also result in surprising distributions of organotins.

In addition to their use in anti-fouling paints, organotin compounds are used as fungicides and molluscicides (the use was prohibited rather early in Japan). They also occur in plastic products, some of which contaminate foods as reported by Takahashi et al. (1999b) who detected elution of dibutyltin during oven baking from cooking sheets used to wrap baked cakes. This implies that, for every application, the amount of use of organotin compounds, which may potentially contaminate the environment and food, needs to be surveyed and examined for counter measures to be effective.

The toxicity of organotins, their persistence, and their continued use make them chemicals of concern. The possibilities of combined effects of different organotins, their global distribution and novel specific toxic effects; suggest the need for integrated research and risk assessment. Without globally integrated assessments followed by appropriate counter measures, risk to humans and other organisms may not be sufficiently diminished.

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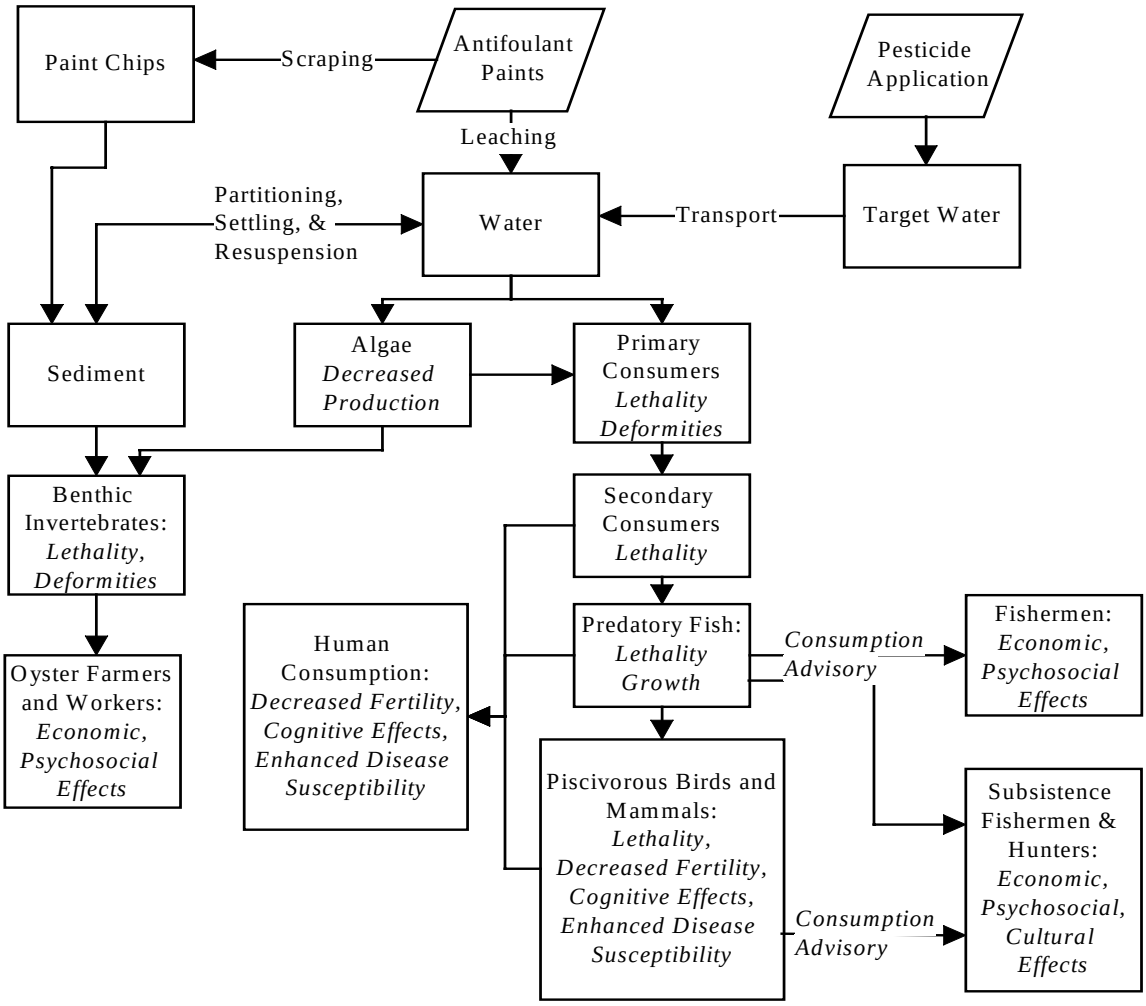

Fig.1 A conceptual model for exposure and effects of humans and marine mammals to tributyltin and triphenyltin compounds

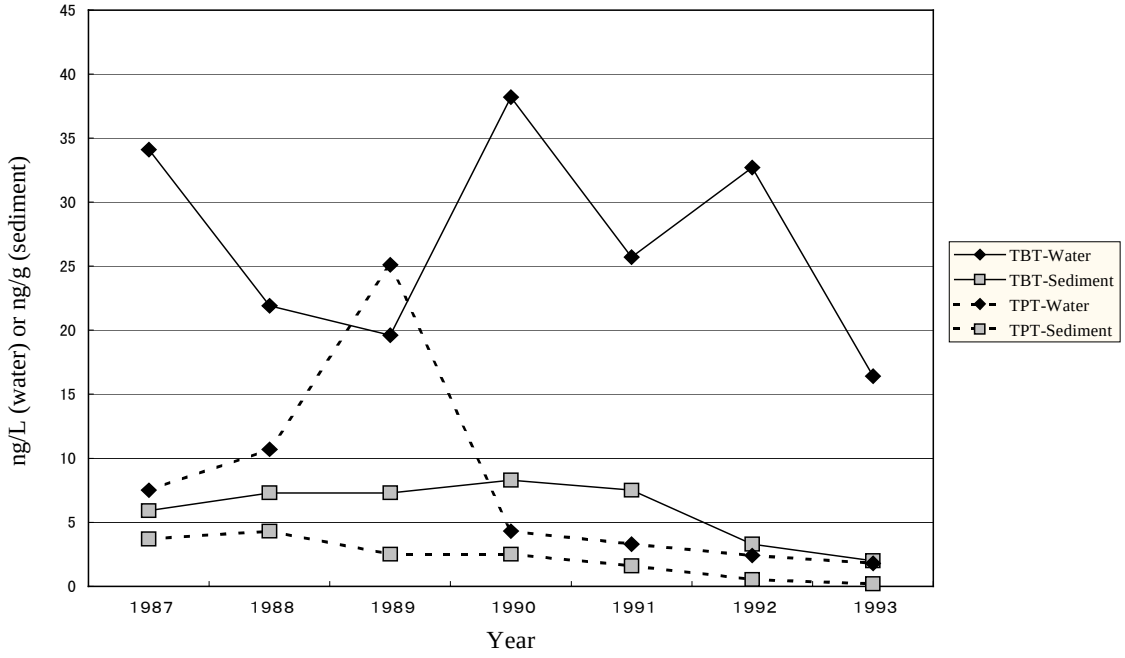

Fig. 2 TBT and TPT concentrations in Tokyo bay area
(National Committee for CICAD)

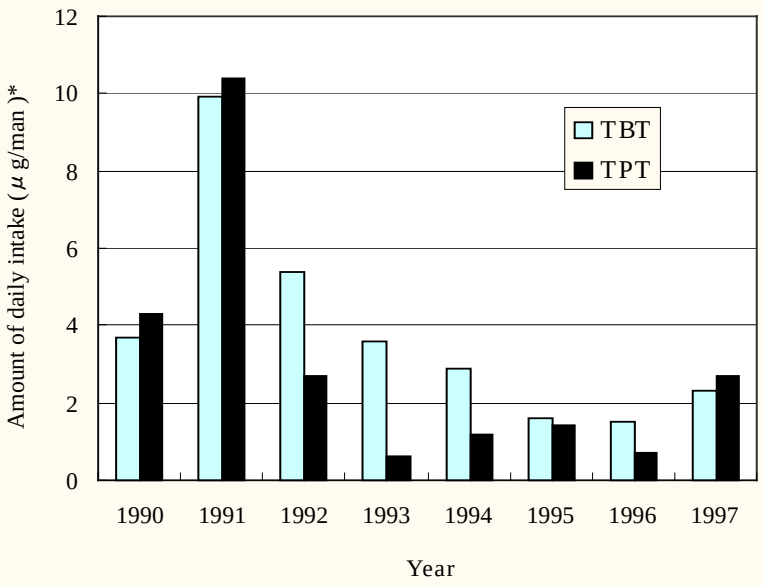

Fig. 3. Estimation of daily intake of TBT and TPT in Japan by the market basket method.

* as triphenyltin chloride or tributyltin chloride

Table 1 Environmental fate, exposure and body burden of humans and organisms in the environment with TBT and TPT
(prepared from IPCS, 1999 a & b and EPA 1997)

	TBT	TPT
Concentrations in the surface water	up to 7.1 µg/l (fresh water area); up to 1.58 µg/l (sea water area)	nearly 200 ng/l (bays & marinas)
Bio-concentration factor	100 - 30,000 in bacteria & algae, 2,000 - 180,427 in molluscs, 24- 1976 in whole fish	32,500 in intestinal sac of a fresh water snail, 7000 in Pacific oyster 257- 4100 in whole fish
Average daily intake (market basket survey)	2.3 µg/day/person (as chloride) in Japan in 1997	2.7 µg/day/person (as chloride) in Japan in 1997
Body burden in liver	84 ng total butyltin compounds/g wet weight - of which 79% were DBT for humans; up to 11,340 ng/g wet weight for dolphins	

Table 2A Concentrations of tributyltin compounds lethal to aquatic organisms (data from IPCS, 1999a, EPA 1997 and Hall et al. 2000)

Taxon (number of tested species)	Criterion	Effective Concentrations (g/l)
Echinoderms (1)	96 h LC_{50}	0.42
Saltwater rotifer (1)	24 h LC_{50}	300
Freshwater rotifer (1)	24 h LC_{50}	19
Freshwater hydrozoans (3)	96 h LC_{50}	1.1 - 1.8
Saltwater molluscs (6)	48-96 h LC_{50}	0.71 - 1800
Freshwater molluscs (4)	24-96 h LC_{50}	12 - 110
Saltwater crustaceans (18)	24-96 h LC_{50}	0.42 - >15
Freshwater insects (3)	24-96 h LC_{50}	3.3 - 16
Saltwater annelids (2)	96 hr LC_{50}	2.0 - 6.8
Freshwater annelids (1)	96 hr LC_{50}	5.4
Saltwater amphioxus (1)	96 hr LC_{50}	<10
Saltwater fishes (9)	48-96 hr LC_{50}	1.5 - 17
Freshwater fishes (5)	96 hr LC_{50}	1.3 - 7.2

Table 2B Chronic or subchronic sublethal toxicity of tributyltin compounds to aquatic organisms (data from IPCS, 1999a, EPA 1997, and Hall et al. 2000)

Organism	Criterion	Effective Concentration (g/l)[1]
Freshwater algae (3 species)	IC_{50} (primary production)	10 - 15
Saltwater algae (5 species)	IC_{50} (primary production)	0.92 - 320
Acartia tonsa (Copepod)	6 day	0.014
Euryptemora affinis (Copepod)	13day Life Cycle test	<0.088 & 0.15
Acanthomysis scuppta (Mysid)	63 day Life Cycle test	0.13
Daphnia magna	21day Life Cycle test	0.14 & 0.25 (2 tests)
Mytilus edulis (Mussel)	33 day CV	0.017
Crassostrea gigas (Pacific oyster)*	Chronic larval mortality Shell thickening	0.05 0.02
Nucella lapillus (Atlantic dogwinkle)*	2 year Life Cycle tests	0.002 (imposex and sterility)
Rainbow trout fingerlings	110 day subchronic	0.2 (histopathology & 20% growth reduction
Pimephales promelas (fathead minnow)	33 day CV, Early Life Stage test	0.26

* marine and estuarine species

[1] Effective concentrations, except where noted, are chronic values (CVs) which are the geometric means of No Observed Effect Concentrations (NOECs) and Lowest Observed Adverse Effects Concentrations (LOECs).

Table 2C. Acute toxicity of triphenyltin compounds to aquatic organisms (modified from IPCS, 1999a)

Organism	Criterion	Levels and/or Note
Debaryomyces hansenii (yeast)	Minimal Inhibitory Concentration	5 μg/ml
Ankisrodesmus (fresh-water alga)	4hr IC_{50} for primary productivity	10 μg/l, static condition, at 20C
Skeletonema costatum: major component of fouling slime*	EC_{50} for carbon fixation, and LC_{50}	0.92 μg/l, and 13.8 μg/l
Daphnia magna (water flea)	48 h LC_{50}	10 μg/l
Nitrocra spinipes (harpacticoid copepod)	96 hr LC_{50}	8 μg/l
Eight fish species	96 hr LC_{50}	*Pimephales promelas* (fathead minnow) most sensitive species, 7.1 μg/l
Pagrus major (red sea bream)*	48-hr LC_{50}	12.6 μg/l

* marine and estuarine species

Table 2D Chronic/subchronic toxicity of triphenyltin compounds to aquatic organisms (modified from IPCS, 1999a)

Organism	Criterion	Levels and/or Note
Natural community of fresh water algae	50% reduction of reproduction and primary production	2 µg/l, Indigenous algae more sensitive than pure cultures
Daphnia magna	21days No-Observed-Effect Concentration	0.1 µg/l
Lymnae stagnalis: a fresh water sludge snail	9 days LC_{100}, or deficiencies in growth, mobility, and embryo development after 5 weeks exposure	10 µg/l for LC_{100}, and 2 µg/l for deficiencies
Thais clavigera (Japanese rock shell)*	Imposex: RPL (relative penis length) in female	RPL significantly increased with injection of 0.1 µg TPT/g wet tissue and culture for 30 days, or at 1 ng/l in water.
Pimephales promelas (fathead minnow)	30-day LC_{50}, NOEC, and LOEC (Lowest-Observed-Effect Concentration)	1.5, 0.15, and 0.23 µg/l, respectively

***** marine and estuarine species

Table 3 Health effects of triphenyltin compounds (modified from IPCS, 1990a & b)

Type of test	Organisms (route of exposure, duration of test)	Results/remarks
Single exposure	Rat (oral)	LD_{50} 160 mg/kg
Short term	Dog (oral, 52 weeks)	NOAEL: 0.21 mg/kg bw/day, based on relative liver weight decrease at effect levels;
	Rat (dermal, 29 days)	NOAEL: 10 mg/kg bw/day, based on erythema, mortality, lymphocyte decrease at effect levels,
	Rat(inhalation, 4-weeks)	NOAEL: 0.014 mg/m^3 based on IgM (an immuno-globulin species) increase at effect levels
Long-term	Mouse (feeding, 80 weeks)	NOAEL: 0.85-1.36 mg/kg bw/day, based on decreased body weight at effect levels;
Genotoxicity	In vivo/In vitro	Mostly negative
Reproduction	Rat (feeding, two generation)	NOAEL: 0.4 mg/kg bw/day, based on decreased litter size, pup weight, relative spleen/thymus weight in weanlings at effect levels
Teratogenicity	Rabbit (gavage, day 6 to day 18 of gestation)	NOAEL for maternal toxicity: 0.1 mg/kg based on decreased body weight gain
Immunotoxicity *	Rat (feeding, two years)	Immunosuppresive. LOAEL: 0.3 mg/kg bw/day, based on reduced immunoglobulin levels and reduction in white blood cell count
Neurotoxicity	Rat (gavage, 6 weeks)	Toxic at 0.36 mg/kg bw/day in maze learning test

* With tributyltin oxide, when weanling rats fed orally up to 4.5 months, NOAEL was 0.025 mg/kg bw/day, based on the depression of IgE titres and impairment of clearance of injected *Trichinella spiralis* at effect levels