Chapter 4
Priority Contaminants, 'New' Toxic Substances, and Analytical Issues

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Summary

Ongoing monitoring of persistent toxic substances (PTSs) in the Arctic has focused on three well-known groups of contaminants: industrial compounds and by-products, chlorinated pesticides, and heavy metals. However, increasing levels of several 'new' contaminants and metabolites are a cause for concern. Brominated flame retardants, polychlorinated paraffins, and perfluoroorganic compounds have recently received international attention, but more data on their presence and possible effects are needed to evaluate their environmental impact.

Interpretation of monitoring results requires reliable and comparable data, a condition not always met. Therefore all laboratories producing human PTS data for AMAP are required to participate in relevant inter-calibration programmes and to achieve acceptable results. Where relevant, measurements should be congener-specific and the data lipid-normalized for the organic pollutants, and speciated for the heavy metals to distinguish toxic and non-toxic forms.

4.1. Persistent toxic substances

Most research and ongoing monitoring work on PTSs in the Arctic have focused on three groups of contaminants: industrial compounds and by-products (e.g., polychlorinated biphenyls – PCBs, and dioxins), pesticides (e.g., lindane, the DDT-group, and cyclodiene analogues), and heavy metals (e.g., mercury – Hg, lead – Pb, and cadmium – Cd) (AMAP, 1998; Hansen *et al.*, 1996; Jensen *et al.*, 1997; Lønne *et al.*, 1997). The Stockholm Convention on Persistent Organic Pollutants (POPs) facilitated by the United Nations Environment Programme (UNEP), and the U.N. Economic Commission for Europe (UN ECE) Protocols for Heavy Metals and POPs also reflect the global concern associated with these contaminants. The UNEP POPs list includes aldrin, chlordane, DDT, dieldrin, dioxins and furans, endrin, heptachlor, hexachlorobenzene (HCB), mirex, PCBs, and toxaphene. The UN ECE POPs Protocol includes the UNEP 12 plus chlordecone, hexachlorocyclohexane (HCH), hexabromobiphenyl and polycyclic aromatic hydrocarbons (PAHs). The UN ECE Heavy Metals Protocol initially focuses on Cd, Pb, and Hg. During the last few years, however, there has been an increasing interest in 'new' toxic substances and metabolites.

The 'new' environmental toxins cover a range of organic compounds and compound classes. These include some of the more persistent polar pesticides currently in use. Other examples are nitro- and aromatic musk and their metabolites from personal care products. Among the industrial chemicals and by-products, phthalates, octachlorostyrene (OCS), polychlorinated naphthalenes (PCNs), polybrominated diphenylethers (PBDEs), polychlorinated paraffins, and perfluoroorganic compounds (e.g., perfluorooctane sulfonate – PFOS) are identified as 'new' toxic substances. Of these, PBDEs, polychlorinated paraffins, and PFOS have recently received particular attention. Due to their distribution and accumulation pattern, the synthetic musks, phthalates and new generation pesticides are generally not considered a particular problem in the Arctic. None of these 'new' compounds are on the current UNEP list of most unwanted POPs.

Increasing interest in the metabolites or halogenated phenolic compounds is partly caused by their structural similarity to natural hormones (see Figure 4·1) and possible action as hormonal mimics (Connor *et al.*, 1997; Hovander *et al.*, 2002). In addition, many of the well-known toxins are chiral (exist in mirror image forms) and hence exist in enantiomeric pairs (Kallenborn and Hühnerfuss, 2001), which have the potential to cause different biological effects. An enantio-selective accumulation has been reported for several organochlorine compounds (Karlsson *et al.*, 2000; Wiberg *et al.*, 2000). That the enantiomers may have different biological effects has in most cases been overlooked when assessing the possible environmental impact of these compounds.

Long-range transport allows many PTSs to reach remote areas such as the Arctic, where few, if any, local sources of these contaminants exist. Depending on the geographic location of sources, weather conditions, and the physico-chemical properties of the contaminants,
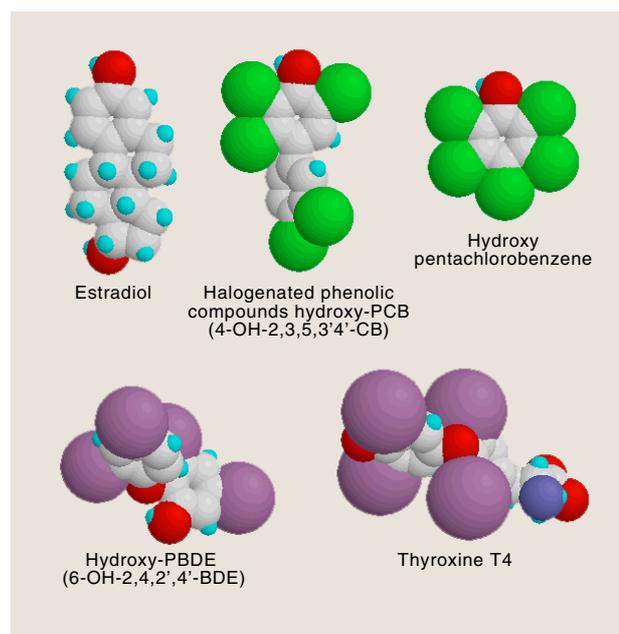

Figure 4·1. Structural similarities between the natural hormones estradiol and thyroxine T4, and the halogenated phenolic compounds hydroxy-PCB, hydroxy pentachlorobenzene and hydroxy-PBDE.

transport to and within the Arctic can occur via the atmosphere, ocean currents, sea ice drift, and river systems (AMAP, 1998; Burkow and Kallenborn, 2000). Due to their persistence and high lipophilicity, several of these compounds bioaccumulate, presenting a possible risk to humans, particularly those who depend on the lipid-rich marine mammals (whale, seal and walrus) for food. Among the many thousands of synthetic bulk chemicals in use today, only a limited number have been tested or evaluated for their hazard potential. To understand the possible consequences for human health and the Arctic environment extensive evaluations are needed. It should be kept in mind that the consequences may only become apparent decades after emissions to the environment have occurred, and thus after wildlife and people have already been exposed. Evaluation criteria must therefore include propensity for long-range transport, persistence, bioaccumulation potential, and hazards for human health and the environment (toxicity). Section 4.2 presents some key information for the most common and most debated PTSs from non-occupational exposure in the Arctic. More information about sources and environmental levels of contaminants in the Arctic can be found in two related assessment reports: the AMAP 2002 assessments of heavy metals (AMAP, 2003b) and POPs (AMAP, 2003c).

4.2. Industrial chemicals and by-products
4.2.1. Dibenzo-*p*-dioxins and dibenzofurans

Commonly known as dioxins and furans, polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are two structurally similar families of, respectively, 75 and 135 congeners. Dioxins and furans are mainly released through relatively low temperature (below 800°C) domestic and industrial incineration processes, with chlorine present, as well as during the manufacture of industrial chemicals including PCBs and pesticides (Alcock and Jones, 1996; Fiedler, 1996). A significant reduction in the emissions of dioxins and furans to the environment has been achieved through the implementation of pollution control measures.

Dioxins and furans are insoluble in water, lipophilic, persistent in the environment, and toxic. In particular, the 2,3,7,8-tetrachlorinated dioxins are known to bioaccumulate, while the more predominant congeners from combustion processes are known to biodegrade. Because they bind to particulate matter, dioxins are normally regarded as a major problem close to the source. In addition to a few local sources, these compounds enter the Arctic ecosystem via long-range atmospheric transport, but not to the same extent as for the other chlorinated PTSs. Diet is the main route of human exposure in the Arctic. Typical ΣPCDD/F values reported in human milk from the Arctic are in the range 10 to 40 pg/g lw (lipid weight) (AMAP, 1998); data on levels in human plasma from the Arctic are, however, sparse.

New methods for sample extraction and clean-up have improved the analytical capability for dioxin/furan trace analysis and pooled blood samples are no longer needed when using the most modern clean-up and quantitative techniques.

Chloracne is a well documented effect following dioxin/furan exposure. Other possible effects include effects on the immune system, cancer, reproductive disturbances, and acute toxic reactions (Fiedler, 1996; Whysner and Williams, 1996).

4.2.2. Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) are a group of 209 congeners, several of which are atropisomers (i.e., exist as enantiomeric pairs due to restricted rotation of the bond between the two phenyl rings). PCBs were commercially produced and sold mainly as Aroclor and Clophen mixtures (Safe, 1994). Worldwide PCB production is estimated at 1.3 million tonnes (Breivik *et al.*, 2002). PCBs have been used extensively since the 1930s for a variety of industrial and commercial purposes, but their manufacture and new uses have now been phased out in many western countries. PCBs have widespread applications, including as dielectric fluids in transformers and large capacitors, as heat exchange fluids, in lubricating oils, as paint additives, in plastics, and in sealants. At present, the major source of PCB exposure seems to be environmental recycling of PCBs from former usage. PCBs are still present in older electrical transformers and at a number of contaminated industrial and waste sites throughout the Arctic. Like most POPs, PCBs have primarily contaminated the Arctic ecosystem through long-range transport from more southern regions.

The physico-chemical properties of PCBs, including low water solubility, high stability (particularly those lacking unsubstituted positions on the biphenyl rings), and semi-volatility, favor long-range atmospheric transport and accumulation in lipid-rich media. Thus, the main source of human exposure is through diet; however, inhalation and dermal routes are likely under occupational exposure scenarios. Typical ΣPCB values in plasma are in the range 1 to 60 μg/L (AMAP, 1998).

Historical levels are not always easy to compare with contemporary measurements due to changing trace analytical techniques and quantitative methods. ΣPCB values are often reported based on different quantitative methods (e.g., as Aroclor 1260 or a selected number of congeners), making comparisons difficult. Co-elution with other chlorinated compounds like chlorobornanes and cyclodiene pesticides has previously made reliable analytical interpretation difficult.

The most persistent congeners in lipid media are CB99, CB118, CB138, CB153, CB170, and CB180. Although regarded as persistent, some PCBs, depending on chlorine substitution, are transformed in the environment by biotic and abiotic processes. Naturally occurring microorganisms are capable of degrading the low chlorinated PCBs with vicinal hydrogen atoms. The presence of PCB metabolites in animals and humans formed by the action of CYP (cytochrome P450) and phase-II enzymes is recognized (Boon *et al.*, 1989), but to date these have not been included in environmental monitoring programmes. Reports have shown that the most abundant hydroxy-PCBs in human blood samples equal the presence of some abundant PCB congeners with sum values in the range 0.1 to 10 μg/L (Bergman *et al.*, 1994; Hovander *et al.*, 2002; Sandau *et al.*, 2000a). Metabolism also includes the formation of diols, phenolic conjugates and glutathione conjugates.

Methyl sulfone metabolites are also reported to bioaccumulate (Letcher *et al.*, 1998), but are present in substantially lower amounts compared to the hydroxy compounds.

Several possible adverse human health effects to PCB exposure have been suggested, including effects on the immune system, cancer, effects on the reproductive system, and cognitive development (Safe, 1994). Some of their toxicity may be linked to the biotransformation products. Due to structural similarities (with hydroxy group in *para*- or *meta*-position), the hydroxy metabolites are assumed to be able to mimic hormonal activities (Connor *et al.*, 1997; Kester *et al.*, 2000). The non-*ortho* and mono-*ortho* substituted PCBs are planar with toxic properties similar to the dioxins.

4.2.3. Chlorinated naphthalenes

Polychlorinated naphthalenes (PCNs) exist as 75 congeners that are structurally similar to the PCBs with comparable chemical and thermal stability (Falandysz, 1998). PCNs were first used commercially in the early 1900s for wood, paper, and textile impregnation, but were shortly thereafter replaced by PCBs. The numerous industrial applications also include usage in electrical equipment (e.g., capacitors and cables), lubricants, solvents, dyes, and sealants. Technical PCN formulations have been found under the names Halowaxes, Seekay waxes and Nibren waxes depending on manufacture. Other sources of PCNs in the environment are technical PCB formulations (up to 0.09% PCN) and thermal processes (e.g., combustion, roasting, metal reclaiming, and the chlor-alkali industry). PCNs are also believed to be formed during combustion of PAHs. In the 1920s, worldwide annual production was approximately 9000 tonnes. One of the largest PCN producers voluntarily ceased production in the late 1970s. However, general information about world production volumes and history is limited. Although the use of PCNs has declined in the past few decades, they are not prohibited in most countries and still occur in many PCB-like applications.

PCNs are transported to the Arctic mainly via long-range atmospheric transport. Partitioning to aerosols is especially important, governing both transport pathways to remote areas and depositional patterns. PCNs are lipophilic and, as for PCBs, the chlorine substitution pattern governs their persistence (Falandysz, 1998). Knowledge of the actual levels and distribution of specific congeners in humans is very limited. Data on human liver and adipose tissue indicate PCN levels 200 to 500 times lower than the total PCB burden (Weistrand and Norén, 1998). Hydroxylated metabolites of PCN have also been reported.

The analytical challenges associated with PCN analysis are the same as those for non-*ortho* substituted PCBs and dioxins; highly sensitive and specific trace-analytical techniques are required. Although all 75 congeners have been synthesized, full congener separation is not yet possible due to co-elution.

Some of the PCN congeners appear to exhibit dioxin-like toxicity of a similar magnitude to some of the co-planar PCBs (Falandysz, 1998; Villeneuve *et al.*, 2000).

4.2.4. Polychlorinated paraffins

Short-chain chlorinated paraffins (SCCPs) are part of the group of polychlorinated-*n*-alkanes (PCAs) with up to 30 carbon atoms and a chlorine content of 30 to 70% by mass (Tomy *et al.*, 1998). PCAs are used as additives to improve water repellent and flame retardant properties in metal working fluids and lubricants, plastics, adhesives, paints, and sealants. The SCCPs have carbon lengths of 10 to 13 and are of particular interest because they have the greatest potential for environmental release and the highest toxicity of the PCAs. Information on historical production volumes of PCAs is difficult to find but annual global production during the 1990s was estimated at 300 000 tonnes, of which 50 000 tonnes were SCCPs (Muir *et al.*, 2001). Due to concerns about their possible environmental impact the use of SCCPs is declining.

SCCPs are relatively mobile, subject to long-range transport, and are found in the Arctic. Studies indicate that SCCPs are less persistent and bioaccumulative than PCBs hence levels in the environment are low compared to PCBs (Fisk *et al.*, 2000). Medium- and long-chain chlorinated paraffins are not yet reported in the Arctic.

In contrast to most other environmental toxins, the number of SCCP congeners is extremely high, and this has resulted in a substantial analytical challenge. No congener-specific analysis exists, as this inability to resolve the individual components causes major problems for quantitation. A high degree of variability has also been reported in the quantitation depending on the analytical technique used.

SCCPs appear to elicit fewer acute and chronic toxic effects when compared to PCBs, but information is very limited. Risk assessments of SCCPs are inconsistent with respect to their conclusions regarding ecological risk, including carcinogenicity, clearly indicating the need for more data (Muir *et al.*, 2001).

4.2.5. Brominated flame retardants

Polybrominated diphenylethers (PBDEs), polybrominated biphenyls (PBBs), and tetrabromobisphenol A (TBBPA) are the three main classes of brominated compounds used as flame retardants (Renner, 2000). Brominated flame retardants (BFRs) are used extensively in a variety of consumer products such as in thermoplastics for televisions and personal computers, building materials, foams for furniture and insulation materials, as well as in textiles. BFRs are either chemically incorporated (covalently bound) in materials or applied as an additive to the material; BFRs from the latter group can more easily migrate into the environment. The major commercial products include the covalently bound TBBPA and its derivatives (representing a third of production), the additive PBDEs (representing a third of production), and a number of other compounds. PBBs for use as an additive flame retardant are no longer produced. The annual usage and variety of compounds manufactured have drastically increased during the last few years, with an annual world production of over 150 000 tonnes in 1998 (Larsen *et al.*, 1999).

The physical properties of BFRs encourage long-range transport and accumulation. That BFRs are found

in air and biological samples from remote areas of the Arctic supports the indications that these substances are globally distributed in the environment. Although de-cabromodiphenyl ether (BDE 209) accounts for most PBDE use, the most commonly found congeners are the *tetra* and *penta* derivatives. Typical values of ΣPBDEs (mainly BDE 47 and BDE 99) in plasma are in the range 5 to 40 ng/L (about 0.5% of levels of ΣPCBs) (Darnerud *et al.*, 2001). Recent findings of increasing PBDE levels in temporal trend studies, and the general lack of data on these substances, underline the importance of further investigations on these compounds (Norén and Mei-ronyté, 2000).

With increasing availability of reference compounds, quantitation of the major congeners can be achieved. However, a complete identification and quantitation of all BFRs is not yet possible, and BDE 209 is often omit-ted when the PBDEs are reported. Studies indicate effec-tive uptake from the gastrointestinal tract and substan-tial breast milk transfer to offspring. The formation of metabolites is also reported.

Although little information is available, data on pos-sible effects suggest that PBDEs are likely to be carcino-gens, endocrine disrupters, and neurodevelopmental toxicants (Hooper and McDonald, 2000).

4.2.6. Perfluorooctane sulfonate

With the possible exception of chlorofluorocarbons (CFCs), fluorinated organics have traditionally received less attention than chlorinated and brominated organics, partly because they are believed to be relatively inert and therefore less likely to have an impact on human health and the environment. A number of different chemical classes belong to this group (e.g., CFCs, aromatics, sul-fonamides, acids and sulfonates). Perfluorooctane sulfo-nate (PFOS), which belongs to the important class of fluorinated surfactants, has, however, received more attention recently (Giesy and Kannan, 2001; Kannan *et al.*, 2001; Moody and Field, 2000). PFOS is used as a refrigerant, a surfactant, and as a component of phar-maceuticals, flame retardants, lubricants, paints, adhe-sives, cosmetics, paper coatings, and insecticides. PFOS has been manufactured for over 50 years and its many useful properties have steadily increased its use, making PFOS a high volume product with an estimated U.S. production of 3000 tonnes in 2000. As a result of the 3M Company's phase out, U.S. production is anticipated to decline.

The strong C–F bond makes fluorinated organics more inert, both chemically and biologically, than the corresponding chlorine or bromine analogues, and hence they are expected to have an environmental per-sistence greater than the more well-known organic con-taminants (Key *et al.*, 1997). In general, however, little is known about their biodegradation and accumulation characteristics. PFOS has been detected in marine mam-mals from the Arctic, but no data exist on levels in hu-mans from this area. The physical properties of fluori-nated organics encourage long-range transport, as they are more volatile than chlorine or bromine analogues.

Part of the reason why PFOS received less attention in the past was because its measurement is complicated. Due to its surface-active properties, extraction is diffi-cult and there is a need for sophisticated LC–MS meth-ods for proper quantitation.

PFOS has been shown to affect cell–cell communica-tion, membrane transport, energy generation, and prox-isome proliferation (Sohlenius *et al.*, 1993; Upham *et al.*, 1998), but concentrations in wildlife are believed to be lower than those required to cause adverse effects.

4.2.7. Octachlorostyrene

Octachlorostyrene (OCS) is an industrial by-product formed during electrolysis of salt solutions to produce chlorine and magnesium, and when purifying aluminum (Deutscher and Cathro, 2001; Selden *et al.*, 1997). Max-imum releases probably occurred in the 1960s, but little is known about global emissions.

Although found in high levels close to industrial sites, OCS has not been regarded as a major contami-nant in the Arctic. However, the metabolite 4-hydroxy heptachlorostyrene has recently been identified as one of the major metabolites in human plasma in the Arctic (Hovander *et al.*, 2002).

No particular problems are associated with OCS analysis.

The potential human health concern with OCS is be-cause it has a binding affinity for both the androgen and estrogen receptor (Satoh *et al.*, 2001). The metabolite is believed to have an influence on thyroid hormone and retinol homeostasis (Sandau *et al.*, 2000b).

4.2.8. Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) constitute a large class of compounds, which comprise hundreds of individual substances. They are produced as a result of incomplete combustion (pyrolysis) of organic matter. Sources are ubiquitous and include notably the burning and coking of coal, wood burning (including forest fires), production of aluminum, emissions from internal combustion engines (particularly diesel), cooking over fire or hot coals, and cigarette smoking. The main sources of non-occupational exposure are cigarette smoke, smoke from wood combustion, and smoked or broiled (over charcoal or fire) food (IARC, 1983).

PAHs released into the atmosphere by these combus-tion processes are rapidly adsorbed onto particulate matter and distributed into the different environmental compartments. PAHs are hydrophobic and insoluble in water and are readily taken up in lipid deposits of aquatic organisms. PAHs are photooxidized by sunlight in air and water. Since PAHs are biodegraded by mi-croorganisms and metabolized by higher organisms, they show little tendency to bioaccumulate. Levels in hu-mans are affected by smoking status, occupational expo-sure and consumption of PAH-containing foods. In non-smokers, the levels of the metabolite 2-naphthol are below 2 μmol/mol creatinine, whereas smokers exhibit average levels of 4 μmol/mol creatinine. Higher levels are encountered in occupationally exposed individuals (ATSDR, 1995).

PAHs may be detected and measured by a number of methods, based on their UV absorption, fluorescence, or molecular mass. Analysis is performed using a separa-tion technique such as high performance liquid chro-

matography (HPLC) or gas chromatography (GC) to enable identification of individual members. Evaluation of human exposure is performed through the measurement of hydroxylated metabolites in the urine (including 1-hydroxypyrene and 2-naphthol) using GC–MS.

Usually PAHs with two to six fused aromatic rings are those of toxicological interest. PAHs are not acutely toxic to humans. However, many PAHs have been shown to be potentially carcinogenic as well as genotoxic. Metabolites (e.g., hydroxides, epoxides, and nitro-PAH) appear to be responsible for these effects (Angerer *et al.*, 1997).

4.3. Chlorinated pesticides
4.3.1. Hexachlorocyclohexanes

Hexachlorocyclohexanes (HCHs) are a group of organochlorine compounds existing in eight isomeric forms including the often-reported α, β- and γ-HCH, the last more commonly known as the pesticide lindane. α-HCH is chiral and hence exists as an enantiomeric pair. The gamma isomer lindane is used as an insecticide on fruit, vegetables, and forest crops. Many countries still use large amounts of lindane and there are some registered uses of lindane in some circumpolar countries. Technical grade HCH, mainly containing the alpha isomer and only 15% γ-HCH, was once used as an insecticide. Total world production is estimated at 0.7 million tonnes of lindane and 10 million tonnes of technical HCH (Li, 1999).

Owing to their physico-chemical properties, HCHs are readily transported to the Arctic, via both atmospheric and aquatic pathways. HCHs partition into all environmental media in the Arctic. Biodegradation seems to be the dominant decomposition pathway in soil and water. Like other POPs, most human exposure to HCHs comes from food consumption. HCHs are not a major contaminant in drinking water. HCHs, especially β-HCH, accumulate readily in fatty tissues and are excreted slowly via feces, breast milk, and urine. Because of its persistence, β-HCH exhibits the highest concentration of the isomers normally reported in human samples. Typical plasma levels are in the range 0.1 to 2 μg/L (AMAP, 1998).

Except for the general difficulties in separating enantiomers, no problems are associated with HCH analysis.

High HCH exposure can affect the liver, the nervous system, the kidney, the reproductive system, and the immune system. HCH is regarded as a possible carcinogen (ATSDR, 1994; Coosen and van Velsen, 1989).

4.3.2. Hexachlorobenzene

Hexachlorobenzene (HCB) was introduced in 1945 as a fungicide for seed treatment. HCB is also an industrial by-product associated with the manufacture of chlorinated solvents, and several metallurgical industrial processes. It is a known impurity in several pesticide formulations that are currently in use. HCB is banned in many countries or its use has been severely restricted. The estimated current global annual emission is 23 tonnes (Bailey, 2001).

HCB is very persistent and bioaccumulates in animals. Dietary intake is the major route of human exposure, with highest concentrations found in oils and fats, meat, poultry, and fish. Exposure via inhalation or through drinking water is considered to be low. Typical plasma levels in Arctic populations are in the range 0.3 to 2 μg/L (AMAP, 1998). HCB is transformed into both pentachlorophenol (PeCP) and conjugates; however, elimination appears to be small compared to adipose deposits (To-Figueras *et al.*, 2000).

In addition to inducing porphyria, HCB has a broad range of toxic effects in experimental animals including immunotoxicity, endocrine effects, and cancer (Fisher, 1999).

4.3.3. DDT group

The use of 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (*p,p'*-DDT) as a pesticide has been declining in the temperate regions of the Northern Hemisphere since the 1960s and especially since the mid-1970s when its production and use were banned by many western nations (Mellanby, 1992). DDT was commonly used as a pesticide on a variety of agricultural crops and is still in use for the control of mosquitoes that spread malaria (vector control). Total global usage was estimated at 2.6 million tonnes up until 1992 (Voldner and Li, 1995). *p,p'*-DDT is easily metabolized to 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethene (*p,p'*-DDE) and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane (*p,p'*-DDD). The DDE/DDT ratio indicates age since release, or closeness to the source of a release. Two minor isomers of the DDT group, *o,p'*-DDT and *o,p'*-DDD, are chiral.

The persistence of the DDT group in the environment and its continued entry into the Arctic region via long-range atmospheric transport has meant that DDT is detectable in almost all compartments of the ecosystem and in human tissues. Levels of total DDT in human tissue in the Arctic are considerably higher than those in most southern populations, reflecting biomagnification in Arctic food chains and the higher consumption of high trophic level species for food in the Arctic. Typical plasma levels are in the range 1 to 9 μg/L (AMAP, 1998). DDT and its metabolites are stored in fatty tissue and excreted very slowly. Due to its lipophilicity, DDT and its metabolites are found in breast milk and can readily cross the placental barrier.

Except for the possibility of decomposition during analysis, there are no general limitations connected to DDT analysis.

Some evidence suggests that the DDT group may suppress the immune system, mimic hormones and be a possible human carcinogen (Fisher, 1999).

4.3.4. Cyclodiene pesticides

The cyclodiene pesticides are a diverse group of compounds including the chlordanes, heptachlor, aldrin, dieldrin, and endrin.

Technical chlordane is a mixture of *cis*- and *trans*-chlordane, *cis*- and *trans*-nonachlor, heptachlor and other chlordane isomers (Dearth and Hites, 1991). The total number of compounds is at least 147, of which 10 are major ones. Most chlordanes are chiral and hence found as racemates (mixture of mirror images) in the technical product. Chlordane was manufactured from

the late 1940s as a broad-spectrum insecticide used on agricultural crops and for termite control. Total global usage has been estimated at 78 000 tonnes (Barrie *et al.*, 1992), and action to ban chlordane has been taken in many countries. It is not registered for use in circumpolar jurisdictions and enters the Arctic ecosystem primarily via long-range transport. The chlordanes are highly volatile, lipid soluble and hence readily accumulate in fatty tissues in the marine food web. In general, only small amounts of chlordane are found in human tissues. However, relatively larger amounts of *trans*-nonachlor and the metabolites oxychlordane and heptachlor epoxide are found. The chlordanes are one of the most abundant environmental pollutants. Typical values (sum of chlordanes) in human plasma are in the range 0.2 to 2 µg/L (AMAP, 1998). No analytical limitations, except for the separation of the chlordane enantiomers, are reported. The compound class is a possible carcinogen and is believed to affect the immune system (Fisher, 1999).

Heptachlor, also used as an insecticide against termites, grasshoppers, and malaria mosquitoes, is now banned in several countries and severely restricted in others. Heptachlor is metabolized in animals to heptachlorepoxide. Typical plasma levels are in the range 0.05 to 0.15 µg/L (AMAP, 1998). As for chlordane, heptachlor is highly volatile, lipid soluble, and bioaccumulates. The compound and its metabolite are classified as carcinogens (Fisher, 1999).

Aldrin is a pesticide used to protect crops such as corn and potatoes from grasshoppers and worms, and to protect wooden structures from termites. Total global production has been estimated at 500 000 tonnes (Barrie *et al.*, 1992). Aldrin is readily metabolized in plants and animals to dieldrin. Dieldrin was traditionally used in agriculture to control soil insects, with a worldwide total production of 34 000 tonnes. Today, primary uses include controlling termites, woodborers, and textile pests. Endrin has been used as an insecticide on cotton and grain, and as a rodenticide to control mice and voles. Aldrin and endrin have been banned or severely restricted in most countries. Action has also been taken to ban or restrict the use of dieldrin, one of the most common pesticides. Due to the persistence and lipophilicity of aldrin and dieldrin, these compounds readily bioaccumulate. Endrin is rapidly metabolized by animals and does not accumulate in fatty tissues to the same extent as the other compounds. The main source of human exposure is through food. Adverse effects include toxicity, immune system depression, and carcinogenic action (Fisher, 1999).

4.3.5. Mirex

Mirex is an insecticide primarily used to control fire ants and other insects. Mirex has also been used as a flame retardant in plastics, rubber, and paint. The compound has never been used in any of the circumpolar jurisdictions and is now banned in many countries. It has been manufactured and applied extensively in the United States and has reached the Arctic via long-range atmospheric transport.

Mirex is one of the most stable and persistent pesticides with an environmental half-life of up to 10 years. Mirex is readily absorbed and stored in fatty tissues.

It bioaccumulates, and is now found at low levels in human tissue. The primary source of exposure is food, especially meat, fish, and game. Transformation to photomirex is slow and elimination is mainly via feces and breast milk. Plasma levels in the range 0.1 to 0.6 µg/L are reported (AMAP, 1998).

Mirex has toxic and possible carcinogenic effects (AMAP, 1998).

4.3.6. Chlorobornanes

Toxaphene is an insecticide mixture introduced by Hercules (USA) consisting of several hundred chorinated bornanes (CHBs, the major product), polychlorinated camphenes (PCCs), bornenes, and bornadiens, containing six to ten chlorine atoms (de Geus *et al.*, 1999; Muir and de Boer, 1995). Comparable mixtures were used under the brand names Strobane and Melipax. Most of the CHBs are chiral. Toxaphene is one of the most heavily used pesticides, with a total world production of 1.3 million tonnes up until 1993 (Voldner and Li, 1993). It was primarily used on cotton, cereal grains, fruits, nuts, and vegetables, as well as to control ticks and mites in livestock. Toxaphene and comparable mixtures are now banned in most countries.

CHBs, the major constituent of toxaphene, are semivolatile and enter the Arctic region via long-range atmospheric transport. The compounds are persistent (half-life in soil up to 12 years), lipid soluble, readily absorbed, and are commonly found in human tissue. Absorbed CHBs may be transformed and excreted; however, some congeners remain for prolonged periods. The two most common congeners are an octachlorobornane (Parlar no. 26) and a nonachlorobornane (Parlar no. 50). Values reported in human plasma are in the range 0.1 to 1 µg/L for both congeners (Deutch and Hansen, 2000).

Quantification has been compromised by difficulties in analysis (separation from PCB and organochlorine pesticides) and in the estimation of the amounts of the various chemicals that make up the CHB mixture. The increased number of reference compounds has improved the capability for acceptable quantitation of the most abundant congeners. However, the lack of standards, as well as differences in how data on total CHB amounts (or the sum of toxaphene-like compounds) are presented, has made comparisons of published data on CHBs difficult.

Several adverse effects of toxaphene, including being a possible human carcinogen, are reported (de Geus *et al.*, 1999). However, structure–activity models have shown that the most toxic CHB congeners are not accumulated (Parlar *et al.*, 2001).

4.3.7. Pentachlorophenol

Pentachlorophenol (PeCP) is made by exhaustive chlorination of phenol or by the hydrolysis (or degradation) of HCB. PeCP is insoluble in water but is readily converted to the soluble sodium salt. Depending on the manufacturing process, PeCP may be contaminated with various dioxins and furans. Worldwide production is estimated at less than 30 000 tonnes per year. As a broad-spectrum low-cost pesticide, PeCP and its salts have been used as algicides, fungicides, insecticides, molluscicides, and her-

bicides. Current use is limited to the treatment of lumber, in particular utility poles. Because of its volatility and water solubility, PeCP evaporates or is leached from wood structures to a large extent (ATSDR, 1999a).

Environmental contamination is widespread, PeCP being found in ambient air, surface and ground waters, sediments, soil, and aquatic and terrestrial organisms. PeCP is degraded by light and microorganisms to form numerous transformation products, of which penta-chloroanisole and tetrachlorocatechol are the most abundant in the environment. PeCP bioaccumulates in fish but in mammalian systems it is rapidly excreted in the urine, either free or conjugated with glucuronide. A recent study of PeCP in blood shows PeCP concentrations in Arctic samples of 0.6 to 8 µg/L plasma (Sandau *et al.*, 2000a).

No particular difficulties are associated with PeCP analysis.

PeCP is a suspected carcinogen, however contaminants in technical grade PeCP may be the actual culprits.

4.3.8. Endosulfan

Endosulfan is a synthetic, sulfur-containing, organochlorinated hydrocarbon used as an insecticide and acaricide. Technical grade endosulfan is a mixture of two geometric isomers (conformers), alpha and beta, which have slightly different physical and chemical properties, in a proportion of 2:1.

Endosulfan is moderately persistent in the environment. In soil, the half-life ranges from 30 to 200 days, and is affected by pH, the presence of microorganisms, and humidity. In water it is hydrolyzed slowly to form sulfur dioxide and endosulfandiol. In mammals, endosulfan is absorbed rapidly though incompletely by the digestive system. Endosulfan is lipophilic but is rapidly converted to a number of hydrophilic metabolites, including endosulfan sulfate, endosulfandiol, endosulfan ether, and hydroxy endosulfan carboxylic acid, which are more easily excreted. Thus it does not accumulate in the fat, and hence shows little potential for bioaccumulation or biomagnification (ATSDR, 2000a).

As a member of the organochlorine class, endosulfan can be determined by GC with electron capture detection (ECD). For environmental and biological specimens, sample clean up and purification is crucial to the reliability of the analysis (ATSDR, 2000a).

4.4. Heavy metals
4.4.1. Arsenic

Arsenic is the archetypal poison, synonymous with homicidal poisoning. The element As is ubiquitous in the environment, associated with mineral deposits of copper, nickel, iron (as arsenopyrite) as well as As oxides and sulfides. Often found as a natural contaminant of groundwater, it has been responsible for large-scale poisoning of human populations in many countries, notably in Bangladesh (Smith *et al.*, 2000) and Taiwan (Tseng, 1977). The worldwide production of As is estimated at 39 000 tonnes per year (USGS, 2001a). Atmospheric pollution stems mainly from coal burning and the smelting of metals. There is no evidence that Arctic regions are particularly affected by As contamination.

Arsenic forms a variety of inorganic and organic compounds. Among the first class, two oxidation states predominate, trivalent (+3) and pentavalent (+5), readily forming oxides, sulfides and acids. Organic forms include methylarsonic acid (MAA), dimethylarsinic acid (DMA), arsenobetaine and arsenocholine, the last two found in seafood. In mammals, inorganic As is rapidly transformed (metabolized) into MMA and DMA and subsequently rapidly excreted in the urine, thus making urine the medium of choice for evaluating recent As exposure. Care must be taken to speciate in order to distinguish between toxic and non-toxic forms.

To interpret the environmental or health impact of As its determination in environmental and biological samples must take into account the various species present. Total As content can be measured by atomic absorption spectrophotometry (AAS) using either hydride generation or graphite furnace (GF). Chemical pretreatment allows a limited speciation to be made, sufficient to distinguish exposure to toxic forms from ingestion of seafood. Inductively-coupled plasma–mass spectrometry (ICP–MS) coupled with HPLC affords complete speciation of common inorganic and organic compounds (ATSDR, 2000b).

The toxicity of As compounds varies from highly toxic to non-toxic in the range As(III) > As(v) > MAA > DMA > arsenobetaine/choline. Chronic As exposure affects several organs with resulting damage to the peripheral nervous system, skin, liver, and heart. Arsenic is recognized as a human carcinogen (Smith *et al.*, 1992).

4.4.2. Cadmium

Cadmium occurs in nature as oxides, sulfides and salts. Cadmium is released into the environment from both natural and anthropogenic sources, with the former including volcanic activity, and weathering and erosion of rocks. Mining, smelting and refining activities account for the majority of anthropogenic emissions. Incineration of municipal wastes containing nickel–cadmium batteries also contributes significantly. Soil levels are elevated close to sources, and usually decrease rapidly with distance away, although emissions from tall stacks may be transported over long distances (IPCS, 1992). Cadmium entering freshwater from industrial sources is rapidly adsorbed onto particulate matter, which eventually settles out. Cadmium is produced as a by-product in the smelting of zinc ores. Annual worldwide production is estimated at 19 000 tonnes (USGS, 2001b). The principal use of Cd is in the manufacture of nickel–cadmium batteries (75%) (ATSDR, 1999b). Other uses include pigments, coatings and plating, stabilizers for plastic, and nonferrous alloys.

Cadmium accumulates in aquatic organisms such as shellfish and crustaceans (Eisler, 1985), as well as in the liver and kidney of mammals (e.g., moose, reindeer/caribou, deer, and horses) (Crête *et al.*, 1987). Many plants, including tobacco, take up Cd. Uptake is enhanced at low soil pH. Occupational exposure results principally from inhalation of dust during manufacturing operations. Because of the dire health consequences, most countries have implemented strict regulations to control Cd exposure in the workplace (ATSDR, 1999b). Non-occupational exposure occurs through the consumption

of contaminated food (in particular organ meat) and cigarette smoking. Cadmium blood levels in Arctic populations are similar to those in other populations and appear to be affected principally by cigarette smoking. In an Inuit population from Nunavik, levels in smokers were 20-fold higher than in non-smokers, ranging from 4.7 to 6.2 µg/L (Benedetti *et al.*, 1992).

GF–AAS and ICP–MS are two techniques of choice for the determination of Cd in environmental and biological samples. Although the analytical techniques are straightforward, care must be exercised to avoid contamination during both the sampling phase and laboratory analysis (ATSDR, 1999b).

Chronic Cd exposure leads to proteinuria and kidney damage, obstructive lung disease, and osteomalacia, the last exemplified by Itai-Itai disease, as observed in Japanese populations in the 1960s (Fushukima, 1978).

4.4.3. Lead

Lead has been used for several millennia. Current worldwide Pb production is estimated at 3 million tonnes per year (USGS, 1996), with primary Pb (as opposed to recycled Pb) produced by the smelting of Pb sulfide ores. Lead present in the environment is mainly of anthropogenic origin (Nriagu, 1989). Localized anthropogenic sources include Pb smelters, battery recycling plants, and peeling paint from houses and industrial structures. Lead-acid battery manufacturing constitutes the principal contemporary use of Pb. Traditional uses such as paints, pigments, gasoline additives, ammunition, and Pb plumbing have all been severely curtailed due to environmental concerns. Leaded gasoline was a major cause of environmental contamination and human exposure during the twentieth century (US EPA, 1991). With the phasing out of leaded gasoline in North America in the 1980s, average blood Pb levels in the population decreased by up to 80% (Pirkle *et al.*, 1994). Environmental levels have also decreased significantly as evidenced for example by a 7.5-fold reduction in the Pb concentration of Greenland snow (Robinson, 1981).

Human exposure to Pb may occur through inhalation of airborne particles, as well as through the diet. Lead is readily absorbed through the lung. Gastrointestinal absorption of Pb is a complex process influenced by dietary factors, nutritional status, and the chemical form of the element. Once absorbed into the bloodstream, Pb is distributed into soft tissues and the skeleton, where it accumulates due to its chemical similarity to calcium. Lead shot has been implicated as a potentially major source of dietary Pb in Arctic hunter populations, since significant amounts of Pb fragments may remain in game, especially birds (Johansen *et al.*, 2001). Mean blood concentrations in humans in the range 10 to 50 µg/L are reported within the Arctic. Cord blood Pb levels in Nunavik were found to be three times higher than in urban Canadian populations (Dewailly *et al.*, 2001a).

Lead in environmental and biological samples may be measured by several analytical techniques including GF–AAS and ICP–MS. The latter technique allows the measurement of isotopic ratios of Pb, which often yields valuable information as to the source of the metal (Gwiazda and Smith, 2000). Prior to the 1980s, accurate determination of trace levels of Pb was a problem for most laboratories. Since then, improved methodology, as well as the generalized use of external proficiency testing programmes, has resulted in a greatly improved situation (Weber, 1996).

Even at low levels, Pb affects the peripheral and central nervous systems, particularly during their development. Hence the unborn and young children are particularly at risk. Higher exposures result in hematological and gastrointestinal symptoms.

4.4.4. Mercury

Mercury exists in many forms in the environment. It is present in the atmosphere mainly as a metallic vapor; it forms different chemical compounds in water, soil and rock; and it occurs in organic forms, found mainly in living organisms. Mercury has a number of unusual properties. It is the only metal that in elemental form is a liquid at room temperature. Mercury conducts electricity and it expands linearly with increasing temperature. Mercury combines easily with most metals, forming alloys known as amalgams, such as those used in dental fillings. These properties have made Hg a widely used product in household, commercial, medical, and industrial applications. Mercury, in various forms, is also one of the most poisonous natural substances known to humans and most other forms of life, making it an effective pesticide, fungicide and preservative. Due to its high toxicity, Hg in the environment has become an issue of international concern, and this has led many countries to implement controls on Hg emissions including phase-out of many uses.

The main ore is cinnabar, with Spain and Italy producing around 50% of the world's supply of the metal. Worldwide production of Hg is estimated at 1800 tonnes per year (USGS, 2001c). The metal is widely used in laboratory work for making thermometers, barometers, diffusion pumps, and many other instruments. It is used in making mercury-vapor lamps and advertising signs, and in mercury switches and other electronic apparatus. Other uses are in pesticides, mercury cells for chlor-alkali plants, dental preparations, anti-fouling paint, batteries, and catalysts (ATSDR, 1999c).

Mercury in the environment originates from both natural and anthropogenic sources. The former includes degassing of the Earth's crust and geothermal activity. Main sources of anthropogenic Hg include the burning of coal and losses from chlor-alkali plants. As a result of environmental concerns, emissions of Hg are declining in Western countries. However, in developing countries emissions are increasing. The future trend in anthropogenic emissions is therefore difficult to predict.

Metallic Hg is practically insoluble in water; it is however methylated in sediments by microorganisms. The highly toxic methylmercury (MeHg) thus formed is readily taken up by aquatic organisms and biomagnified through the food chain. Methylmercury exposure has been extensively documented in Arctic and subarctic populations since the 1970s (Hansen and Danscher, 1997), notably in Canada (Kosatsky and Dumont, 1991; Wheatley and Paradis, 1998). In some instances, hair was used as a surrogate for blood, and levels were converted using an appropriate conversion factor. Levels

correlate with the consumption of fish or sea mammals. In non-consumers, blood values are generally < 2 μg/L. In people who consume large amounts of fish, however, levels as high as 600 μg/L have been observed, with means of 20 to 40 μg/L. These levels can be compared to the 'no risk' level of 20 μg/L (WHO, 1990).

The physical and chemical characteristics of Hg make it easy to measure and speciate. Analytical problems are related to the very low levels found in some types of environmental sample and to the complexity of some matrices (ATSDR, 1999c).

Methylmercury affects the nervous system and can cause paresthesia, ataxia, and tunnel vision. *In utero* exposure (as seen in Minamata disease) may result in severe neurological damage, including cerebral palsy (Harada, 1995). No confirmed diagnosis of MeHg poisoning has been made in Arctic populations.

4.4.5. **Selenium**

Selenium (Se) is a metalloid and the element exists under three allotropic forms; red, gray and amorphous. Its four stable valence states are -2, 0, +4 and +6. In the environment, elemental Se is stable in soil and barely soluble in water. Selenites (+4) and selenates (+6) are soluble in water and thus more bioavailable. Selenates are biotransformed into organic compounds such as selenomethionine and selenocysteine, which are subsequently bioaccumulated by aquatic organisms (ATSDR, 1996).

Selenium is a relatively rare element, being sixty-ninth in abundance within the Earth's crust, with an average concentration of 0.05 to 0.09 mg/kg. It is produced as a by-product of the processing of copper ore. Annual worldwide usage is estimated at 1500 tonnes. Much of the Se produced (46%) is used in photocopying for the coating of the transfer cylinders. Other uses include electronics, glassmaking, and pigments. A variety of other uses account for the remaining production. Medically, Se is used as a catalyst in the preparation of pharmaceuticals, as an ingredient in antidandruff shampoos, as a constituent in fungicides, and as a supplement in animal feeds. Selenium may enter the environment as a result of human activity, principally within fly ash resulting from the combustion of coal (ATSDR, 1996).

The determination of trace amounts of total Se in environmental and biological matrices can be accomplished by several techniques including fluorometry (using 2,3-diaminonaphtalene as a fluorophore), neutron activation, GC (formation of volatile piazselenol), AAS (GF or hydride generation) as well as ICP–MS (ATSDR, 1996). It is often useful to determine which species of Se, whether organic or inorganic, is present. Most of the techniques mentioned are, however, not suitable for this since they require prior mineralization of the sample. Coupling HPLC to ICP–MS does allow the identification and quantitation of individual Se species (Michalke *et al.*, 2001).

Selenium is an essential element, present in several protein systems. It appears to offer protection from Hg poisoning as indicated by animal experiments (Cuvin-Aralar and Furness, 1991) and epidemiological studies. However, even a moderate excess of Se can lead to toxicity.

4.4.6. **Tributyltin compounds**

Tributyltin (TBT) compounds contain three butyl groups covalently bound to tetravalent tin. The main commercial compound is tributyltin oxide, however tributyltin hydroxide, tributyltin chloride, and tributyltin carbonate are also found in the environment. The biocide tributyltin oxide is used extensively as an antifouling agent in numerous formulations of marine paint. It is slowly released from the painted surface as the polymer is hydrolyzed in seawater, thereby entering the marine environment (Champ and Seligman, 1996).

Because of its low water solubility and lipophilic character, TBT is readily adsorbed onto particles and may persist in sediments for several years. It bioaccumulates in organisms, with the highest concentrations found in liver and kidney. Uptake from food is more important than uptake directly from water. However, TBT is rapidly metabolized and excreted from aquatic and terrestrial mammals and has not been shown to biomagnify in higher organisms. TBT has been detected in marine sediments in harbors throughout the world, including the Arctic region (Chau *et al.*, 1997; Ruiz *et al.*, 1996). As a result, most industrialized countries regulate the use of TBT, and its use on vessels shorter than 25 m is banned. As a consequence, environmental levels have decreased steadily since the 1980s. Populations of non-target affected marine organisms such as snails and molluscs have shown recovery since the regulations were put in place (Evans, 1999).

Determination of trace amounts of TBT in water and biota is classically performed by GC after derivatization. Detection limits are in the sub-ppb range (Sadiki and Williams, 1996). A novel technique, stir bar sorptive extraction with thermal desorption-capillary GC–ICP–MS allows the determination of ppq-level (i.e., one part in 10^{15}) traces of organotin compounds in environmental samples (Vercauteren *et al.*, 2001).

TBT is an endocrine disrupter for certain species of snail and other types of mollusc, but has not been shown to similarly affect higher organisms. In humans, acute exposure to organotin compounds (industrial exposure or laboratory accidents) has led to severe central nervous system damage, as well as to skin irritation (Baaijens, 1986). Although no data were found concerning low-level effects of TBT in humans, *in vitro* studies using human cells indicate potential immunological effects (Whalen *et al.*, 1999). Butyltin compounds were recently identified and measured in human blood from Michigan (Kannan *et al.*, 1999) with total concentrations ranging up to 100 μg/L.

4.5. **Quality control and quality assurance**

Reliable and comparable data are the basis for the AMAP assessment. In order to achieve this, a quality assurance and quality control (QA/QC) programme has been established by the AMAP Human Health Expert Group. This includes guidelines for sampling, transportation and storage, as well as analytical performance criteria including a ring test programme.

Basic prerequisites must be adhered to if quality is to be achieved and maintained. These include competence of personnel, adequacy of infrastructure and equipment,

documentation of all relevant procedures, traceability of measurements, and calibration. Various legislative bodies and international standardization organizations have promulgated guidelines addressing these requirements. ISO guide 17025 'General Requirements for the Competence of Calibration and Testing Laboratories' (ISO, 1999) is generally accepted as an appropriate basis for laboratory quality systems. It is however not sufficient for laboratories to adopt good practices. They must be able to demonstrate conclusively that the data they produce are consistently reliable.

Chemical trace analysis of contaminants in human samples is challenging. Due to risk of accidental exposure to diseases such as HIV, protocols and regulations concerning sample handling need to be carefully followed. Well-designed analytical procedures are required to overcome the difficulties associated with performing complex analyses on human media. These may include low concentrations of the analytes, small sample volume, a high number of contaminants, blank problems for compounds still in use, and interfering compounds. For liposoluble compounds, lipid normalization must also be performed. To ensure valid results, parameters such as identification, detection and quantitation limits, accuracy and precision, as well as the method's robustness must be evaluated. In addition, data treatment, reporting format and data storage must be harmonized.

A key issue is QC, which incorporates a range of activities such as the establishment and implementation of appropriate in-house QA routines, the use of relevant reference materials, and participation in inter-laboratory comparison programmes (also known variously as proficiency testing programmes, external QA schemes, or ring tests). The AMAP Human Health QA/QC system has been established to accomplish the last. At the request of the AMAP Human Health Expert Group, the Centre de Toxicologie of the Institute Nationale de Santé Publique du Québec in Canada has developed QA/QC activities in support of the AMAP Human Health monitoring programme. Main activities to date include running intercomparison programmes on relevant reference samples based on human material. This includes preparation and distribution of test samples, collection and interpretation of data, and the communication of results. In addition to the heavy metals, human samples for the organic contaminants (PCBs, standard pesticides, lipids, new organic xenobiotic compounds, and metabolites) will be provided. All laboratories producing data for AMAP are required to participate in the intercomparison programme and to achieve acceptable results.

4.6. Conclusions and recommendations

Heavy metals and UNEP-listed POPs are of continued concern for human health and should not be neglected. In addition, increased levels of many 'new' POPs and metabolites are a cause of significant concern. However, more data on their presence and possible effects are needed before their environmental impact, including possible implications for human health, can be properly evaluated. These knowledge gaps should be addressed in ongoing and future monitoring work. Where relevant, data reported should be congener-specific and lipid-normalized for the POPs, and speciated for the heavy metals to distinguish toxic and non-toxic forms. Selection criteria for choosing new target compounds must also be developed.

The key component for interpretation of monitoring results is reliable and comparable data. Therefore it is required that all laboratories producing human contaminant data for AMAP participate in the AMAP Human Health intercomparison programme with acceptable results.