

Reviews of Environmental Contamination and Toxicology

VOLUME 184

Reviews of Environmental Contamination and Toxicology

Continuation of Residue Reviews

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VOLUME 184

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Reviews of Environmental Contamination and Toxicology

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Springer

New York: 233 Spring Street, New York, NY 10013, USA
Heidelberg: Postfach 10 52 80, 69042 Heidelberg, Germany

Library of Congress Catalog Card Number 62-18595.

Printed in the United States of America.

ISSN 0179-5953

Printed on acid-free paper.

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Printed in the United States of America.

ISBN 0-387-22398-3

SPIN 10954799

springeronline.com

Foreword

International concern in scientific, industrial, and governmental communities over traces of xenobiotics in foods and in both abiotic and biotic environments has justified the present triumvirate of specialized publications in this field: comprehensive reviews, rapidly published research papers and progress reports, and archival documentations. These three international publications are integrated and scheduled to provide the coherency essential for nonduplicative and current progress in a field as dynamic and complex as environmental contamination and toxicology. This series is reserved exclusively for the diversified literature on “toxic” chemicals in our food, our feeds, our homes, recreational and working surroundings, our domestic animals, our wildlife and ourselves. Tremendous efforts worldwide have been mobilized to evaluate the nature, presence, magnitude, fate, and toxicology of the chemicals loosed upon the earth. Among the sequelae of this broad new emphasis is an undeniable need for an articulated set of authoritative publications, where one can find the latest important world literature produced by these emerging areas of science together with documentation of pertinent ancillary legislation.

Research directors and legislative or administrative advisers do not have the time to scan the escalating number of technical publications that may contain articles important to current responsibility. Rather, these individuals need the background provided by detailed reviews and the assurance that the latest information is made available to them, all with minimal literature searching. Similarly, the scientist assigned or attracted to a new problem is required to glean all literature pertinent to the task, to publish new developments or important new experimental details quickly, to inform others of findings that might alter their own efforts, and eventually to publish all his/her supporting data and conclusions for archival purposes.

In the fields of environmental contamination and toxicology, the sum of these concerns and responsibilities is decisively addressed by the uniform, encompassing, and timely publication format of the Springer-Verlag (Heidelberg and New York) triumvirate:

Reviews of Environmental Contamination and Toxicology [Vol. 1 through 97 (1962–1986) as Residue Reviews] for detailed review articles concerned with any aspects of chemical contaminants, including pesticides, in the total environment with toxicological considerations and consequences.

Bulletin of Environmental Contamination and Toxicology (Vol. 1 in 1966) for rapid publication of short reports of significant advances and discoveries in the fields of air, soil, water, and food contamination and pollution as well as

methodology and other disciplines concerned with the introduction, presence, and effects of toxicants in the total environment.

Archives of Environmental Contamination and Toxicology (Vol.1 in 1973) for important complete articles emphasizing and describing original experimental or theoretical research work pertaining to the scientific aspects of chemical contaminants in the environment.

Manuscripts for *Reviews* and the *Archives* are in identical formats and are peer reviewed by scientists in the field for adequacy and value; manuscripts for the *Bulletin* are also reviewed, but are published by photo-offset from camera-ready copy to provide the latest results with minimum delay. The individual editors of these three publications comprise the joint Coordinating Board of Editors with referral within the Board of manuscripts submitted to one publication but deemed by major emphasis or length more suitable for one of the others.

Coordinating Board of Editors

Preface

Thanks to our news media, today's lay person may be familiar with such environmental topics as ozone depletion, global warming, greenhouse effect, nuclear and toxic waste disposal, massive marine oil spills, acid rain resulting from atmospheric SO_2 and NO_x , contamination of the marine commons, deforestation, radioactive leaks from nuclear power generators, free chlorine and CFC (chlorofluorocarbon) effects on the ozone layer, mad cow disease, pesticide residues in foods, green chemistry or green technology, volatile organic compounds (VOCs), hormone- or endocrine-disrupting chemicals, declining sperm counts, and immune system suppression by pesticides, just to cite a few. Some of the more current, and perhaps less familiar, additions include *xenobiotic transport*, *solute transport*, *Tiers 1 and 2*, *USEPA to cabinet status*, and *zero-discharge*. These are only the most prevalent topics of national interest. In more localized settings, residents are faced with leaking underground fuel tanks, movement of nitrates and industrial solvents into groundwater, air pollution and "stay-indoors" alerts in our major cities, radon seepage into homes, poor indoor air quality, chemical spills from overturned railroad tank cars, suspected health effects from living near high-voltage transmission lines, and food contamination by "flesh-eating" bacteria and other fungal or bacterial toxins.

It should then come as no surprise that the '90s generation is the first of mankind to have become afflicted with *chemophobia*, the pervasive and acute fear of chemicals.

There is abundant evidence, however, that virtually all organic chemicals are degraded or dissipated in our not-so-fragile environment, despite efforts by environmental ethicists and the media to persuade us otherwise. However, for most scientists involved in environmental contaminant reduction, there is indeed room for improvement in all spheres.

Environmentalism is the newest global political force, resulting in the emergence of multi-national consortia to control pollution and the evolution of the environmental ethic. Will the new politics of the 21st century be a consortium of technologists and environmentalists or a progressive confrontation? These matters are of genuine concern to governmental agencies and legislative bodies around the world, for many serious chemical incidents have resulted from accidents and improper use.

For those who make the decisions about how our planet is managed, there is an ongoing need for continual surveillance and intelligent controls to avoid endangering the environment, the public health, and wildlife. Ensuring safety-

in-use of the many chemicals involved in our highly industrialized culture is a dynamic challenge, for the old, established materials are continually being displaced by newly developed molecules more acceptable to federal and state regulatory agencies, public health officials, and environmentalists.

Adequate safety-in-use evaluations of all chemicals persistent in our air, foodstuffs, and drinking water are not simple matters, and they incorporate the judgments of many individuals highly trained in a variety of complex biological, chemical, food technological, medical, pharmacological, and toxicological disciplines.

Reviews of Environmental Contamination and Toxicology continues to serve as an integrating factor both in focusing attention on those matters requiring further study and in collating for variously trained readers current knowledge in specific important areas involved with chemical contaminants in the total environment. Previous volumes of *Reviews* illustrate these objectives.

Because manuscripts are published in the order in which they are received in final form, it may seem that some important aspects of analytical chemistry, bioaccumulation, biochemistry, human and animal medicine, legislation, pharmacology, physiology, regulation, and toxicology have been neglected at times. However, these apparent omissions are recognized, and pertinent manuscripts are in preparation. The field is so very large and the interests in it are so varied that the Editor and the Editorial Board earnestly solicit authors and suggestions of underrepresented topics to make this international book series yet more useful and worthwhile.

Reviews of Environmental Contamination and Toxicology attempts to provide concise, critical reviews of timely advances, philosophy, and significant areas of accomplished or needed endeavor in the total field of xenobiotics in any segment of the environment, as well as toxicological implications. These reviews can be either general or specific, but properly they may lie in the domains of analytical chemistry and its methodology, biochemistry, human and animal medicine, legislation, pharmacology, physiology, regulation, and toxicology. Certain affairs in food technology concerned specifically with pesticide and other food-additive problems are also appropriate subjects.

Justification for the preparation of any review for this book series is that it deals with some aspect of the many real problems arising from the presence of any foreign chemical in our surroundings. Thus, manuscripts may encompass case studies from any country. Added plant or animal pest-control chemicals or their metabolites that may persist into food and animal feeds are within this scope. Food additives (substances deliberately added to foods for flavor, odor, appearance, and preservation, as well as those inadvertently added during manufacture, packing, distribution, and storage) are also considered suitable review material. Additionally, chemical contamination in any manner of air, water, soil, or plant or animal life is within these objectives and their purview.

Normally, manuscripts are contributed by invitation, but suggested topics are welcome. Preliminary communication with the Editor is recommended before volunteered review manuscripts are submitted.

Tucson, Arizona

G.W.W.

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Organohalogen Contaminants in Delphinoid Cetaceans

Magali Houde, Paul F. Hoekstra, Keith R. Solomon,
and Derek C.G. Muir

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I. Introduction

For centuries, marine mammals have been the cornerstone of industrial and economic activities in many countries, as well as an important part of the subsistence harvesting of several aboriginal populations. As a consequence of human-related activities such as commercial whaling, habitat degradation, and declining fish stocks, as well as accidental capture in fishing gear and physical and acoustical disturbance by ship traffic, many populations of marine mammals have been depleted compared to historic population estimates (Reeves et al. 2003).

An additional threat to the health of marine mammals is contamination by chemical pollutants. Assessment of chemical residues in marine mammal tissues

Communicated by George W. Ware.

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has been conducted since the mid-1960s (Aguilar et al. 2002). The concern about the potential toxicity of chemical pollutants to physiological systems of marine mammal began when a series of die-offs occurred within a short period of time in different regions of the world. During the late 1980s, pinniped epizootics caused the deaths of approximately 20,000 northern European harbour seals (*Phoca vitulina*), hundreds of grey seals (*Halichoerus grypus*) (Osterhaus and Vedder 1988), and thousands of Baikal seals (*Phoca sibirica*) from Lake Baikal, Russia (Grachev et al. 1989). Additionally, during this period, more than 7000 bottlenose dolphins (*Tursiops truncatus*) were washed ashore along the central and southern Atlantic coastline of the United States (Kuehl et al. 1991). At the beginning of the 1990s, massive die-offs of striped dolphins (*Stenella coeruleoalba*) from the Mediterranean Sea (Aguilar and Borrell 1994a; Aguilar and Raga 1993; Kannan et al. 1993a) and bottlenose dolphins from the Gulf of Mexico (Kuehl and Haebler 1995) also occurred. In 2000, thousands of Caspian seals (*Phoca caspica*) from the Caspian Sea were found dead during another epizootic (Kennedy et al. 2000). Although deaths from die-offs were primarily attributed to distemper virus (or morbillivirus) infection (Aguilar and Raga 1993; Heide-Jørgensen et al. 1992; Kennedy et al. 2000), chemical contaminants have been suggested as contributing factors in these marine mammal epizootics.

Characterizations of chemical contaminants in tissues of Atlantic bottlenose dolphins that died during the American epizootic in 1987 reported significant concentrations of polychlorinated biphenyls (PCBs) (Kuehl et al. 1991). Likewise, assessment of environmental contaminants in the blubber of Mediterranean Sea dolphins indicated concentrations of PCBs two- to three times higher in striped dolphins found dead during the outbreak compared to free-ranging individuals sampled before and after the epizootic (Aguilar and Borrell 1994a). The high concentration of PCBs found in victims of mass mortalities, in addition to the known increased susceptibility to viral infections in experimentally exposed laboratory mammals such as mice, ducks, guinea pigs, and rhesus monkeys to PCBs (Friend and Trainer 1970; Thomas and Hinsdill 1978; Vos and De Roij 1972), led to the speculation about a possible suppression of immune functions associated with environmental pollution.

Few contaminant studies have been conducted on cetaceans, compared to pinnipeds, because of logistical, ethical, and legal constraints. The order *Cetacea* is divided into two suborders: Mysticeti, which are the baleen whales, and Odontoceti, which are toothed whales. In cetaceans, most chemical contaminant studies have been conducted on members of the toothed whale superfamily Delphinoidea (including three families: *Delphinidae*, *Phocoenidae* and *Monodontidae*), and these are reviewed here.

II. Persistent Organohalogen Contaminants

A. Physicochemical Properties

Exposure assessment of marine mammals to environmental contaminants is an important part of the management and conservation of wildlife populations. Persistent organohalogen contaminants (PHCs) are a major part of the investigation

of marine pollution. Industrial chemicals such as PCBs and various organochlorine pesticides such as dichlorodiphenyltrichloroethane (DDT), chlordanes (CHL), hexachlorocyclohexanes (HCH), and hexachlorobenzene (HCB) are commonly studied PHCs in marine mammals. Other persistent pollutants, including tris(4-chlorophenyl)methane (TCPM) and tris(4-chlorophenyl)methanol (TCPMe), which may originate from the production of synthetic high polymers and light-fast dyes for acrylic fibers (Jarman et al. 1992), the insecticide toxaphene (Vetter et al. 2001a), perfluorinated acids (PFAs) such as perfluorooctane sulfonates (PFOS) and related compounds (Giesy and Kannan 2002), and polybrominated flame retardants, such as polybrominated diphenyl ethers (PBDEs) (McDonald 2002), are of concern because of their widespread distribution in marine ecosystems and their potential toxicity. Additionally, compounds from natural origins, such as halogenated dimethyl bipyrolles, have been globally detected in marine mammals (Tittlemier et al. 2002). Brominated and chlorinated dimethyl bipyrolles appear to be produced in the northern Pacific by an unknown pathway or mechanism, and their spatial distribution shows a different pattern than that of anthropogenic organohalogen contaminants (Tittlemier et al. 2002).

PHCs vary in their chemical structures and physicochemical properties such as vapor pressure, octanol–water partition coefficient, and Henry’s law constant. In general, PHCs are chemically stable, resistant to biological or abiotic chemical breakdown, and, with the exception of perfluorinated acids, are lipophilic. This combination of physicochemical properties results in the environmental persistence of PHCs and their global dispersion and bioaccumulation in lipid-rich tissues of marine mammals. Moreover, the food chain transfer of PHCs and other contaminants to toothed whales has resulted in concentrations at several orders of magnitude greater than in species feeding at lower trophic levels, such as fish and baleen whales, as a result of biomagnification of contaminants through the food chain (Hoekstra et al. 2003).

B. Global Transport

The dispersion of PHCs in the marine environment depends on the physicochemical properties of compounds (particularly vapor pressure and air–water partition coefficient). Less volatile compounds, such as DDT and highly chlorinated PCBs, are usually found close to their emission source, as compared to the highly volatile chlorobenzene and HCH isomers, which are more globally distributed (Iwata et al. 1993; Li et al. 2002).

Long-range transfer of PHCs that are released in the environment may occur through oceanic and riverine transport. Global transfer of volatile and semivolatile PHCs can also occur through the volatilization of those contaminants from terrestrial soils and marine waters into the atmosphere, with ultimate deposition in remote regions through dry deposition of particles, gas exchange, or via precipitation scavenging of rain and snow (Macdonald et al. 2000). As a consequence of this long-range transfer, known as the “grasshopper effect” or global distillation (Mackay and Wania 1995), considerable concentrations of PHCs have

been found in the air, water, snow, and ice and in biological samples of marine organisms inhabiting polar regions (de Wit et al., 2004). The highest concentrations of HCH in seawater, for example, are found in the Arctic environment. The extent of degradation (e.g., via photolysis, hydrolysis, microorganisms, or free radicals) of contaminants in the atmosphere, in marine waters, or in the nearshore sediment varies with chemical structure. PCBs have been found to degrade in the atmosphere due to reaction with hydroxy radicals (Mandalakis et al. 2003), whereas HCHs have been found to be slowly degraded by microorganisms in ocean water (Harner et al. 2000; Li et al. 2002).

C. Sources and Spatial Distribution

In 2001, more than 120 countries signed the Stockholm Convention on Persistent Organic Pollutants, targeting 12 specific PHCs (i.e., aldrin, DDT, dieldrin, endrin, HCB, mirex, toxaphene, PCBs, polychlorinated dioxins, and furans, and chlordanes, including heptachlor) (UNEP 2001). This treaty, ratified in May 2004, bans 8 chlorinated pesticides, prohibits PCB production, and establish a long-term goal of eliminating DDT use. However, the treaty permits public health exceptions for the use of DDT in mosquito control to fight malaria in developing countries. Many industrialized nations have already banned the manufacture and use of DDT, which has resulted in a marked decrease of the global concentrations of this contaminant in marine ecosystems during the past 30 years (Aguilar et al. 2002). Unlike DDT, PCB concentrations have generally declined slowly or not at all over time in the marine ecosystem. The inadequate disposal, improper storage, accidental release, and ongoing use of PCBs in building materials and electrical equipment all contributed to the continuous input of these toxicants into the environment (Aguilar et al. 2002; Breivik et al. 2002a; Tanabe 1988).

To evaluate the spatial distribution of PHCs, a worldwide survey was conducted in 1989–1990 by Iwata et al. (1993) to assess PHC concentrations in air and surface water from various oceans. The survey indicated a higher level of atmospheric contamination in the Northern Hemisphere compared to the Southern Hemisphere (Iwata et al. 1993). These results may be explained by the greater number of industrialized countries found in the northern region of the globe and relatively greater releases from more intense industrial activities as well as indirect release from commercial use. Breivik et al. (2002b) suggested that approximately 97% of the global historical use of PCBs has occurred in the Northern Hemisphere. As well, the most elevated concentrations of DDT were found in the surface water of tropical Asia (Iwata et al. 1993) and may be attributed to its ongoing use in these regions (Prudente et al. 1997) and its decreased mobility compared to more volatile PHCs such as HCB and α -HCH. Global soils surveys have shown that highest and lowest concentrations of PCBs were found in Europe and Greenland, respectively (Meijer et al. 2003). These observations were supported by Connell et al. (1999) in a systematic comparison of lipophilic chemicals in air, water, sediment, and biota of the Northern and Southern Hemi-

spheres. More specifically, in North America, lowest concentrations of PCBs and DDTs in marine biota were found in Alaska and the western part of the Canadian Arctic compared to the eastern region (de March et al. 1998). Similar spatial trends were observed in water and zooplankton from Alaska and the Canadian Arctic (Hoekstra et al. 2002) as well as ringed seals (*Phoca hispida*) from the circumpolar region (Muir et al. 2000).

HCH isomers are widely distributed in the Northern Hemisphere waters (Li et al. 2002). These compounds are retained in cold water, resulting in an accumulation of HCH in the arctic marine ecosystem (Macdonald et al. 2000). Atmospheric concentrations of HCH have decreased during the past 15 years following application bans and restricted use (Macdonald et al. 2000). However, the insecticide γ -HCH is still widely used in North America and Europe (Li et al. 1998). The volatile HCB originates from pesticide usage, manufacturing, and combustion (Bailey 2001). In a global survey of HCB in background surface soils, the highest concentrations of this contaminant were found in the Northern Hemisphere (Meijer et al. 2003), as seen for PCBs. However, HCB concentrations in North America and Northern Europe have declined during the past 35 years based on measured concentrations in the atmosphere, sediment cores, fish, and bird eggs (Bailey 2001).

Emerging contaminants, such as PFAs and PBDEs, are following different trends. PFAs have a carbon chain in which all hydrogens have been replaced by fluorine, which confers thermal and chemical stability to the molecule. These compounds have been used since 1950 in a variety of household and industrial applications (e.g., surfactants, refrigerants, lubricants, paints, adhesives, paper coating) (Key et al. 1997). Perfluorinated acids have been found to be widely distributed in the environment and highly resistant to abiotic or metabolic degradation (Giesy and Kannan 2001, 2002). PBDE flame retardants are used in a wide range of manufactured products (e.g., computers, television sets, electrical cables), cars, and textile coatings (Darnerud et al. 2001). These lipophilic compounds have chemical structures very similar to PCBs and bioaccumulate in tissues (Haglund et al. 1997). Numerous studies show that PBDE concentrations are increasing in the environment (Darnerud et al. 2001; Ikononou et al. 2002; Law et al. 2003a).

III. Marine Mammals and PHCs

The accumulation of persistent and bioaccumulative contaminants in the marine environment may impair the health of aquatic wildlife such as marine mammals. Many species of delphinoids experience lifelong exposure to persistent contaminants because of their elevated trophic position, longevity, and proximity of their coastal habitats to industrial and agricultural areas. As a result of trophic transfer of PHCs, odontocetes are exposed to greater amounts of contaminants through their dietary exposure (Morris et al. 1989) compared to Mysticetes, which feed at a lower trophic level (Hoekstra et al. 2003). Studies on lipid composition of striped dolphin tissues demonstrated that concentrations of

DDTs, HCHs, and highly chlorinated PCBs were correlated to triglycerides content mainly found in the blubber (Kawai et al. 1988). In general, cetaceans have large and dynamic lipid reserves for thermoregulation, energy storage, and buoyancy, which correspond also to a large accumulation capacity for lipophilic chemicals. Fat reserves may be mobilized in times of illness, starvation, pregnancy, and lactation, consequently increasing the potential bioavailability of lipophilic contaminants (Aguilar 1987).

A. Biotransformation

In mammals, xenobiotics circulating in the bloodstream are chemically transformed into more hydrophilic by-products by hepatic biotransformation processes to facilitate their excretion from the organism. The hydrophobicity of chlorinated xenobiotics, such as PCBs, depends on the degree and pattern of chlorination of the molecule. Lower chlorinated substances have structural features, such as adjacent unsubstituted carbon atoms, that make them generally less resistant to biotransformation compared to highly chlorinated ones. Biotransformation, however, can also result in the formation of more persistent and (or) biologically active metabolites, such as the conversion of *p,p'*-DDT to *p,p'*-DDE or the conversion of certain PCBs to hydroxylated and methyl sulfone (MeSO₂) PCBs (Letcher et al. 2000a).

Biotransformation of xenobiotics occurs principally in the liver and is divided into two phases. Phase I is responsible for the insertion of a polar group into the molecule, most often by the oxygen-mediated actions of cytochrome P450 (CYP450) or by removal of a chlorine molecule by dehalogenation (Parkinson 1996). Families of microsomal CYP450 play key roles in the detoxification or activation of xenobiotics in addition to their essential roles in the biosynthesis and catabolism of endogenous substrates such as steroid hormones, bile acids, fatty acids, and liposoluble vitamins (Honkakoski and Negishi 2000). Phase II of biotransformation consists of the conjugation of the xenobiotic functional groups present or introduced/exposed during phase I with endogenous compounds such as glutathione, amino acids, glucuronide, or sulfate (Parkinson 1996). Most of these reactions result in the increased hydrophilicity of the xenobiotics and therefore enhance their elimination. However, certain metabolic compounds such as MeSO₂-PCBs and MeSO₂-DDEs are sufficiently lipophilic to bioaccumulate in tissues (Letcher et al. 1998, 2000a). Other PHCs such as PBDEs have been shown to biotransformed to hydroxylated PBDE (HO-PBDE) metabolites in studies with laboratory rodents and fish, but there is presently no published information on PBDE metabolism in any cetacean species or population (Hakk and Letcher 2003). One recent exception was a report of hydroxylated PCBs (HO-PCBs) and HO-PBDEs in the plasma of killer whale (*Orcinus orca*) fed a diet of wild Pacific salmon (Bennett et al. 2002).

B. Pattern of Accumulation

In marine mammals, the uptake of PHCs from the diet exceeds the rate of metabolism and excretion. As a result, concentrations of lipophilic PHCs tend

to increase with age in males and juvenile females (Cockcroft et al. 1989; Wells et al. 1994). When reaching maturity, females can transfer large quantities of pollutants to their offspring through gestation and during lactation via the lipid-rich milk (Addison and Brodie 1977; Borrell et al. 1995; Cockcroft et al. 1990), thus reducing their load of body contaminants. In long-finned pilot whales (*Globicephala melas*), 60% to 100% of the mother's contamination load was transferred by the lipid-rich milk to the offspring, compared to 4% to 10% through the placenta (Borrell et al. 1995). Maternal reproductive history is an important factor determining the contamination load transferred to the offspring. The firstborn calf receives a much higher burden of contaminants than subsequent offspring (Cockcroft et al. 1989; Ylitalo et al. 2001). Cockcroft et al. (1989) reported that 80% of the total contamination load of the mother was transferred to the firstborn in South African bottlenose dolphins. On the other hand, lipophilic PHCs continue to increase with age in adult males (Granby and Kinze 1991; Westgate et al. 1997), a phenomenon also observed in postreproductive female long-finned and short-finned pilot whales (*G. macrorhynchus*) (Tanabe et al. 1987a; Tilbury et al. 1999), as well as in postreproductive female killer whales (Ross et al. 2000). PCBs in male belugas (*Delphinapterus leucas*) have been shown to reach a plateau in older individuals (Stern et al. 1994) as they reach a near steady state with their environment.

C. Mechanisms of Action

Cytochrome P450 Induction Certain xenobiotics can stimulate the synthesis of enzymes involved in biotransformation processes, such as cytochrome P450. Three main inducible cytochrome P450 subfamilies (i.e., isozymes CYP1, CYP2, and CYP3) are known to be implicated in the biotransformation of marine pollutants (e.g., PCBs, chlorinated dioxins). CYP isoenzymes have different, sometimes overlapping, substrates. The cytochrome metabolic capacity varies with gender, age, tissue, and species as well as PHC exposure.

The CYP1A family catalyzes planar organics such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), which is considered as one of the most potent synthetic toxicants, and PCBs with no (or limited) *ortho*-, *meta*-substituted chlorine atoms on the biphenyl rings (i.e., dioxin-like PCBs). Induction of CYP1A enzyme synthesis occurs through the aryl hydrocarbon receptor (AhR). CYP2B and CYP3A catalyze reactions in molecules with no *meta*-, *para*-substituted chlorine (with at least one *ortho*-substituted chlorine) possessing a nonplanar configuration. Current knowledge of metabolic activity in cetaceans suggests that their metabolic capacity to degrade xenobiotics may be low compared to that of terrestrial mammals or pinnipeds (Boon et al. 1997; Tanabe et al. 1988, 1997a).

Biochemical and immunochemical analyses have revealed enzymes from the subfamily CYP1A in pinnipeds and cetaceans (Goksøyr 1995; Li et al. 2003; Teramitsu et al. 2000; Watanabe et al. 1989; White et al. 1994). Immunochemical assays have demonstrated the presence of CYP1A, CYP2B, and CYP3A isoenzymes in the liver of harbour seals (van Hezik et al. 2001). Moreover, AhR

has recently been characterized in beluga whale liver tissue, suggesting that these animals are capable of metabolizing dioxin-like contaminants (Jensen and Hanh 2001).

In cetaceans, CYP1A has been identified in the liver of hunted and stranded belugas from the Canadian Arctic, and concentrations have been strongly correlated with non-*ortho* and mono-*ortho* PCB congeners in blubber (Muir et al. 1999a; White et al. 1994). White et al. (1994) found that CYP1A was a primary catalyst for EROD (7-ethoxy-*O*-deethylase) and AHH (aryl hydrocarbon hydroxylase) activities in Arctic belugas, with EROD activity levels falling within an overlapping range of concentrations measured in short-finned pilot whales, striped dolphins, and killer whales caught off the coast of Japan (Watanabe et al. 1989) and pilot whales stranded on Cape Cod (White et al. 2000). These results suggest that exposure of these delphinoids to high body burdens of contaminants, including PCBs, may be responsible for the induction of the CYP1A-like proteins (White et al. 1994, 2000). Based on PCB accumulation patterns, Muir et al. (1996a) suggested that belugas from the St. Lawrence estuary may have developed greater cytochrome activities (CYP1A/2B) in response to PCB exposure compared to less-contaminated arctic belugas. Similarly, Letcher et al. (2000b) reported a greater degrading capacity of PCB and DDE methyl sulfone precursors in free-ranging belugas from the St. Lawrence estuary compared to free-ranging belugas from western Hudson Bay, Canada. Letcher et al. (2000b) postulated that the differences of metabolic capacities between the two populations were associated with higher CYP enzyme activities in the southern St. Lawrence population.

The presence and activity of CYP1A suggest that PCB congeners with *ortho-meta*-unsubstituted chlorine atoms, in combination with at most one *ortho*-chlorine atom, can be metabolized by cetaceans (Boon et al. 1997; Reijnders 1994), albeit in a limited fashion compared to other mammals. On the other hand, low hepatic catalytic biomarkers of CYP2B-like enzymes have been observed in arctic belugas and pilot whales (Watanabe et al. 1989; White et al. 1994, 2000). Indirect characterization of CYP450 was conducted by evaluating the pattern of tissue PHC residues relative to those found in the environment. Norstrom et al. (1992) found a much higher abundance of nonplanar PCB congeners in Canadian Arctic belugas and narwhals, which suggested a low activity for CYP2B-type metabolism compared to a higher metabolic activity for CYP1A. Letcher et al. (2000b) suggested that CYP2B-like-mediated biotransformation may be induced in beluga whales based on the formation of methyl sulfone metabolites of PCB and DDE in their tissues. Nonetheless, cetaceans seem to have lower CYP2B-like activity than seals (Goksøyr 1995). The characterization and activity of these enzymes have yet to be determined in cetaceans.

Less is known about cytochrome enzymes from the subfamily CYP3A, which are very active in testosterone and bile acid metabolism (Honkakoski and Negishi 2000). These enzymes have wide substrate specificity and are involved in drug and xenobiotic metabolism (Honkakoski and Negishi 2000). CYP3A enzymes have been identified in pinnipeds and some species of whales such as