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Chemical Pollution in Low- and Middle-Income Countries

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Contents

Executive Summary

In the current Millennium Development Goals' framework, three of the eight goals directly refer to health-related issues, while several other goals relate to determinants of health. Although much still needs to be done beyond 2015 to reduce the burden of communicable and non-communicable diseases, a still neglected issue is the health and environmental impact of the unsafe use and management of chemicals. This relates directly to the targets of Millennium Development Goal 7. These targets focus on the loss of environmental resources and biodiversity as well as setting other health targets.

This report draws attention to the neglected issue of anthropogenic chemical pollution in low- and middle-income countries.

The daily use of chemicals is omnipresent and only a few industrial sectors do not use chemical products. Consideration of chemical pollution issues are mainstream in the developed world where policy and practice engage in finding and implementing appropriate solutions. However, limited information and scientific evidence has yet been compiled on the use, fate, and impact of anthropogenic chemical pollutants, such as pesticides, pharmaceuticals, heavy metals from the mining sector, e-waste pollutants, and other industrial chemical substances, in the specific context of low- and middle-income countries.

This situation is alarming and becomes even more severe as chemical production and demand increases with population growth, urban development, improvements in living standards, and increased pressure to achieve high agricultural yields. Furthermore, chemical production is increasingly moved from high-income to low- and middle-income countries to reduce costs and maintain competitiveness. It is inevitable that with increased production of chemical substances and their use, there is a need for a comprehensive global overview of and insight into the exposure and effect of anthropogenic chemical pollutants on human and environmental health. There is also need for an assessment of the awareness and practices of stakeholders.

Looking in detail at the situation in low- and middle-income countries is justified by the increasing production and use of chemicals in these countries and the expected elevated release of toxins into the environment. Often obsolete techniques are applied, governmental infrastructure is lacking, and the disposal of waste is poorly managed, regulated or controlled. Furthermore, compared to the availability of scientific studies in high-income settings, the pathways of anthropogenic pollution in low- and middle-income situations are less evidenced by research and less well understood.

The scarcity of publicly available data currently makes it impossible to fully assess and quantify the risks of chemical pollutants to human and environmental health in low- and middle-income countries. Although different reports and scientific studies are available with site-specific information, a broader framework at the global level is still lacking. This report attempts to fill this gap. It provides a structured framework by distinguishing various types of chemical substances and sectors – pesticides, pharmaceuticals (for human health care and veterinary use), mining, e-waste, and residual industries (cement, paper, rubber, textile, and leather).

This report provides an overview of the current situation based on existing published information and reveals the most important and hazardous sources of those anthropogenic pollutants. It then advocates and encourages further discussion around this sensitive issue. Each section of this report covers different aspects of chemical pollution. Each section starts with a description of the specific chemical characteristics and the groups of chemicals of highest environmental concern. It goes on to describe their input pathways, their use – including trends and impacts – and issues of special concern. The section ends with the best practices observed and documented.

Based on a comprehensive literature search regarding anthropogenic chemical pollutants in low- and middle-income countries, a clear picture emerges of some fundamental issues that show a repeating pattern. Implementation of and compliance with international regulations still need to be significantly improved, especially in low- and middle-income countries. Although several international initiatives, such as the Stockholm, Basel, and Rotterdam Conventions, and the Strategic Approach to International Chemicals Management (SAICM) exist, their application in these countries of concern remains questionable. It is obvious, although difficult to quantify, that the use of hazardous chemicals in low- and middle-income countries poses a grave threat to the environment and to human health, often affecting the already vulnerable and poor fraction of the population. Overall data on industrial production and exports, as well as on the import and use of hazardous chemicals is still significantly lacking. Without a comprehensive overview at the national level it is very difficult to assess the overall relevance of the different substances in a specific spatial context. Only when more data on production and use are available or accessible, can better evidence on input pathways, spatial distribution, and the associated risks to human and environmental health be established. At sites already identified as critical, more research is needed to develop efficient and low cost techniques for environmental remediation that are feasible for application in low- and middle-income countries.

The management of chemicals and their use are seldom considered priority issues by government agencies. Developing effective sticks and carrots, by politicians providing clear and enforced legal settings, or governments providing economic incentives, will have the potential to engender improvement. An important step in raising awareness and starting to mitigate the hazardous chemical pollution of the environment and reducing human exposure is to create a sound knowledge base for decision makers and local authorities. This will help them become aware of the existing risks and appropriate technologies that can be applied in the production and consumption of chemical commodities or mining products. This also includes an urgent need to raise the individual awareness of the appliers and consumers related to the effect of chemical compounds on their own and others' health as well as on the environment.

More than 1.5 billion[1] hectare (2012) of arable land are in low- and middle-income countries – around 75% of the global total. The most environmentally hazardous and controversial substances with the highest bioactivity used on these lands are pesticides. The US Environmental Protection Agency (EPA) estimates that worldwide about 2.4 million tonne of active pesticide ingredients – single or a mixture of substances used for preventing, destroying, repelling, or mitigating any pest – are used each year. This amounts to an average annual use of pesticides of about 1.53 kg/ha. With population growth and increased intensification of agriculture, the use and application of pesticides is steadily increasing. Currently, about 1300 active pesticide substances are in use. These can vary significantly in their chemical characteristics, modes of action, effectiveness, and impacts. Pesticides are highly bioactive even at low concentrations and exposure to pesticides is known to impair human and environmental health. Extremely hazardous pesticides, which are banned in high-income countries, are still being stockpiled or even used in low- and middle-income countries. This use, linked to poor education on the handling of pesticides, limited awareness of their toxicity, the lack of regulations, and an overall lack of appropriate measures of risk mitigation, results in millions of people suffering from pesticide poisoning.

The use of pharmaceuticals to treat human and animal diseases is considered indispensable. More than 3000 active pharmaceutical ingredients are currently in use. These include analgesics, antibiotics, anticancer, antivirals, beta-blockers, contraceptives, lipid regulators, sedatives, impotence drugs, and others. The consistent use of pharmaceuticals results in an omnipresent contamination of the environment by active pharmaceutical ingredients or their transformation products. Increasingly, research in environmental toxicology and environmental chemistry, driven by improved analytical techniques, has resulted in better knowledge about pharmaceuticals in the environment and their effects on ecosystems. The occurrence and fate of pharmaceuticals in the environment have been extensively assessed and documented for high-income countries, whereas data is limited for the low- and middle-income country context. This is critical as the bulk of pharmaceutical production is in these countries. For example, China, India, and Pakistan are all producing large amounts of active pharmaceutical ingredients as a result of increasing demand and their lower production costs. Often the wastewater effluents, released without treatment into the environment, are important sources of pollution for such compounds. Use of active pharmaceutical ingredients increases with the availability of cheap generic drugs, improving living standards, and population growth. Finally, the rapid increase in intensive livestock farming (aquaculture and cattle, poultry, and pork) goes hand in hand with an increased use of active veterinary pharmaceutical ingredients. The consequences for human health resulting from the presence of active pharmaceutical ingredients in the environment are the development of antibiotic-resistant strains of bacteria (e.g. tuberculosis) or antiviral drug-resistant influenza viruses. Pharmaceuticals are found in many organisms in the environment and influence their development, reproduction, and behavior. The effects of this pollution with pharmaceuticals carry over into the population and even into the food web interactions in ecosystems.

Rising demand for raw material and ores from low- and middle-income countries relates particularly to metals and resources used in high-technology industry. Extractions of these minerals produce large quantities of waste. As more high-grade ore deposits are depleted, lower grade ores are exploited whereby even more waste is produced. To produce 0.3 mg of gold, 79 tonne of mine waste is generated. For 1 tonne of copper, 110 tonne of tailings (waste ore) and 200 tonne of waste rocks are generated. Mining energy commodities such as gas, oil, coal, or

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[1] 1 billion = 1,000 million – 10^9

radioactive uranium ore, although not discussed in this report, are known to affect environmental and human health significantly. This report distinguishes four steps in the mining sector that are of concern when analyzing the importance of chemical pollution – ore exploitation, extraction and enrichment, transport, and ore refining. The consequences of ore exploitation comprise not only the generation of mining waste, but also waste from the use of explosives. These include the mixtures of ammonium nitrate and fuel oil, trinitrotoluene, and nitroglycerine, which may have adverse effects on environmental and human health by polluting vulnerable ecosystems. Extracting and enriching the compounds of interest often implies the use of chemical substances. Gold, silver, and platinum group elements are often processed by leaching with cyanides or using mercury for amalgamation, which are then released in an uncontrolled way into the environment. For lead, zinc, and copper milling, flotation, smelting, and sulfuric or hydrochloric acid leaching methods are used, whereas iron is principally extracted by magnetic separation. Pollution from small-scale mining operations, which are widespread and typical in low- and middle-income countries, is a serious concern as regulation and control is hardly feasible. Common chemicals of environmental concern, which are used for the processing and extraction of ores and minerals include hydrochloric acids, sulfuric acid, potassium cyanide and cyanide acids, soda ash, sulfur dioxide, coal tar, and aluminum and zinc sulfates. However, the quantities of these chemicals used and the risks they pose to human and environmental health are difficult to assess. This report focuses on the most hazardous heavy metals, metalloids, and minerals that are released accidentally as side products, posing risks to the environment.

The management of waste from electrical and electronic equipment represents an emerging and growing problem. The continuous expansion of the electronics market and shortened innovation cycles stimulating the replacement of electrical and electronic equipment increase the amount of obsolete equipment. This type of waste comprises a diversity of hazardous compounds especially when poorly managed and regulated, which is often the case in low- and middle-income countries. Although international initiatives try to prevent the export and trade of e-waste from industrial countries they have limited impact. The International Labour Organization highlights that 80% of all e-waste that is sent to low- and middle-income countries ends up in informal and uncontrolled e-waste recycling sites. This poses a risk to human and environmental health given the often obsolete recycling techniques used and the very limited health protection measures afforded the workers.

The significance of chemical pollution from other industrial sectors was difficult to assess given the limited data available or accessible. This report describes issues around the use of chemical substances in the textile, leather, paper, and rubber industries. It identifies the major chemicals of concern and their potential negative impacts on human and environmental health.

Despite data being scarce and/or fragmented, it is safe to conclude that the situation is alarming and that there is a trend that this situation is getting worse. In all the sectors evaluated, significant amounts of a large variety of chemical compounds are used, which enter the environment in often uncontrolled manner and can have negative impacts on environmental health. The negative effects of chemical pollution on human health, either caused by direct exposure, or indirectly, e.g. via the environment or food, are also significant. Because of the lack of data, the real threat for humans and the environment can only be estimated. To improve the situation of chemical pollution, the following four recommendations have been made:

i) data availability and data collection

More comprehensive data, including the complete chemical life cycle, assessments of effects on environmental and human health, and comprehensive risk assessments are needed, on various scales. Data at global scale are needed to support international policy development as well as international conventions and protocols. Increasing international attention will also help national policy makers to make chemical pollution a priority topic. Country-level evidence is crucial for the development of national policies. Finally, since mitigation actions are implemented at local/catchment scale, more detailed information, with significant spatial and temporal resolution, is needed at this level. As a first step, it is suggested that existing data could/should be made publicly available.

ii) development of concepts and tools for monitoring and data collection

Available concepts and tools for monitoring and data collection need to be adapted or newly developed for LAMICs, so that evidence on exposure routes, environmental concentrations and effects of chemical pollutants can be collected. This under the consideration of i) functionality under the respective climatic situation, ii) efficiency and cost-effectiveness, iii) feasibility of use by local people with limited technical skills and expertise, iv) applicability for all relevant spheres (air, soil, water and anthroposphere), v) the ability to capture both exposure and effect assessments and vi) the ability to allow the development of locally relevant risk maps and mitigation options.

iii) development of mitigation options

Despite the fact that chemical pollution is of global importance and influenced by global trends, local mitigation measures are key to improving the situation for human and environmental health. There are no „one size fits all" solutions. A wide portfolio of mitigation options must be developed and evaluated. Ideally, finding and implementing mitigation solutions is a process taking place not in isolation but by including boundary conditions and local challenges and using a base of solid and detailed knowledge about the local situation.

iv) raise awareness in society, private sector and industry, politics and regulatory authorities as well as support the development & implementation of legislation and management tools

Awareness of the existing problem or the risk of the issue becoming a problem is a precondition for change. Society, including policy makers, regulatory authorities and producing industries must be better informed with clearer messages. In this regard, scientists and research play an important role as they can provide facts in an unbiased and neutral way. Furthermore, scientists can also support decision making under uncertainty. Interdisciplinary research including relevant stakeholders in the research process assures that the critical questions can be voiced and tackled by researchers, that necessary and required data can be collected in a focused, practical manner, that mitigation and management tools can be developed in a concerted action, and that evidence can support and drive policy and legislation.

Introduction

Chemical pollution - an underestimated risk

Many polluted sites are in the low- and middle-income countries of Latin and Central America, Africa, and the Asia-Pacific region.

Unintentional poisoning may often be associated with the inappropriate use and environmental management of toxic chemicals.

Chemical substances play an important role in our daily lives. One example is the common practice of using large amounts of pesticides to increase yields in agriculture. Similarly, the use of pharmaceuticals to treat animal and human diseases is indispensable and widespread. Increasing agricultural and livestock production, population growth, improving standards of life, increased productivity and changes in production sites, and the trade and use of chemicals highlight the increasing importance of chemical substances in the global economy. The increasing production and use of a growing number of substances generally comes hand in hand with higher exposures and thus increased risks for human and environmental health. This is particularly of concern when governmental policies and enforcement are deficient, data on the production, use, exposure scenarios, and toxicities are lacking, or if inappropriate corporate practices are in place. Such concerns are globally relevant, but become increasingly significant in the context of low- and middle-income countries. The shift of production and use from high-income countries to low- and middle-income ones can be clearly observed.

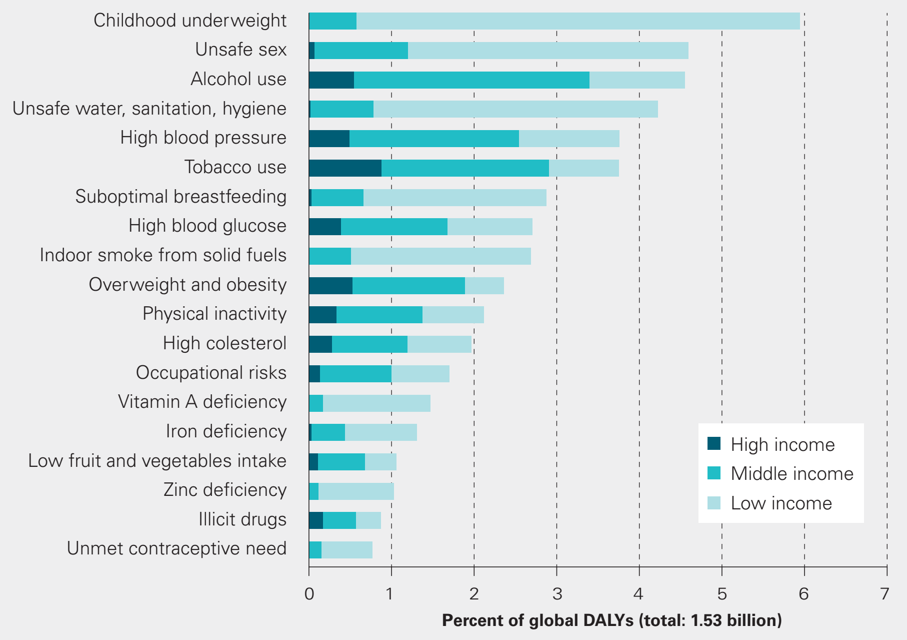

Figure 1: *Proportions of the main health risk factors – in percent of global disability-adjusted life years (DALYs) – for high-, low-, and middle-income countries (World Health Organization, 2009).*

In the past, when discussing the health risks to the populations of low- and middle-income countries, the focus has been on issues such as availability of food, sexually transmitted diseases, and diarrheal diseases. Figure 1 shows the proportions of the main health risk factors – in percent of global disability-adjusted life years[2] (DALYs; World Health Organization, 2009) – for high-income countries and low- and middle-income countries. For low- and middle-income countries the risks of chemical pollutants have not yet been determined as relevant although evidence points to a considerable risk factor.

Few reports are available or accessible that give a comprehensive overview on chemical pollution in low- and middle-income countries. Most reports on global challenges and risks in low- and middle-income countries focus on health, food security, climate change, and socio-economic aspects. Two examples of reports with a focus on chemical pollution are the United Nations Environmental Programme's report on Global Chemicals Outlook – Towards Sound Management of Chemicals (United Nations Environment Programme, 2013c) and the annual reports of the Blacksmith Institute (Blacksmith Institute and Green Cross, 2011, 2012), produced in cooperation with Green Cross, on The World's Worst Pollution. The Blacksmith Institute revealed that the number of people affected by industrial waste (focusing mainly on heavy metals) is comparable to the number of people affected by tuberculosis or malaria when using DALYs as the unit of measurement. The top ten pollution problems with their respective contaminated sites, shown in the Blacksmith Institute's publication, highlight that many of the polluted sites are located in the low- and middle-income countries of Latin and Central America, Africa, and in several countries of the Asia-Pacific region (Blacksmith Institute and Green Cross, 2011).

In low- and middle-income countries, the production and use of pesticides, pharmaceuticals, and chemical substances for ore extraction in mining and use in the construction, textile, and apparel industries are often linked to a release of extremely hazardous and bioactive substances. These substances include heavy metals, pharmaceuticals, pesticides, detergents, solvents, or persistent organic pollutants (POPs). These pollutants, as single compounds or in mixtures, may have negative impacts on human health and the environment (Buccini, 2004; Blacksmith Institute and Green Cross, 2011; United Nations Environment Programme, 2010, 2013c).

A map showing unintentional deaths from poisoning (Figure 2) reveals that in many low- and middle-income countries the annual numbers of deaths from unintentional poisoning range from 30 to 450 cases per million inhabitants, with high levels especially in Belarus, Kazakhstan, Ukraine, South Asia, and West Africa. The World Health Organization (WHO) emphasizes that in such countries unintentional poisoning may often be associated with the inappropriate use and environmental management of toxic chemicals.

The annual report of The World's Worst Toxic Pollution Problems 2011 (Blacksmith Institute and Green Cross, 2012, Figure 3) shows the number of mining sites (e.g. for minerals and ores) as well as polluted industrial and agricultural sites and it becomes clear that most of these sites are in low- and middle-income countries. The impact of anthropogenic chemical pollution is even higher when the emissions or discharges of these substances are not – or are inadequately – regulated, enforced, or controlled, or if obsolete production or treatment technologies are applied. Unfortunately, this is frequently the case in low- and middle-income countries (African Ministerial Conference on Environment and United Nations Environment Programme, 2004; International Labour Organization, 2012; United Nations Environment Programme, 2013c).

Impact of anthropogenic chemical pollution is higher when the emissions are inadequately regulated, enforced, or controlled, or if obsolete production or treatment technologies are applied.

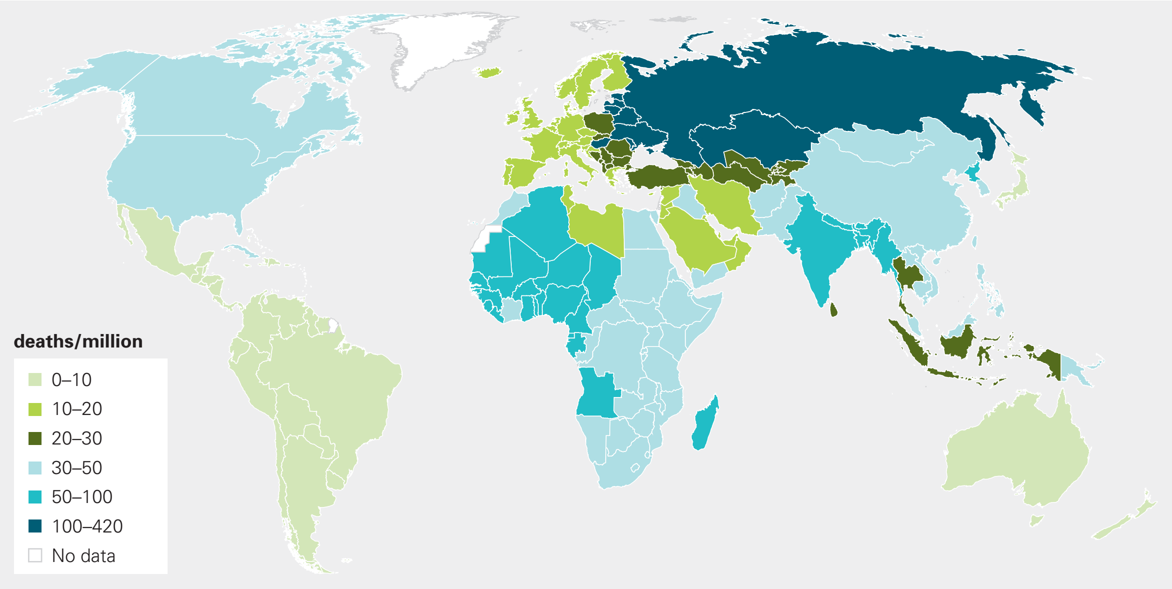

Figure 2: *Global map with estimated deaths from unintentional poisoning in deaths per million (World Health Organization, 2005).*

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[2] DALY is used as a measure to integrate the years of life lost from premature death with the years of healthy life lost as a result of illness and disability.

High human exposure to hazardous substances is also a consequence of poor working conditions.

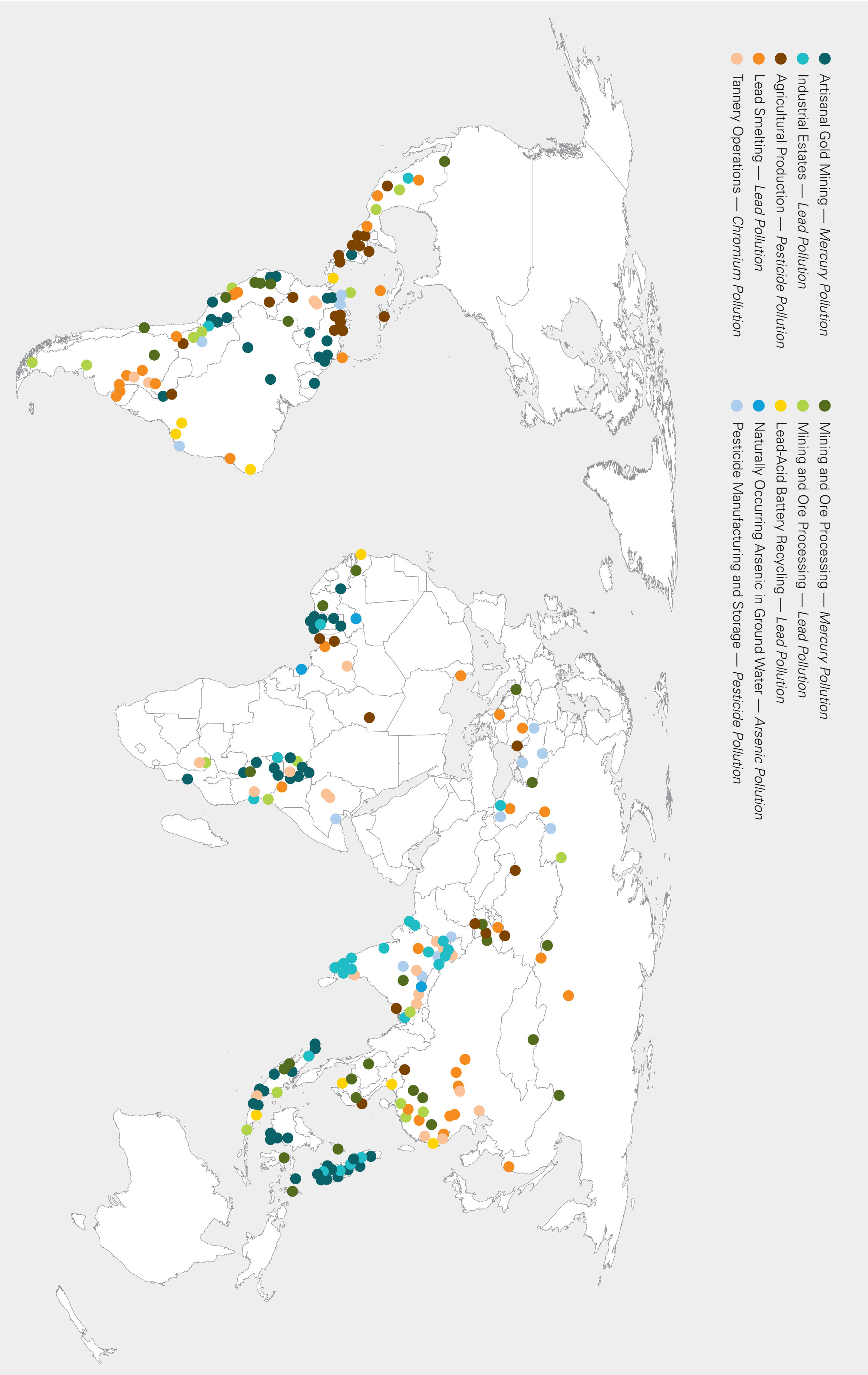

Figure 3*: Top ten pollution problems and the major sites of contamination (Blacksmith Institute and Green Cross, 2011).*

The impacts are further exacerbated as industries and dumping sites are often near to or in densely populated areas, thereby increasing the risk of human exposure. High human exposure to hazardous substances, especially for workers, is also a consequence of poor working conditions as safety measures are seldom in place or respected and occupational incidents are frequent (El Sebae, 1993; Quarantelli, 2003; Blacksmith Institute and Green Cross, 2011). Such behavioral aspects, together with awareness issues – the fact that operators, workers and local communities are minimally aware of the consequences and impacts of hazardous emissions – contribute to high exposure and the resulting health risks (Blacksmith Institute and Green Cross, 2012). This problem is, however, not restricted to industrial settings and/or urban environments. The same is true for pesticide use in agriculture. Unawareness, lack of appropriate technology, or incomplete regulations result in increased exposures and risks for human and environmental health (Kesavachandran et al., 2009).

Lack of government enforcement and a disregard of the laws or regulations for the application, production, and disposal of chemicals and other waste material, result in a vast amount of chemicals being released into the environment (Blacksmith Institute and Green Cross, 2012; International Labour Organization, 2012; United Nations Environment Programme, 2013c). Cases are documented where obsolete chemicals were stockpiled under insecure and unprotected conditions. As a result, these chemicals were leached into the soil, contaminated aquifers, or were transported by air or water (rainfall runoff or erosion) and discharged into river systems and lakes (Food and Agriculture Organization, 2001; Elfvendahl et al., 2004). Wildlife and humans living adjacent to insecure dumping sites were drinking polluted water, or eating plants grown in and animals raised on contaminated soil, and, most probably, were taking up increased amounts of hazardous chemicals (Oaks et al., 2004; Tue et al., 2010; Bedi et al., 2013).

In summary, the global situation, the degree of chemical pollution, and the impact on the environment and human health are yet unclear as evidence is limited, especially in low- and middle-income countries. This is a consequence of the limited number of governmental or other independent monitoring systems that have been implemented and/or the lack of capacity to do so. The lack of a strategy and capacity to oversee the use of hazardous chemicals in industrial activities is a major bottleneck to obtaining sound data – a basic requirement to ensure appropriate management. Obtaining a clear oversight of activities is also hindered by the existence of many informal businesses (often small-scale enterprises), which, by definition, are not legalized and are, therefore, also difficult to quantify and monitor (Artisanal Gold Council 2015; International Labour Organization, 2012). Lack of sound data limits the possibilities to undertake a good risk assessment and this again limits the possibilities to advocate for a higher priority at the political level. Showing the consequences of chemical exposure is further complicated as such pollutants often show chronic effects that require the accumulation of data over a long period of time. Monitoring pollutants is also challenging as often there is a lack of analytical technologies and capacity in these countries.

As anthropogenic pollutants are often not considered as significant risk factors, they tend to be disregarded by policy measures. Similarly, the political will is often too low to change this situation and, when working with a limited budget, the issue of chemical pollutants most often does not receive high priority.

The future of chemical pollutants in low- and middle-income countries

Trends show a clear global increase in the production of chemical substances and this increase is particularly large in low- and middle-income countries (PricewaterhouseCoopers, 2012). Expected demographic changes, such as population growth, increasing life expectancy, improving living standards, and modern lifestyles are likely to increase the demand for chemicals and consequently stimulate global production and the increased use of hazardous ones.

The United Nations Environment Programme (2013c) in its Global Chemicals Outlook 2013 shows how the chemical industry has grown continuously over the last decades (Figure 4). Output from the chemical industry has increased globally from US$171 billion in 1970 to US$4120 billion in 2010, although these figures do not consider inflation or changes in prices. When focusing on economies in transition (Figure 4B), an exponential rate of growth is visible for low- and middle-income countries, whereas in developed regions this growth is linear. Rapid growth can be observed especially after the time of the financial crisis around 2008/2009. One explanation for this exponential growth in outputs in low- and middle-income countries is the shift of the production facilities of the chemical industry from high- to low- and middle-income countries.

This trend is confirmed by data from the European Chemical Industry Council (Cefic, 2013) and from figures published in the United Nations Industrial Development

Obsolete chemicals are stockpiled under insecure and unprotected conditions. As a result, these chemicals are leached into the soil, contaminate aquifers, or are transported by air or water (rainfall runoff of erosion) and discharged into river systems and lakes.

Impact on the environment and human health are yet unclear as evidence is limited, especially in low- and middle-income countries.

Rapid growth of global chemical production goes hand in hand with a shift of the production facilities to low- and middle-income countries.

Chemical intensification in low- and middle-income countries is stimulated by increase in local demand and increase in the number of producing facilities for the local and global market.

Organization's International Yearbook of Industrial Statistics 2013 (Appendix Figures 1–4; United Nations Industrial Development Organization, 2013). Recently, several multinational chemical companies have opened new production facilities in low- and middle-income countries to reduce production costs (United Nations Environment Programme, 2013c). Chemical intensification in low- and middle-income countries is thus stimulated by both a local increase in demand as well as an increase in the number of facilities producing for local as well as high-income country markets (United Nations Environment Programme, 2013c).

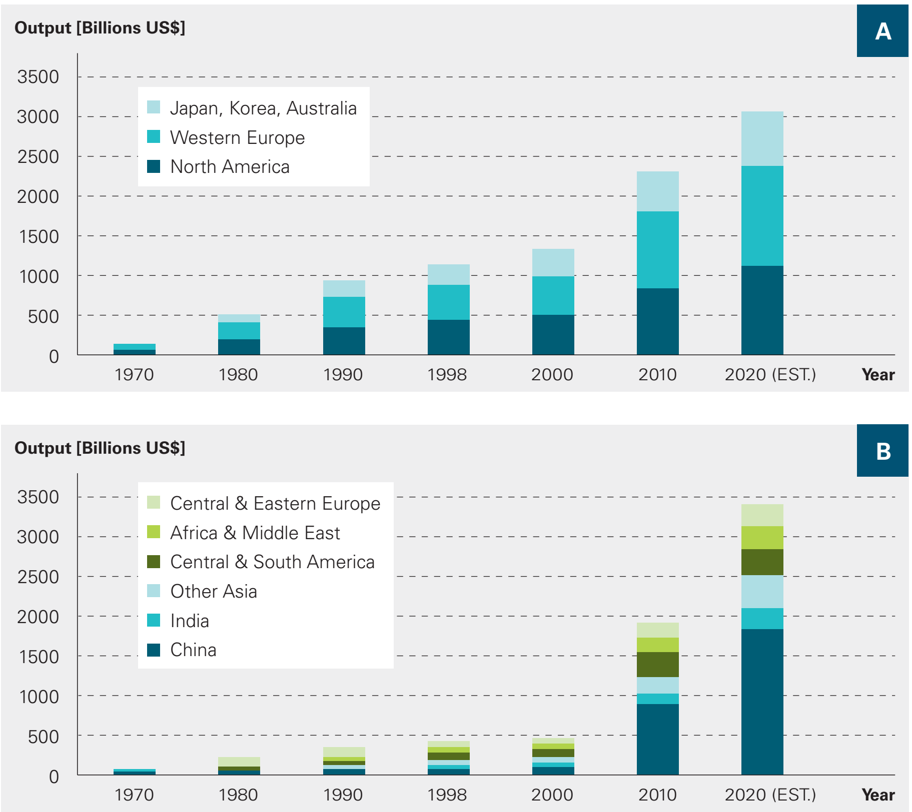

Figure 4: *Output of the chemical industry in developed regions (A) and developing regions and countries with economies in transition (B; United Nations Environment Programme, 2013c)*

The increase in the number and size of the production facilities in low- and middle-income countries is likely to go hand in hand with an increase in chemical pollution, exposure, and impact on human and environmental health. Such an intensification of chemical production will affect the lower-income countries most; it is these countries that will face the greatest difficulties in reacting to this increase with appropriate policy, technology, or management measures (African Ministerial Conference on Environment and United Nations Environment Programme, 2004; United Nations Environment Programme, 2013c; European Chemical Industry Council, 2013; United Nations Industrial Development Organization, 2013). In addition, education and raising awareness will be major challenges in general, and in low- and middle-income countries in particular.

Objectives of this report

As highlighted in the first section **Chemical pollution - an underestimated risk**, the situation regarding chemical pollution in low- and middle-income countries is seldom well documented, and if it is, then it is only in small-scale scientific studies. Nevertheless, several signals point to an alarming situation with a worsening trend.

Therefore, the main objectives of this report are to:

- Develop a systematic structure to describe the different sectors of chemical use, the various chemical substance classes or individual compounds, and their importance and potential impact on human and environmental health
- Obtain the best possible comprehensive overview of the existing situation by studying all the relevant literature for each sector and to assess the main chemicals used, their pathways into the environment, human exposure to them, and their impacts on environmental and human health
- Identify high risk areas in which the welfare of human beings and the environment might be threatened and endangered
- Suggest possible measures to mitigate environmental and human health risks in the production and use of hazardous chemical substances by improving practices to reduce exposure, remediate polluted areas, or encourage innovative 'green' technologies in the production and application of chemical substances (Hanrahan et al., 2007; United Nations Environment Programme, 2013, 2013b)

- Identify significant gaps in knowledge where more research is necessary and use this to advocate for increased research resources to develop evidence that can be used for policy making and in practice to address the environmental conditions in regions at risk

- Advocate for more global attention to the issue of chemical pollution in low- and middle-income countries and for more structured and reliable country-level monitoring that can be complied with at a larger scale to examine the global situation and changes over time.

This report is not written primarily for a scientific audience, but rather it targets bilateral and multilateral organizations, government and non-governmental organizations, and representatives of the industry; anyone with an interest and stake in public health, industrial development, or environmental protection. For the scientific audience it indicates areas where more research is required and seeks to motivate researchers to engage in the overall topic of chemical pollution in low- and middle-income countries. Information about the actual levels of chemical pollutants in low- and middle-income countries and their impacts on environmental and human health is needed. Any possible collaboration with Eawag in providing and exchanging data about the production, export, and release of chemicals into the environment, as well as on the impacts on human and environmental health is welcomed. The aim is to find and establish together strategies to:

- Assess and monitor these hazardous pollutants in the environment
- Assess their impacts on environmental and human health
- Mitigate exposure to the environment and humans, with a strong focus on low- and middle-income countries.

Categorizing chemical pollutants

A first step when compiling this report was to specify and structure the broad term of anthropogenic chemical pollution. This report differentiates, according to various production sectors, where chemical substances are used and where pollution occurs that is relevant in the low- and middle-income country context (Buccini, 2004; Farrell et al., 2004; Pesticide Action Network Asia and the Pacific, 2010; Blacksmith Institute and Green Cross, 2011, 2012, 2013; International Labour Organization, 2012; United Nations Environment Programme, 2013c; Weber et al., 2014). The sectors covered by this report are:

For each of the sectors, the most relevant chemical pollutants are determined and classified into different categories according to their physicochemical characteristics and/or their environmental behavior. We also describe these characteristics and their potential risks to human and environmental health.

For each sector, the most hazardous pollutants are described, information is compiled regarding their input and exposure pathways, their trend of use, future expected pollution, and their negative impacts on humans and the environment.

Within each sector, cases of significant environmental and human concern are introduced describing causes and effects. An overview is given regarding good practices, which have been implemented already under specific conditions or which are recommended for implementation as mitigation measures to reduce emission or environmental impact, or which would help to mitigate the adverse effects on human health.

The report ends with conclusions and with an analysis of the current research gaps. It recommends future potential research questions and research requirements.

Limitations of this report

This report is based on an analysis of the literature and databases using scientific publications, news articles, reports, and reliable websites. Furthermore, personal contact was established with specific government and non-governmental organizations specializing in this topic and with individuals with experience of and expertise in chemical pollution. The maps shown in this report were compiled with the help of the geographic information system software ArcGIS, whereby data included in the maps are open source information obtainable from various international, government and non-governmental organizations.

This report does not cover all chemical substances of concern. The authors took an informed decision to leave out certain substances to make it more manageable given the timeframe for finalizing this report, but at the cost of restricting its scope. Natural geogenic pollutants, such as arsenic (As) and fluorine (F), are not covered in this report although it is well-known that high concentrations of these substances in groundwater of certain regions of the world impact severely on the health of humans drinking such water without appropriate treatment. Furthermore the report does not cover nutrients, such as nitrogen and phosphorous, the main causes of eutrophication. Also nanoparticles, chemical substances related to fossil fuels, radioactive compounds, air pollution, and greenhouse gases are not dealt with.

As mentioned in various sections of this report, one major bottleneck the authors faced when compiling this report was the lack or limited availability of chemical pollution data at the country level or with regard to specific industrial sectors in low- and middle-income countries. Only a few databases exist with more or less comprehensive country data on the use of chemicals or the concentrations of chemical pollutants in the environment (Food and Agriculture Organization, 2013; Weber et al., 2014; United States Geological Survey, 2013; Step Initiative, 2015). Data on industrial activity, production, and use of chemical substances is not available to the public, especially in the context of low- and middle-income countries.

Agricultural Chemical Pollutants

Chemical characteristics and their potential risks

Introduction

According to calculations with the publicly available data of the Food and Agriculture Organization of the United Nations (FAO; 2013), there were 1563 billion hectare (ha) of both arable land and land with permanent crops available worldwide in 2012. Of this, about 75% is located in low- and middle-income countries.

In agriculture, the most environmentally hazardous and controversial substances with the highest bioactivity are pesticides. Large volumes of these are applied annually (Wesseling et al., 1997). According to the US EPA (United States Environmental Protection Agency, 2015a), a pesticide is defined as a single substance or a mixture of substances used for preventing, destroying, repelling or mitigating any pest (e.g. insects, mice, and other animals, unwanted plants, fungi, and microorganisms).

Along these lines, the EPA estimated that worldwide about 2.4 million tonne of active pesticide ingredients are used each year. This means that given the global area of arable land and permanent crops, the average annual use of pesticides is about 1.53 kg/ha (United States Environmental Protection Agency, 2011; Food and Agriculture Organization, 2013). Hence, chemical substances are used intensively for the removal of unwanted pests and plants on crops and in fields since mechanical removal is considered too time, labor, and cost intensive. In line with population growth and increased intensification of agriculture, the application of pesticides has also increased and intensified in low- and middle-income countries (Henriques et al., 1997; Ecobichon, 2001). Other substances of environmental concern, like phosphorous, nitrogen, and other fertilizers, which are causing eutrophication, do not fall within the scope of this study. However that is not to say that they are not of environmental concern.

Currently, about 1300 active pesticide substances are known (European Commission, 2015). They vary markedly in their chemical characteristics, modes of action, effectiveness, and impacts. According to their use, toxicity, chemical structure, and persistence, the most hazardous insecticides (I) and herbicides (H) are (Fishel, 2014a, b, 2015; International Agency for Research on Cancer, 2015; European Commission, 2015):

- Bipyridylium (H)
- Carbamates (I,H)
- Organochlorines (I)
- Organophosphates (I)
- Pyrethroids (I)
- Triazines (H)

In general, in low- and middle-income countries more investigation about the fate, occurrence, and the human and environmental health risks of pesticides is required.

Toxicological potential

Most of the pesticides used are not highly specific to one target organism. They are not easily degradable as shown by their half-lives, which range from several days to years. Also, they are applied in large quantities all over the world (~1.5 kg/ha; Deer, 2004). Adding to this, especially in low- and middle-income countries, pesticides that are banned already in high-income countries, such as Europe or the USA, are still used or stockpiled in low- and middle-income countries where regulations, environmental controls, infrastructure, and the risk awareness of those hazardous pollutants are lacking (Kesavachandran et al., 2009; Carneiro et al., 2012). Several of these pesticides, especially the organochlorines, have a high toxic and bioaccumulation potential (Bedi et al., 2013). In addition, metabolites of degraded pesticides and their effects on environmental and human health are often unknown or unclear (Somasundaram and Coats, 1991; Belfroid et al., 1998). Pesticides used in low- and middle-income countries, their environmental relevance, their physicochemical properties, and the trends in their use are summarized in Table 1. The human toxicological potential of substances is indicated by their lethal dose for 50% of the organisms tested – the (LD$_{50}$)[3] values for rats – and their eco-toxicological potential as indicated by the environmental quality standards (Ecotox Centre, 2015). The environmental quality standards, MAC-EQS (maximum allowable concentrations) and AA-EQS (annual average concentrations), represent the acute and chronic environmental concentrations of chemical agents that, if exceeded, indicate a risk to aquatic organisms in surface water bodies.

Application of pesticides has increased and intensified in low- and middle-income countries.

About 1300 active pesticide substances are in use. They vary in their chemical characteristics, modes of action, effectiveness, and impacts.

Pesticides that already are banned in high-income countries are still used or stockpiled in low- and middle-income countries.

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[3] LD$_{50}$ is a standardized measure for expressing and comparing the toxicity of chemicals.

Main Issues

- It is known that pesticides are highly bioactive even at low concentrations and exposure to pesticides can impair human and environmental health (van der Werf, 1996; Roldán-Tapia et al., 2005; Wesseling et al., 2005; Relyea, 2009; World Health Organization, 2010b; Wu et al., 2011a; Xu et al., 2013)
- The major part of the global arable land and land with permanent crops (about 75%) is located in low- and middle-income countries (Food and Agriculture Organization, 2013) and where the highest amounts of pesticides (around 2.4 million tonne/year) are used globally (United States Environmental Protection Agency, 2011)
- Extremely hazardous pesticides, which are banned in many high-income countries, are still stockpiled in low- and middle-income countries. Additionally, banned pesticides or pesticides that cannot be properly handled in low- and middle-income countries are being used in these countries under inappropriate conditions (Dinham, 2003; Elfvendahl et al., 2004; Wesseling et al., 2005; Pesticide Action Network Asia and the Pacific, 2010)
- Millions of people suffer from pesticide poisoning in low- and middle-income countries (Kesavachandran et al., 2009) mainly because of poor education regarding the handling of pesticides, lower awareness of the toxicity of pesticides, and a lack of regulations governing pesticide use (Kesavachandran et al., 2009; Dawson et al., 2010; Pesticide Action Network Asia and the Pacific, 2010).

According to the WHO's estimates, about 3 million people around the globe are severely poisoned annually by pesticides. Of these, at least 10% died and 99% of these poisoning incidents happened in low- and middle-income countries. Suicides by ingesting pesticides contributed to about two-thirds of all acute pesticide poisoning cases (Jeyaratnam, 1990; Jeyaratnam and Chia, 1994; Kesavachandran et al., 2009). However this number may be underestimated since in low- and middle-income countries health care centers remain difficult to access and thus many cases of poisoning are not registered and remain unreported. The chronic effects on environmental and human health resulting from exposure to pesticides are often not included in such risk assessment studies (Kesavachandran et al., 2009; Dawson et al., 2010; Pesticide Action Network Asia and the Pacific, 2010). A comprehensive research literature study revealed that the main groups of the most hazardous pesticides used in uncontrolled ways and in high quantities in low- and middle-income countries are organochlorines, organophosphates, bipyridylium herbicides, carbamates, and triazines (Kesavachandran et al., 2009; Pesticide Action Network Asia and the Pacific, 2010). The environmental behavior and toxicity of typical representatives of those pesticide groups considered most harmful in low- and middle-income countries are described in more detail in the following chapter.

3 million people annually are poisoned by pesticides. 99% of these poisoning incidents happened in low- and middle-income countries.

Chronic effects on environmental and human health by exposure to pesticides are often not included in risk assessment studies.

Pesticides of environmental concern

A) Organochlorine (OC) insecticides

Organochlorine (OC) insecticides are of particular concern for environmental and human health. Lindane, dichlorodiphenyltrichloroethane (DDT), aldrin, dieldrin, endosulfan, heptachlor, and heptachlor epoxide are OC insecticides (Lewis et al., 2015).

Consumption

The use of most OC insecticides is declining because of international restrictions. For example, the Stockholm Convention 2004 restricted or prohibited the production, import, export, and inappropriate stockpiling of OC insecticides that contain POPs, such as aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, taxophene, chlordecone, α- and β-hexychlorocyclohexane, and lindane (United Nations Environment Programme, 2013d). Nevertheless, OC insecticides still pose risks to environmental and human health. The OC insecticide of most concern for its effects on the environment in several low- and middle-income countries is DDT. DDT was banned in many parts of the world in the 1970s and 1980s because of its environmental persistence and moderate toxicity (National Geographic, 2006). However, DDT has begun to be used again more frequently since 2000, mainly in sub-tropical and tropical low- and middle-income countries in Africa, Latin America, and South Asia. This is because it is an effective and long-lasting insecticide for controlling insects that spread malaria, dengue fever, typhus, and cholera, and because its low cost makes it affordable in poor regions (Loganathan and Kannan, 1994; African Ministerial Conference on Environment and United Nations Environment Programme, 2004; European Commission, 2015). The recommended method for using DDT as a vector control for insects that transmit malaria, dengue fever, typhus, and cholera in low- and middle-income countries is to spray a very low concentration on house walls as an insect repellent. In the past, DDT has also been widely used in agriculture. In low- and middle-income countries, the use of DDT should be strictly controlled and regularly monitored (National Geographic, 2006). High-income countries already generally restrict the use of DDT. Globally, much less is used now than previously (Loganathan and Kannan, 1994). Nevertheless, since the ban on OCs, tonnes of DDT have been stockpiled under inappropriate conditions in low-income countries where they pose a risk to environmental and human health (Elfvendahl et al., 2004; Dasgupta et al., 2010). To date, reliable comprehensive data on the production of OCs and the use of old stocks of OCs are not available.

Environmental behavior and occurrence.

The physical and chemical properties of OC insecticides vary considerably. For instance, lindane and its other hexychlorocyclohexane isomers have higher vapor pressures and water solubilities, but lower adsorptions than chlordanes and DDT and, therefore, have less potential for bioaccumulation. However, all OC insecticides are known to persist in environmental systems for extended periods. Table 1 presents the physiochemical properties of significant OC insecticides. Volatile and semi-volatile OCs, such as lindane, persist in the atmosphere. The global climate transports volatile OCs from warmer to colder polar regions where they accumulate in the water and ice (Goldberg, 1975). In contrast, lipophilic compounds accumulate in soils and biota and affect wildlife and humans. Biotransformation eliminates residues slowly (Figure 5). Decades after the ban on OC insecticides, the levels of residues in human and bird adipose tissue are declining very slowly (Loganathan and Kannan, 1994). The top predators, the last links in the food chain, are most affected as a consequence of the enrichment of lipophilic OC insecticides by biomagnification at successive trophic levels (Bro-Rasmussen, 1996). Clearance rates in biota are higher in rivers and lakes than in semi-closed seas, where OC concentrations have slightly decreased, and in oceans, where they have remained constant. In aquatic biota in tropical regions, concentrations of OCs have increased slightly since 1970. The increase in concentrations may be the result of the persistence of OCs and because several of these, mainly DDT, are still used to prevent the spread of vector-borne diseases, such as dengue fever and malaria.

In 2003, OC insecticide concentrations in the Tonghui River, China, ranged from 134.9 to 3788 ng/L. Concentrations of OC insecticides in sediments ranged from 1.79 to 13.98 ng/g dry weight (Zhang et al., 2004). On the east coast of Thailand, oysters contained concentrations of OC insecticides up to 16.71 ng/g wet weight (Cheevaporn et al., 2005). In 2008, Devanathan et al. showed that the concentrations of DDT in breast milk in low- and middle-income countries were higher than those in higher-income countries (Devanathan et al., 2009). In New Delhi the mean level of DDT in human breast milk was 1500 ng/g lipid weight and in Chennai 1200 ng/g lipid weight, while in Malaysia the mean level was 1600 ng/g lipid weight. Breast milk sampled in the Democratic Repu-

Use of organochlorine insecticides is declining due to international restrictions. However, in sub-tropical and tropical low- and middle-income countries DDT is used again more frequently since 2000.

All organochlorine insecticides are known to persist in environmental systems for extended periods. Volatile and semi-volatile organochlorines persist in the atmosphere and accumulate in the water and ice of colder polar regions. Lipophilic compounds accumulate in soils and biota and affect wildlife and humans.

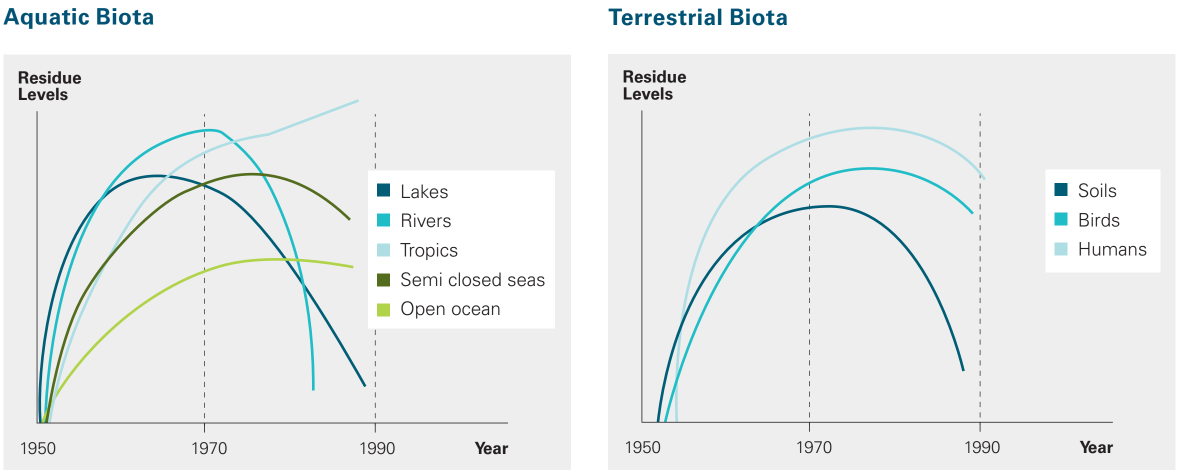

__Figure 5__: Pollution trends of organochlorine insecticides in aquatic and terrestrial biota (Loganathan and Kannan, 1994)

blic of Vietnam had a DDT concentration (mean value) of 2200 ng/g lipid weight, in China (Hong Kong) it was 2870 ng/g lipid weight, and in Mexico, 4100 ng/g lipid weight. In contrast, human breast milk sampled in the USA had DDT residues of 65 ng/g lipid weight, Germany 240 ng/g lipid weight, Japan 340 ng/g lipid weight, United Kingdom 470 ng/g lipid weight, and Australia 1200 ng/g lipid weight (Devanathan et al., 2009).

Toxicity

OC insecticides have a bad reputation because of their toxic potential. There is evidence of the negative effect of OCs on endocrine activity (Kojima et al., 2004; Lemaire et al., 2004), their carcinogenic potential (Ibarluzea et al., 2004), and their potential to promote neuropsychiatric impairment and diseases such as Parkinson's Disease (Fleming et al., 1994). Furthermore, the DDT metabolite dichlorodiphenyldichloroethylene is known to cause eggshell thinning by impairing or inhibiting prostaglandin synthesis in eggshell gland mucosa (Lundholm, 1997). Bobwhite quail (*Colinus virginianus*) exposed to 60 to 85 µg DDT/g body weight as an oil solution or 300 µg DDT/g body weight in a crystalline form showed acute toxic effects. After chronic exposure (63 days) to 3.07 mg DDT by oral ingestion, 70% of the tested bobwhite quail died (Coburn and Treichler, 1946).

B) Organophosphates (OP) and Carbamates

Continuous application of organophosphates and carbamates increases environmental concentrations especially in lakes, groundwater, and soils, although they degrade more easily than organochlorines.

The most hazardous organophosphates are: Azinphos-methyl, chlorpyrifos, diazinon, dichlorvos, dimethoate, ethephon, malathion, methamidophos, naled, and oxydemeton-methyl. The carbamates aldicarb, aldoxycarb, aminocarb, bendiocarb, carbofuran, dimetan, dimetilan, dioxacarb, methiocarb, methomyl, oxamyl, and propoxur are very toxic. Bufencarb, carbosulfan, pirimicarb, promecarb, thiodicarb, and trimethacarb are moderately toxic carbamates (Morais et al., 2012).

Consumption

Most OPs and carbamates are used in insecticides, herbicides, and fungicides (Table 1). Today, most WHO Class I and II OPs and carbamates are banned in most parts of the world. Large amounts of Class II or lower OPs and carbamates are still widely used (Table 1).

Detecting carbamates is a challenge even when using relatively modern techniques, such as liquid chromatography (LC) with post-column fluorescence detection or LC-diode array ultraviolet (UV) detection.

Environmental behavior and occurrence

Compared to OCs, OPs and carbamates are less persistent and bioaccumulative (Henriques et al., 1997; Klaassen, 2013). Table 1 presents the physiochemical properties of several OPs and carbamates. In soil samples taken in 2002 and 2003 from agricultural areas around Hisar, Haryana (India), the maximum concentrations of the OPs chlorpyriphos, malathion, and quinalphos were 0.172, 0.008, and 0,01 µg/g, respectively (Kumari et al., 2008).

In 2000, groundwater from an agricultural area in the Yaqui Valley, in northwest Mexico, had 5.4 µg/L of the carbamate methiocarb, and surface water had 18 µg/L of the carbamate metabolite of carbofuran, 3-hydroxycarbofuran. In this region, groundwater is an important source of drinking water, especially in rural areas, thus contamination of groundwater by pesticides is a serious health risk for local communities (García de Llasera and Bernal-González, 2001). Consequently, although OPs and carbamates degrade more easily than OCs and have shorter half-lives, these pesticides still occur in water samples at µg/L or ng/L concentrations because of their continuous use in agriculture over months or years (Gruber and Munn, 1998). In low- and middle-income countries, especially in sub-tropical and tropical regions, pesticides may be used throughout the year because there is no winter. Continuous application increases environmental concentrations, especially in standing water (lakes), groundwater, and soils. Inappropriate application of pesticides, applying too much, neglecting to consider wind direction or surface runoff, or applying to agricultural areas near wells or aquifers that are used as drinking water sources, can lead to high concentrations (Wesseling et al., 2005; Pesticide Action Network Asia and the Pacific, 2010). Although large amounts of carbamates are widely used, monitoring data and data on environmental concentrations are not as available as for OCs and OPs, mainly because of the challenge of detecting carbamates. García de Llasera and Bernal-González, (2001) showed that it is even difficult to detect carbamates using relatively modern techniques, such as liquid chromatography (LC) with post-column fluorescence detection or LC-diode array ultraviolet (UV) detection.

Toxicity

Although the chemical structures of OPs and carbamates differ, they act in a similar way. Both inhibit the enzyme acetylcholinesterase. Carbamates are considered to be less toxic than OPs as they bind less tightly to acetylcholinesterase (Henriques et al., 1997). Inhibiting the enzyme acetylcholinesterase kills many insects. However, vertebrates and mammals are also highly susceptible because inhibiting acetylcholinesterase causes neuropsychological sequelae (Fukuto, 1990; Story and Cox, 2001). For instance, in human pesticide poisoning, symptoms of acetylcholinesterase inhibition are miosis, salivation, sweating, lacrimation, rhinorrhea, abdominal cramping, vomiting, diarrhea, urinary incontinence, bronchospasm, dyspnea, hypoxemia, bradycardia, bronchial secretions, pulmonary edema, and respiratory failure (Morais et al., 2012). School children exposed to OPs and carbamates in infancy suffer significant consequential damage. This includes, for example, deficient inhibitory motor control or difficulties in the acquisition phase of verbal learning tasks (Kofman et al., 2006).

Vertebrates and mammals are also highly susceptible to carbamates, as inhibiting acetylcholinesterase causes neuropsychological pathological conditions.

In Costa Rica in 2001, drifts of the OP methamidophos, which was being used to prevent agricultural pests, affected 78 children. In 2003 the number was 40 children and in 2004, 61 children were affected (Wesseling et al., 2005). Carbamates and OPs also impair reproduction in vertebrates (Pawar and Katdare, 1984) and mammals (Gosselin et al., 1984) because of their estrogenic potential (Schulte-Oehlmann et al., 2011). Furthermore, carbamates and OPs are suspected of causing cancer (Schlatter and Lutz, 1990). The toxic potential of OPs, and especially carbamates, varies considerably. For instance, aldicarb, aldoxycarb, aminocarb, bendiocarb, oxamyl, and propoxur have an estimated LD$_{50}$[4] value for humans of less than 50 mg/kg. Bufencarb, carbosulfan, pirimicarb, promecarb, thiocarb, and trimethacarb are moderately toxic with estimated LD$_{50}$ values of from 50 to 200 mg/kg. Fenocarb, carbaryl, and isoprocarb have low toxicity with an estimated LD$_{50}$ of less than 200 mg/kg (Erdman, 2004). From the eco-toxicological point of view, crustaceans are much more sensitive to OPs than to carbamates: *Daphnia magna* and *Hyalella azteca* showed acute LC$_{50}$s of 0.6 and 0.1 µg/L after exposure to the OP chlorpyrifos for 48 hours, and LC$_{50}$s of 3990 and 583 µg/L after exposure to the carbamate aldicarb for 48 hours. Vertebrates generally seem to be less sensitive to exposure to OPs and carbamates than crustaceans. The fish *Pimephales promelas* had higher LC$_{50}$ values than crustaceans – 162.7 µg/L after exposure to chlorpyrifos for 48 hours and 8860 µg/L after exposure to aldicarb for 48 hours. Nevertheless, chronic exposure of fish to OPs and carbamates led to alterations in swimming (Matton and LaHam, 1969) and feeding (Bull and McInerney, 1974) behavior, changes in social interactions (Symons, 1973), widened opercula, and increased hyperexcitability (Zinkl et al., 1991). In plants, the herbicide carbamates, for example carbetamide, inhibit cell division by disturbing the nucleic acid metabolism and protein synthesis (Audus, 1976; Ocampo and Barea, 1985; Morais et al., 2012), and they are also known to inhibit photosynthesis (Moreland, 1980).

C) Triazines

Atrazine, atraton, simazine, prometon, and propazine are members of the triazine-derivate herbicides of environmental concern (Köck-Schulmeyer et al., 2013).

Consumption

The triazine derivate atrazine is one of the most widely used herbicides worldwide (Azevedo et al., 2010). According to a quantitative analysis for atrazine, the EPA estimated that the annual consumption of atrazine was about 35,000 tonne, in 2001 (United States Environmental Protection Agency, 2006). Usually, the herbicide is used to eliminate unwanted plants before the emergence of the crop. Most of it is used before the cultivation of crops such as corn, sugarcane, sorghum, and sweet corn. In addition to its agricultural application it is used in forestry for non-selective plant control on roads, railway lines, and industrial areas (United States Environmental Protection Agency, 2006; Azevedo et al., 2010).

The triazine derivate atrazine is one of the most widely used herbicides worldwide. Although banned in the EU since 2003 triazines are still in use in the USA and many low- and middle-income countries.

Environmental behavior and occurrence

The investigations of Köck-Schulmeyer et al. (2013) showed that triazines, triazine- derivates, and the transformation products atrazine, desethylatrazine,deisopropylatrazine, simazine, and terbuthylazine are hard to remove from water systems. Given their nitrogen and chlorine atoms, triazines have polar and persistent characteristics.

The physicochemical properties of atrazine are presented in Table 1. From 2007 to 2009, Köck-Schulmeyer et al. (2013) measured concentrations of triazines, its derivates, and its metabolites ranging from 20 to 169 ng/L (mean values) in the effluents of wastewater treatment plants (WWTPs) from Catalonia (north-east Spain), although they have been banned in the EU since 2003 (Sass and Colangelo, 2006). In addition, the maximum concentration of 1990 ng/L simazine was measured in effluents from one Catalonian WWTP (Köck-Schulmeyer et al., 2013). In addition to these high environmental concentrations in Spain, triazines occur in water samples in other countries and in low- and middle-income countries as well. These herbicides are still in use in the USA and various low- and middle-income countries (Gfrerer et al., 2002; Sass and Colangelo, 2006; Kesavachandran et al., 2009). For instance, in 2002, in the Liaoning Province, eastern China, atrazine concentrations of up to 1600 ng/L were detected in Liao-He River water (Gfrerer et al., 2002). Furthermore, according to the environmental relevance of pesticides from wastewater treatment plants index (ERPWI), atrazi-

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[4] LD$_{50}$ is a standardized measure for expressing and comparing the toxicity of chemicals.

ne and simazine, as well as diazinon and diuron, were listed as the most problematic compounds within the scope of their study. The ERPWI considers the occurrence and removal of pesticides in wastewater treatment installations and the toxicity of pesticides to algae, daphnia, and fish (Köck-Schulmeyer et al., 2013).

Toxicity

Triazines act as strong herbicides by inhibiting photosynthesis. Accordingly, processes that are correlated with photosynthesis, for example, stomatal movement, transpiration, ion movement, and other energy-dependent processes, are affected by triazines as well (Ebert and Dumford, 1976). Furthermore, animal tests with rats showed that exposure to triazines causes neuroendocrine development and reproduction impairments because of the antiandrogenic properties (Stevens et al., 1994; McMullin et al., 2004). The uptake of atrazine leads to the suppression of the luteinizing hormone surge in ovariectomized estrogen-primed adult female rats, and it was shown that atrazine has antiandrogenic properties after conducting *in vitro* and *in vivo* studies. Moreover, it was revealed that these herbicides affect parts of the central nervous system, for example, causing hypothalamic dysfunction and disrupting the pituitary function (McMullin et al., 2004). Other effects on humans and wildlife include changes in organ weights and damage to the heart and liver. Tremors were observed as well (Fishel, 2015). Because of the adverse effects of the triazine compound atrazine, the EPA recommended that atrazine concentrations in drinking water should not exceed 3 µg/L to prevent chronic effects on humans and animals (Fishel, 2015). For the algae *Chlamydomonas reinhardtii* and *Pseudokirchneriella subcapitata*, mean EC_{50} values (96 hour), ranged from 176 to 117 µg atrazine/L. The triazine metribuzin seems to be more toxic by showing lower EC_{50} mean values ranging from 23 to 43 µg/L when used with the same algae. For the macrophytes *Ceratophyllum* demersum and *Lemna minor*, EC_{50} values of 22 and 92 µg/L were measured for atrazine and 14 and 36 µg/L for metribuizin (Fairchild et al., 1998). Invertebrates are much less sensitive to triazines. For example, for zebrafish *(Danio rerio)* embryos, a LC_{50} (48 hour) value of 36.8 mg/L was determined (Wiegand et al., 2000).

Effects on humans and wildlife by triazines include changes in organ weights and damage to the heart and liver.

D) Bipyridylium herbicides

Diquat and paraquat are the most popular bipyridylium herbicides (Pesticide Action Network UK, 1996).

Consumption

These are non-selective contact herbicides, causing wilting of foliage as a result of the rapid destruction of plant cell membranes even after a few hours of exposure (Fishel, 2014a). Diquat is mainly used for agricultural purposes to desiccate certain crops, for example, alfalfa, clover, potato, grain sorghum, and soybean, to simplify harvesting. It is used to control free-floating and submerged weeds in aquatic systems as well (Food and Agriculture Organization and World Health Organization, 1995). Paraquat is mostly used as a desiccant prior to harvesting of plants or it is applied as a weed killer to quickly eliminate unwanted plants before favored crops are sown (Fishel, 2014a).

Environmental behavior and occurrence

The distribution patterns of diquat and paraquat are quite similar. Given their low vapor pressures and their relatively high solubilities in water, they do not have the tendency to evaporate out of the water phase (Food and Agriculture Organization and World Health Organization, 1995; Rodriguez Jr et al., 2002; Sigma-Aldrich, 2014b). Paraquat and diquat are stable under neutral and acidic conditions, but in alkaline environments (pH > 12) they are hydrolyzed (Roberts et al., 2002). However, although they are soluble in water, they more likely adsorb to organic material and accumulate in soils and sediments. Because of their high affinity to bind to soil surfaces and their, therefore, lower availability in the soil pore water, their potential for microbial degradation is limited (Riley et al., 1976; Roberts et al., 2002; Fishel, 2014a). Regardless of these limitations for microbial degradation, there are some microbial species and fungi that are able to metabolize these herbicides alone or through co-metabolism processes (Funderburk and Bozarth, 1967; Carr et al., 1985; Roberts et al., 2002). Nevertheless, these herbicides pose a risk to aquatic environmental health mainly because of continuous exposure. Agricultural surface runoff transports these substances into flowing and still water systems, harming aquatic organisms, particularly algae and macrophytes (Sáenz et al., 1997; Sigma-Aldrich, 2014b). However, because of its adsorption to soils, it is not transported into ground water aquifers (Roberts et al., 2002). Fortunately, these compounds are not extensively transferred into plants (Fuerst and Vaughn, 1990), they can be removed quite easily from plant surfaces and water through sunlight and photo-degradation processes, or they can be removed through absorption to the soil (Slade, 1965, 1966; Roberts et al., 2002). Nevertheless, it has to be noted that these herbicides are much disputed, especially for use in low- and middle-income countries, because of their high acute toxicity (Wu et al., 2012a). In these regions, no data about environmental concentrations are available.

Toxicity

According to the material safety data sheets of Sigma-Aldrich, these agents are categorized as Category 1 chemicals, which have chronic aquatic toxicity (Sigma-Aldrich, 2014a, b) and are particularly known for their high acute toxicity as well (Sigma-Aldrich, 2014a, b). The toxic effects of these compounds are caused by several steps:

- After the exposure of plants and animals to bipyridylium herbicides (paraquat and diquat) the compounds are reduced, leading to the formation of radicals

- These radicals then reduce the molecular oxygen and promote formation of superoxide radicals

- Through further complex processes and reactions, other toxic oxygen species are formed, for example, hydroxyl radicals, hydrogen peroxides, and singlet oxygen

- The formation of these toxic species, lipid peroxidation, and the adverse effects to cell membrane integrity, results in fast dehydration (Fuerst and Vaughn, 1990).

Vertebrates and crustaceans seem to be less sensitive to exposure of bipyridylium herbicides. For instance, studies show that the LC_{50} of paraquat for the fish *Lepomis macrochirus* is 13 mg/L after 96 hours of exposure and the EC_{50} for *Daphnia magna* after 48 hours of exposure is 2.8 mg/L (Sigma-Aldrich, 2014b). For the algae *Selenastrum capricornutum* and *Chlorella vulgaris* even very low mean EC_{50} values (96 hour) of 670 and 140 μg paraquat/L were determined for the endpoint growth (Sáenz et al., 1997).

Although paraquat and diquat are known for their potential for geo-accumulation, they are not suspected to bio-accumulate in fruits and food because of their high potential for photochemical degradation (Food and Agriculture Organization and World Health Organization, 1995). To humans and mammals, the acute toxicity of diquat and paraquat is high (Category 2; Sigma-Aldrich, 2014a, b), especially the dermal uptake, and uptake through inhalation during application is life-threatening. The uptake of these agents causes organ damage, particularly to lungs and skin (Clark et al., 1966; Sigma-Aldrich, 2014a, b). Malfunctions of the respiratory system and adverse effects to the nervous system and kidneys are caused when these herbicides are inhaled. Exposure to high volumes causes progressive pulmonary fibrosis and epithelial proliferation that can lead to death (Rodriguez Jr et al., 2002). The LD_{50} of paraquat for rats through oral uptake is 57 mg/kg body weight, whereas the LD_{50} through dermal uptake for rabbits is 325 mg/kg (Sigma-Aldrich, 2014b). Furthermore, these substances are well-known for causing damage to the central nervous system (Clark et al., 1966; Wu et al., 2012a; Prakash et al., 2013) and paraquat is even suspected to cause Parkinson's disease (Wu et al., 2012a; Moretto and Colosio, 2013). According to the EPA, the maximum concentration of diquat and paraquat in drinking water, 20 μg/L or 3 μg/L, respectively, should not be exceeded (Rial-Otero et al., 2006). For humans the highest risk is through accidental uptake or skin contact during unsafe application of these herbicides. Unsafe applications include the use of inappropriate methods, not using personal protective equipment, or occupational accidents.

Mainly because of its high acute toxicity and its potential to endanger aquatic systems, paraquat has gained a bad reputation – during the last decades it has become one of the most controversial herbicides worldwide (Dinham, 2003). In addition, paraquat was being used very frequently to commit suicide, especially in developing countries (Dinham, 2003). Several public organizations, such as the Berne Declaration of Switzerland, Swedish Society for Nature Conservation, Foro Emaús of Costa Rica, Pesticide Action Network of Asia and the Pacific (PANAP), and Pesticide Action Network (PAN) UK, support a phasing out of paraquat. They emphasize that paraquat is mainly used in low- and middle-income countries in Asia and Central and South America, where proper handling of these hazardous herbicides cannot be guaranteed because of a lack of knowledge of the safe handling of pesticides and regulations governing its use (Dinham, 2003). Furthermore, it is questionable why, when paraquat is banned in several countries (including Austria, Denmark, Finland, Germany, Hungary, Slovenia, Sweden, and Switzerland), its use in low- and middle-income countries is still permitted.

E) Pyrethroids

The pyrethroids can be classified into two types, Type I without and Type II with cyano groups. The cyano-pyrethroids (Type II pyrethroids) – cyhalothrin, cypermethrin, deltamethrin, cyfluthrin, fenvalerate, flucythrinate, and

Bipyridylium herbicides are more likely to adsorb to organic material and accumulate in soils and sediments. Their high affinity to bind to soil surfaces and lower availability in the soil pore water limits their potential for microbial degradation.

The uptake of diquat and paraquat through the skin, and inhalation during application is acutely life threatening to humans and mammals.

fluvalinate – are the pyrethroids of higher concern because they are more toxic than the Type I pyrethroids (Roberts and Reigart, 2013).

Consumption

After application, pyrethroids adsorb to particles and organic matter and are transferred to rivers and streams with surface runoff and erosion.

Pyrethroids are synthetic analogues of natural pyrethrins obtained from chrysanthemum flowers (*Chrysanthemum cinerariaefolium)*. They are modern insecticides. Compared to natural pyrethrins, pyrethroids are designed to have an increased toxicity to targeted insects, have more persistence in the environment, and to have a good knockdown activity to pests. At the same time, they are designed to have a lower mammalian toxicity than other pesticides (Palmquist et al., 2012). Nevertheless, since synthetic pyrethroids became popular as substitutes for banned OCs, OPs, and carbamates, their application and the accompanying concern caused by these substances has constantly increased (Sayeed et al., 2003). Today, they are often used in agriculture, homes, and gardens, and for the treatment of ectoparasitic diseases in humans and animals. In some products, they are often combined with other strong OP or carbamate insecticides to enhance their effects (Roberts and Reigart, 2013).

Environmental behavior and occurrence

Fish and invertebrates seem to be highly susceptible to exposure to pyrethroids.

These synthetic compounds are known for their lipophilic characteristics, their persistence, and their high stability to photolytic degradation. Their low vapor pressures and high octanol-water coefficients show that they have a low potential to volatilize, but they have a high affinity to adsorb to organic matter and soils (Weston and Lydy, 2010; Palmquist et al., 2012; Lewis et al., 2015). Therefore, according to their physicochemical properties (Table 1) pyrethroids are most likely adsorbed to organic matter and particles. After application, these pesticides are transferred to rivers and streams by sediment movement through surface runoff. Investigations have shown that these pesticides occurred significantly in eroded sediments (Gan et al., 2005), which is indicative of their high potency for sorption to soil and organic particles (Luo and Zhang, 2011). For instance, in the Ubombo and Ingwavuma districts in KwaZulu-Natal province, South Africa, the maximum concentration of the pyrethroid cypermethrin found in the soil of the Makhathini flat was 1651 µg/kg and the maximum concentration found in the water of the same area was 40.7 µg/L. In the Ndumo agricultural area, concentrations of up to 467.3 µg/kg were measured in soil samples, while concentrations in the water samples were 23.19 µg/L. In Ophansi, 261 µg/kg of cyfluthrin was detected in soils, whereas in the water no cyfluthrin could be detected. Even in Tembe Elephant Park, a nature reserve, surprisingly high concentrations – up to 467.3 µg/kg – of cyfluthrin were found although, officially, no pesticides have been applied in this region (Sereda and Meinhardt, 2005). These concentrations confirm that these compounds tend to sorb to organic matter, soil, and suspended sediments because the concentrations in soils exceed those found in the water samples. The concentrations found in water and sediments are both of environmental concern.

Toxicity

In contrast to the OPs, the pyrethroids do not impair the central nervous system of animals exposed to them, but, rather, they affect the functioning of the peripheral nervous system. Pyrethroids prolong the opening time of voltage-gated sodium channels on nerves. Consequently, this alteration in nerve function leads to a series of short bursts or a prolonged burst, caused by repeated stimulus-dependent nerve depolarization or discharges of nerve signals (Soderlund and Bloomquist, 1989). For humans, exposure to Type I pyrethroids causes effects like restlessness, hyperexcitation, prostration, and body tremors. Exposure to Type II pyrethroids leads to hyperactivity, incoordination, convulsions, and writhing (Soderlund and Bloomquist, 1989; Fishel, 2014b). The pyrethroids are well-known for being less toxic to mammals and birds, because they do not have a high potential for bioaccumulation and they are easily degradable through the liver systems of mammals and birds. However, in contrast, non-target insects, invertebrates, and fish are highly susceptible to these chemicals (Fishel, 2014b).

On the one hand, as described before, pyrethroids are less toxic to mammals and birds than most of the other pesticides, for example, carbamates, OCs, and OPs, because they are more selective to insects and they are more easily metabolized. On the other hand, fish and invertebrates seem to be highly susceptible to exposure to pyrethroids. For instance, for the fish *Danio rerio,* the LC_{50} values range from 1.9 to 27.6 µg/L after exposure to permethrin for 2 days (United States Environmental Protection Agency, 2014a)

For crustacean invertebrates, the 10 day LC50 values for pyrethroids in general ranged from 2 to 140 ng/L in water samples (for *Americamysis bahia* and *Ceriodaphnia dubia*) and from 4 to 110 ng/L (for *Hyalella Azteca*) in sediments (Hladik and Kuivila, 2009). In summary, given their photolytic stability, their high lipophilic characteristics, and their high acute toxicity to fish and invertebrates, pyrethroids pose a risk to environmental health and especially to aquatic systems.

Table 1: Selection of hazardous pesticides used in low- and middle-income countries

Name [A]	**Type/ chemical family**	**WHO toxicity classification** [B] (World Health Organization, 2010b)	**Use trend** [C]	**Henry's law constant (at 25°C)**	**Log K_{OW} (at 25°C)**	**Water solubility [g/L]**	**LD_{50} for rats [mg/kg body weight]** (World Health Organization, 2010b)	**Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]**
BIPYRIDILS								
🟧 Paraquat	Herbicide	II	➡	$1.23*10^{-12}$ (Lewis et al. 2015)	-4.5 (20°C) (Lewis et al. 2015)	620 (20°C) (Lewis et al. 2015)	150	NA/NA
CARBAMATES								
🟧 Carbaryl	Insecticide	II	➡	$3.3*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.4 (Gramatica and Di Guardo, 2002)	0.120 (27°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	300 [D]	0.23/NA (National Institute for Public Health and the Environment - RIVM, 2008)
🟩 Carbendazim	Fungicide	IV	⬆	$2.1*10^{-11}$ (Gramatica and Di Guardo, 2002)	1.5 (Gramatica and Di Guardo, 2002)	0.008 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	> 10,000	0.34/0.57 (Ecotox Centre, 2015)
🟧 Carbofuran	Insecticide	Ib	⬇	$3.1*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.3 (Gramatica and Di Guardo, 2002	0.320 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	8	0.02/NA (Institut National de l'Environnement Industriel et des Risques - INERIS, 2008a)
🟧 Carbosulfan	Insecticide	II	⬇	$1.83*10^{-5}$ (Lewis et al. 2015)	7.42 (Lewis et al. 2015)	0.00011 (20°C) (Lewis et al. 2015)	101 (Lewis et al. 2015)	NA/NA
🟧 Fenobucarb	Insecticide	II	➡	$5.9*10^{-8}$ (Gramatica and Di Guardo, 2002)	2.8 (Gramatica and Di Guardo, 2002)	Practically not soluble (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	620	NA/NA
🟩 Mancozeb	Fungicide	IV	⬆	$1.76*10^{-10}$ (20°C) (Lewis et al. 2015)	1.8 (European Commission, 2015)	0.000006 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	>8000	0.07/0.7 (European Commission,2015)
ORGANOCHLORINES								
🟩 2,4-D	Herbicide/ Alkyl chlorophenoxy	II	⬇	$1.40*10^{-9}$ (20°C) (Lewis et al., 2015)	2.8 (Travis and Arms, 1988)	23.180 (25°C) (European Commission, 2015)	425-764 (European Commission, 2015)	0.2/1.3 (Ecotox Centre, 2015)
🟧 Butachlor	Herbicide	III	⬇	$5.1*10^{-8}$ (Gramatica and Di Guardo, 2002)	4.5 (Gramatica and Di Guardo, 2002)	0.020 (20°C) (Lewis et al., 2015)	2200	NA/NA
🟩 Chlorothalonil	Fungicide	IV	➡	$1.36*10^{-5}$ (20°C) (Lewis et al., 2015)	2.9 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.0006 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	>10.000	0.035/1.2 (Maycock et al., 2012a)
🟩 Clomazone	Herbicide/ oxazolidone	II	➡	$1.67*10^{-6}$ (Lewis et al., 2015)	2.54 (Lewis et al., 2015)	1.102 (20°C) (Lewis et al., 2015)	1369 (Lewis et al., 2015)	2/NA (Institut National de l'Environnement Industriel et des Risques - INERIS, 2008b)
🟧 DDT	Insecticide	II	⬇	$8.3*10^{-6}$ (Gramatica and Di Guardo, 2002)	6.9 (Gramatica and Di Guardo, 2002)	0.000001 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	113	0.025/NA (European Commission, 2008)

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C: 🟠 Presumable decreasing trend in use; 🟡 Trend in use is uncertain – approximation is difficult; 🟢 Presumable increasing trend in use.

D: The LD_{50} was not a single value, but rather a value within the wider than usual range adopted for the WHO's recommended classification of pesticides by hazard.

E: Usually, the LD_{50} values for oral uptake are taken. E indicates that the LD_{50} values are for dermal uptake.

F: Converted from Henry's constant k_H^{cp} [atm m³/mol] to k_H^{cc} [dimensions less] using the EPA online tools for site assessment calculation (United States Environmental Protection Agency, 2015b).

G: Approximated by and ad hoc value; less data available.

Name ^{A}	Type/ chemical family	WHO toxicity classification ^{B} (World Health Organization, 2010b)	Use trend ^{C}	Henry's law constant (at 25°C)	Log K_{OW} (at 25°C)	Water solubility [g/L]	LD_{50} for rats [mg/kg body weight] (World Health Organization, 2010b)	Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]
ORGANOCHLORINES								
🟩 Difenoconazole	Fungicide	II	→	$7.31*10^{-10}$ (20°C) (Lewis et al., 2015)	4.4 (Mensink, 2008)	0.015 (25°C) (Schummer et al., 2010)	1453	0.76/7.8 (National Institute for Public Health and the Environment - RIVM, 2008)
🟧 Endosulfan	Insecticide	II	↓	$6.5*10^{-5}$ (Gramatica and Di Guardo, 2002)	3.8 (Gramatica and Di Guardo, 2002)	0.00033 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	80	0.005/0.01 (European Commission, 2008)
🟩 Fipronil	Insecticide	II	→	$1.60*10^{-7}$ (20°C) (Lewis et al., 2015)	4.0 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.0024 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	92	0.012/NA (Biocidal Products Committee, 2011)
🟩 Imidacloprid	Insecticide	II	→	$4.10*10^{-11}$ (20°C) (Lewis et al., 2015)	0.33 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.61 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	450	0.067/0.2 (National Institute for Public Health and the Environment - RIVM, 2008)
🟩 MCPA ^{G}	Herbicide	II	→	$1.10*10^{-8}$ (Lewis et al., 2015)	2.56 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.3 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	700 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	1.34/15.2 (Ecotox Centre, 2015)
🟧 Niclosamide	Fungicide	IV	→	$2.15*10^{-12}$ (20°C) (Lewis et al., 2015)	4.56 (20°C) (Lewis et al., 2015)	0.005 (20°C) (Lewis et al., 2015)	5000	NA/NA
🟧 Propanil	Herbicide/ anilide	II	→	$1.82*10^{-8}$ (Lewis et al., 2015)	2.29 (Lewis et al., 2015)	0.095 (20°C) (Lewis et al., 2015)	960 (Lewis et al., 2015)	NA/NA
🟩 Propiconazole	Fungicide	II	→	$4.2*10^{-9}$ (Gramatica and Di Guardo, 2002)	3.7 (20°C) (Lewis et al., 2015)	0.15 (20°C) (European Commission, 2015)	1520	1.0/NA (Marion Junghans (Ecotox Centre); personal communication)
ORGANOPHOSPHATES								
🟧 Acephat	Insecticide	II	↓	$2.15*10^{-11}$ (Lewis et al., 2015)	-0.85 (Lewis et al., 2015)	790 (20°C) (Lewis et al., 2015)	945 (Lewis et al., 2015)	$57/570^{I}$ (Marion Junghans (Ecotox Centre); personal communication)
🟩 Chlorpyrifos	Insecticide	II	→	$3.0*10^{-6}$ (Gramatica and Di Guardo, 2002)	5.0 (Gramatica and Di Guardo, 2002)	0.001 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	135	0.03/0.1 (European Commission, 2008)
🟧 Dichlorvos ^{G}	Insecticide	Ib	↓	$1.50*10^{-2}$ (20°C) (Lewis et al., 2015)	1.43 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	10 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	17 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.0006/0.0007 (European Parliament and Council of the European Union, 2013)

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D: The LD_{50} was not a single value, but rather a value within the wider than usual range adopted for the WHO's recommended classification of pesticides by hazard.

E: Usually, the LD_{50} values for oral uptake are taken. E indicates that the LD_{50} values are for dermal uptake.

F: Converted from Henry's constant k_H^{cp} [atm m^3/mol] to k_H^{cc} [dimensions less] using the EPA online tools for site assessment calculation (United States Environmental Protection Agency, 2015b).

G: Approximated by and ad hoc value; less data available.

Name [A]	Type/ chemical family	WHO toxicity classification [B] (World Health Organization, 2010b)	Use trend [C]	Henry's law constant (at 25°C)	Log K_{OW} (at 25°C)	Water solubility [g/L]	LD_{50} for rats [mg/kg body weight] (World Health Organization, 2010b)	Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]
ORGANOPHOSPHATES								
Dimethoate	Insecticide	II	→	$1.0*10^{-10}$ (Gramatica and Di Guardo, 2002)	0.8 (Gramatica and Di Guardo, 2002)	39.8 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	150 [D]	0.07/0.977 (Ecotox Centre, 2015)
Fenthion	Insecticide	II	→	$1.4*10^{-6}$ (Gramatica and Di Guardo, 2002)	4.1 (Gramatica and Di Guardo, 2002)	0.055 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	586[E]	0.003/NA (National Institute for Public Health and Environment - RIVM, 2008)
Glyphosate	Herbicide	III	↑	$8.5*10^{-11}$ (European Commission, 2015)[F]	-3.2 (European Commission, 2015)	10.5 (20°C) (European Commission, 2015)	4230	196/389 (Maycock et al., 2012b)
Malathion	Insecticide	III	↑	$4.9*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.4 (Gramatica and Di Guardo, 2002)	0.145 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	2100 [D]	0.013/NA (National Institute for Public Health and the Environment - RIVM, 2008)
Monocrotophos	Insecticide	Ib	↓	$6.5*10^{-13}$ (Gramatica and Di Guardo, 2002)	-0.2 (Gramatica and Di Guardo, 2002)	818 (20°C) (Lewis et al., 2015)	14	0.00008/NA (National Institute for Public Health and the Environment - RIVM, 2008)[I]
Parathion-methyl	Insecticide	Ia	↓	$2.30*10^{-6}$ (20°C) (Lewis et al., 2015)	3.0 (20°C) (Lewis et al., 2015)	0.55 (20°C) (Lewis et al., 2015)	14	0.011/NA (National Institute for Public Health and the Environment - RIVM, 2008)
Phenthoate	Insecticide	II	→	$6.34*10^{-5}$ (Lewis et al., 2015)	3.69 (Lewis et al., 2015)	0.011 (20°C) (Lewis et al., 2015)	249 (Lewis et al., 2015)	NA/NA
Phorate	Insecticide	Ia	↓	$4.4*10^{-6}$ (Gramatica and Di Guardo, 2002)	3.6 (Gramatica and Di Guardo, 2002)	0.050 (20°C) (Lewis et al., 2015)	2	0.000165/NA (National Institute for Public Health and the the Environment - RIVM, 2008)[I]
Phosphamidon	Insecticide	Ia	↓	$6.5*10^{-12}$ (Gramatica and Di Guardo, 2002)	0.4 (Gramatica and Di Guardo, 2002)	Completely mixable (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	7	0.03/NA (National Institute for Public Health and the Environment - RIVM, 2008)[I]
Profenofos	Insecticide	II	→	$2.2*10^{-8}$ (Gramatica and Di Guardo, 2002)	4.7 (Gramatica and Di Guardo, 2002)	0.02 (25°C) (United States Environmental Protection Agency, 2000)	358	NA/NA
Quinalphos	Insecticide	II	→	$2.38*10^{-6}$ (20°C) (Lewis et al., 2015)	4.44 (20°C) (Lewis et al., 2015)	0.0178 (20°C) (Lewis et al., 2015)	62	NA/NA
Triazophos	Insecticide	Ib	↓	$1.30*10^{-6}$ (20°C) (Lewis et al., 2015)	3.55 (Lewis et al., 2015)	0.035 (20°C) (Lewis et al., 2015)	82	0.001/0.02 (National Institute for Public Health and the Environment - RIVM, 2008)
PYRETHROIDS								
Cyfluthrin	Insecticide	Ib	↑	$7.78*10^{-5}$ (20°C) (Lewis et al., 2015)	6.0 (European Commission, 2015)	0,000002 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	15 [D]	0.0006/NA (Andersson and Kreuger, 2011)
Cyhalothrin	Insecticide	II	→	$4.62*10^{-11}$ (20°C) (Lewis et al., 2015)	6.85 (Ochiai et al., 2004)	0.000004 (20°C) (Lewis et al., 2015)	144 [D]	0.00002/0.00047 (National Institute for Public Health and the Environment - RIVM, 2008)
Cypermethrin	Insecticide	II	↑	$3.70*10^{-6}$ (20°C) (Lewis et al., 2015)	5.3 (20°C) (Lewis et al., 2015)	0.000009 (20°C) (Lewis et al., 2015)	250 [D]	0.00008/0.0006 (Ecotox Centre, 2015)
Deltamethrin	Insecticide	II	↑	$4.20*10^{-6}$ (20°C) (Lewis et al., 2015)	6.2 (European Commission, 2015)	<0.0001 (20°C) (European Commission, 2015)	135 [D]	0.0000031/0.0003 (National Institute for Public Health and the Environment - RIVM, 2008)
Esfenvalerate	Insecticide	II	↑	$1.01*10^{-6}$ (Lewis et al., 2015)	6.24 (Lewis et al., 2015)	0.000001 (20°C) (Lewis et al., 2015)	88.5 (Lewis et al., 2015)	0.0001/0.0009 (National Institute for Public Health and the Environment - RIVM, 2008)

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TRIAZINES								
Atrazine	Herbicide	III	→	$2.3*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.6 (Gramatica and Di Guardo, 2002)	0.035 (22°C) (Agency for Toxic Substances and Disease Registry, 2003)	2000[D]	0.6/2 (European Parliament and Council of the European Union, 2008)
OTHERS								
Cymoxanil	Fungicide/ urea derivative	II	↑	$1.53*10^{-8}$ (Lewis et al., 2015)[F]	0.67 (Lewis et al., 2015)	0.78 (20°C) (Lewis et al., 2015)	760 (Lewis et al., 2015)	3/NA (Andersson and Kreuger, 2011)
Dinocap[G]	Fungicide/ dinitrophenol	II	→	$5.96*10^{-6}$ (Lewis et al., 2015)	6.5 (20°C) (Lewis et al., 2015)	0.000183 (20°C) (Lewis et al., 2015)	766 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	NA

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G: Approximated by and ad hoc value; less data available.

Input pathways of pesticides

The input pathways of pesticides in low- and middle-income countries and higher-income countries have similarities and differences.

In high-, and low- and middle-income countries, pesticides after application can leach into the subsoil and groundwater aquifers through irrigation or they can be transported into rivers, streams, and groundwater systems through surface runoff after rainfall events, thus posing risk to environmental and human health. However, in high-income countries, ground water and surface waters are more strictly controlled and wastewater treatment facilities for surface water purification are common. In contrast, in most of the low- and middle-income countries, water controls and wastewater treatment facilities are lacking or not available. This results in higher environmental concentrations of pesticides, especially if contaminated and untreated river water is used for irrigation over several years (Clarke et al., 1997; Corcoran et al., 2010; Heeb et al., 2012; Ismail et al., 2012; Sapari and Ismail, 2012).

In addition, the amounts of pesticides released into the environment through individual input sources differ to a greater extent between high- and low- and middle-income countries. For example, in high-income countries with their more strict controls and regulations and improved education in pesticide handling and storage, less cases of acute pesticide poisoning are observed during application and, presumably, smaller amounts of pesticides are exposed and released to the environment (Jeyaratnam and Chia, 1994; Kesavachandran et al., 2009). Consequently, smaller amounts accumulate in soil/sediments, biota, and food (crops, fruits). For instance, the amount of DDT found in human breast milk is much higher in low- and middle-income countries than in high-income countries (Devanathan et al., 2009). However, it must be noted that reliable, comprehensive, and comparative data about the amounts of pesticides released in high- and in low- and middle-income countries are not available yet. Even in high income countries, studies of the environmental distribution and the individual sources of pesticides need to be conducted to gain a better understanding of their environmental behavior and their risk to environmental and human health (Wittmer et al., 2010).

In private gardens in urban regions of high-income countries, pesticides are mainly used to protect plants. Herbicides, fungicides, and algaecides are applied to terraces and floors or they are contained in wall paints and renderings to get rid of unwanted plants or to prevent plants, algae, and fungi growing for aesthetic reasons (Wittmer et al., 2010, 2014). In private households in several urban regions located in low- and middle-income countries, pesticides are used for cultivating plants for private purposes. Or they are used as vector control agents against malaria and other pathogenic diseases that are transferred by insects. In that case, more hazardous and persistent pesticides – carbofuran, DDT, dichlorvos, endosulfan, monocrotophos, profenofos, etc., which are banned in Europe or most other high-income countries – are often used (Mabaso et al., 2004; National Geographic, 2006). In high- and low- and middle-income countries, inappropriate disposal and cleaning of contaminated equipment can act as additional point sources of pesticide pollution, as well (Pesticide Action Network Asia and the Pacific, 2010; Wittmer et al., 2010). In low- and middle-income countries, inappropriate stockpiles of obsolete pesticides, originating from industrial countries, are acting as additional point sources of high amounts of hazardous pesticides (Elfvendahl et al., 2004; Dasgupta et al., 2010).

Hazardous and persistent pesticides - carbofuran, DDT, dichlorvos, endosulfan, monocrotophos, profenofos, etc. - are often used for control of disease transmitting vectors in low- and middle-income countries.

Use of pesticides and pollution trends and impacts

Data availability

It is generally difficult to obtain reliable data on pesticide use. In addition, comprehensive data about the production of pesticides is even more difficult to get hold of. This is true for high-income countries and it is particularly problematic for low- and middle-income countries. In general, according to the National Health Surveillance Agency and the Observatory of Pesticides of the Universidade Federale do Paraná, Brazil, it is safe to assume that during the last decade, the world pesticide market increased by 93%. The Brazilian market alone increased by 190% (Carneiro et al., 2012). Apart from that, in low- and middle-income countries, weakly implemented regulations and policies governing pesticide use and import, the stockpiling of obsolete pesticides, and poor education in pesticide storage and handling, have led to a high risk of occupational acute and chronic pesticide poisoning. These issues make it more difficult to assess data about pesticide production, import, and use. Currently, it is not possible to reliably assess the number of people affected by pesticide poisoning. Nevertheless, the WHO estimates that every year, around 3 million people globally might suffer from severe pesticide poisoning and the estimated number of unreported cases seems to be unpredictably high (Kesavachandran et al., 2009). In low- and middle-income countries it is impos-

Currently, it is not possible to reliably assess the number of people affected by pesticide poisoning. Nevertheless, the WHO estimates that every year, around 3 million people globally might suffer from severe pesticide poisoning and the estimated number of unreported cases seems to be very high.

sible to document systematic and authentic data about pesticide poisoning for many reasons. These include the lack of medical facilities, the farmers' lack of knowledge of the symptoms of pesticide poisoning, and the uncontrollable use of pesticides, particularly in remote small agricultural establishments.

In general, it can be said that worldwide, from 2 million to 2.4 million tonne of pesticides are consumed annually (Gupta, 2004; United States Environmental Protection Agency, 2011). According to the studies of Kesavachandran et al. (2009) and Gupta (2004) around 45% of this is consumed in Europe alone, 25% in the USA, and about 20–25% in low- and middle-income countries. Of all pesticides, the consumption of herbicides is highest, representing 47.5%, followed by insecticides at 29.5%. Fungicides account for 17.5% and others for 5.5% (Gupta, 2004). In our report, we focus mainly on the pesticides most used, and the pesticides having the highest negative effects on environmental and human health – herbicides and insecticides. Nevertheless, although such data is not readily available, some hot spots with high use of those pesticides can be identified (Figure 6).

Future trends and hot spots

The list of pesticides presented in Table 1 and the investigations of Roberts et al. (2003) show that exposure to OPs, OCs, bipyridylium herbicides, and carbamates poses high risks to human and environmental health. Several publications of international organizations and research institutes show that there are serious issues, especially in low- and middle-income countries, related to policies and regulations, application, storage, and disposal of pesticides (El Sebae, 1993; Eddleston et al., 2002; Pesticide Action Network Asia and the Pacific, 2010; United Nations Environment Programme and Food and Agriculture Organization, 2013; United Nations Environment Programme, 2013c, 2014). Today, the WHO Class II pesticides (as shown in Table 1) seem to be the most used and most hazardous ones, since the production of WHO Class I pesticides is being phased out and their use and trade abolished in the most parts of the world (Roberts et al., 2003). Implementation of the Rotterdam and Stockholm Conventions has resulted in the international trade in several obsolete and dangerous pesticides being abolished and has triggered a phasing out of the most toxic and persistent Class I and several Class II (WHO classification) pesticides. These include aldrin, chlordane, chlordecone, dieldrin, endrin, heptachlor, hexachlorobenzene, hexachlorocyclohexane, lindane, mirex, pentachlorbenzene, endosulfan, and toxaphene. In future, the consumption of OCs will decrease because of restrictions on and prohibitions of these compounds. This is because of their high persistence and their high toxicologic and bioaccumulative potentials. However, the use of pyrethroids will increase as they are used as substitutes for the banned OCs, OPs, and carbamates because of their lower toxicity to mammalian species (Fishel, 2014b; Luo and Zhang, 2011; Palmquist et al., 2012). Furthermore, the use of the lower toxic OPs and carbamates of WHO Class III or Class IV pesticides will increase as well.

Research shows that there are serious issues related to policies and regulations, application, storage, and disposal of pesticides, especially in low- and middle-income countries.

Figure 6 presents the worldwide average annual use of pesticides. Between 2001 and 2010, this ranged from 0 to 80 kg pesticide/ha of arable land according to data available from FAO (Food and Agriculture Organization, 2013). According to the datasets, the hot spots for pesticide application, with dosages ranging from 5.2 to 76 kg pesticides per ha of arable land, are the Bahamas, Maureta-

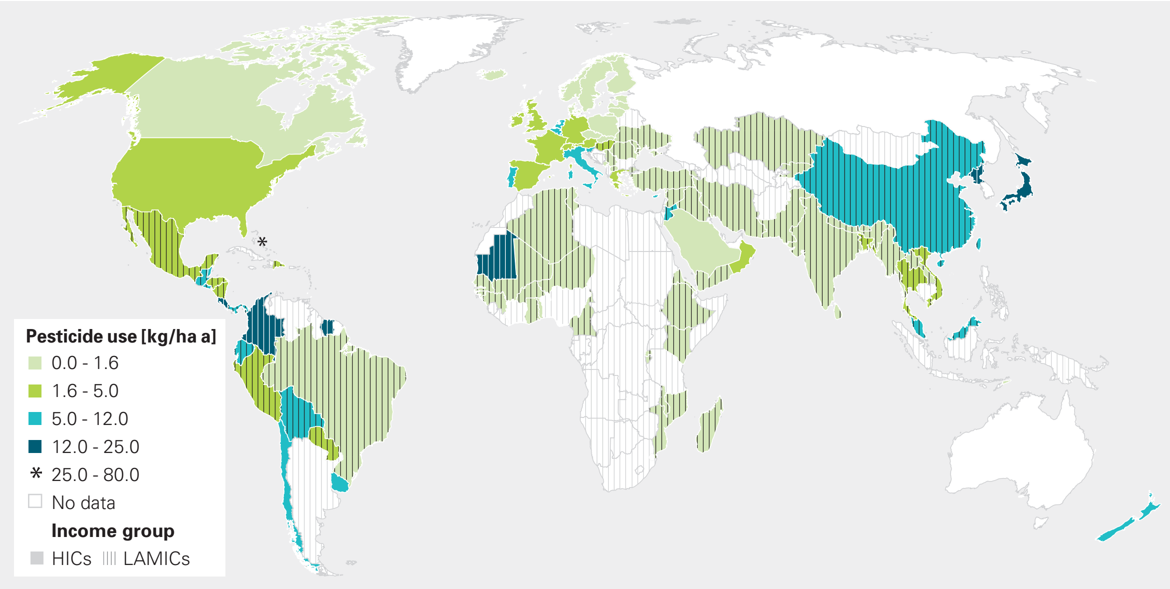


***Figure 6**: Average annual pesticide use for the period 2001–2010 ranged from 0 to 80 kg pesticide/ha of arable land (Food and Agriculture Organization, 2013). The shaded areas represent low- and middle-income countries.*

nia, Costa Rica, Colombia, North Korea, Suriname, China, Belize, Panama, Jordan, Ecuador, Guatemala, Malaysia, Bolivia, and El Salvador, in descending order of rate of application. However, these data have to be treated with caution since for several regions, especially Africa, South America, and Asia, there is a lack of data. This is especially the case for the rural regions and smaller agricultural communities in low- and middle-income countries where it is difficult to estimate the real amounts of pesticides applied. Often farmers in these regions are buying their pesticides unofficially and they do not really know the concentrations of the pesticides applied on their fields. For this reason, the amounts of pesticide applied may be underestimated for several regions (Pesticide Action Network Asia and the Pacific, 2010).

Figure 6 shows the average annual pesticide use for the period 2001–2010 and this forms the base layer for the components of Figure 7.

Figure 7 shows the worldwide average use of pesticides per hectare of arable land along with the annual average production (2005–2009) of crops requiring high volumes of pesticides. These include the permanent crops coffee (Rama and Jaga, 1992; Yang et al., 2011) and lemons and limes (Ortelli et al., 2005), and the temporary crop soybeans (Pizzutti et al., 2007) as the top layer (data from FAO; Food and Agriculture Organization, 2013). Although for the cultivation of palm trees (a permanent crop) less pesticides are required, as compared to most other commodities, data about palm oil production is shown as well. Mainly this is because it is well-known that for the cultivation of palm trees, large amounts of the extremely acutely toxic herbicide paraquat are used. In addition, these tropical trees are commonly cultivated in many different low- and middle-income countries (Teoh, 2010). By considering these data on crop production, it can be assumed that in middle America, northern and southern South America, west central Africa, southeast Africa, South Asia, and Oceania, higher amounts of pesticides might be used for the cultivation of these agricultural commodities than is suggested by the average pesticide use.

Impacts on environmental and human health

Of the amount of pesticide applied, only 0.1% to 0.3% comes into contact with the target pests directly or indirectly. Thus, 99.7 to 99.9% of the applied pesticide is dispersed into the environment and reaches non-target organisms, including humans.

Pimentel (1995) predicted that of the amount of pesticide applied, only 0.1% to 0.3% comes into contact with the target pests directly or indirectly. Thus, 99.7 to 99.9% of the applied pesticide is dispersed into the environment and reaches non-target organisms, including humans. This might certainly be the case if obsolete methods and equipment are used in applying the pesticides. Mostly, pesticides can be dispersed into the environment through the air. If they are sprayed manually using a backpack spray tank or mechanically by a lawn sprinkler system, a plane, or a tractor, the unintentional drift of these substances can range from hundreds of meters up to several kilometers (Pimentel, 1995) depending on the method, weather conditions, and the degree of education of the person applying the pesticide. Afterwards residues of the pesticides remain and adsorb to plants, soils, and sediments, given their high potential for bioaccumulation. Additionally, pesticides can be leached out into drinking water aquifers by the rain and irrigation water or they can be transported by surface runoff into river systems. Humans can take up hazardous pesticides directly by inhaling the pesticide spray or ingest them by drinking or eating contaminated water or food. Some pesticides, such as paraquat, can even be absorbed directly through the skin during the preparation of the pesticide solution, through handling, or during the mixing process (Wester et al., 1984; Dinham, 2003).

After exposure, pesticides often have adverse impacts on human health. Most of them, particularly the OPs, OC, and carbamates, are known to cause malfunctions in the brain and peripheral nervous system. Chronic exposure can lead to neurological, neurobehavioral, and psychiatric diseases and diminish intelligence (Salvi et al., 2003; Wu et al., 2012a). The pesticides which cause inhibition of cholinesterase – OCs, OPs, and carbamates – can affect the respiratory system. An affected respiratory system can be indicated by symptoms like coughing, discharging phlegm, and wheezing. In addition, pesticides can cause contact allergies and skin eruptions (Kesavachandran et al., 2009). Furthermore, OPs, OCs, and carbamates are known for causing malfunctions in reproduction through their endocrine disruptive potential. Moreover, there is evidence that chronic pesticide exposure can lead to several forms of cancer (López et al., 2007; Kesavachandran et al., 2009; Bedi et al., 2013). There are a many examples of private and occupational accidents involving pesticide poisoning in low- and middle-income countries that have led to adverse effects on human health or even to death. For instance, in the state of Mato Grosso do Sul,

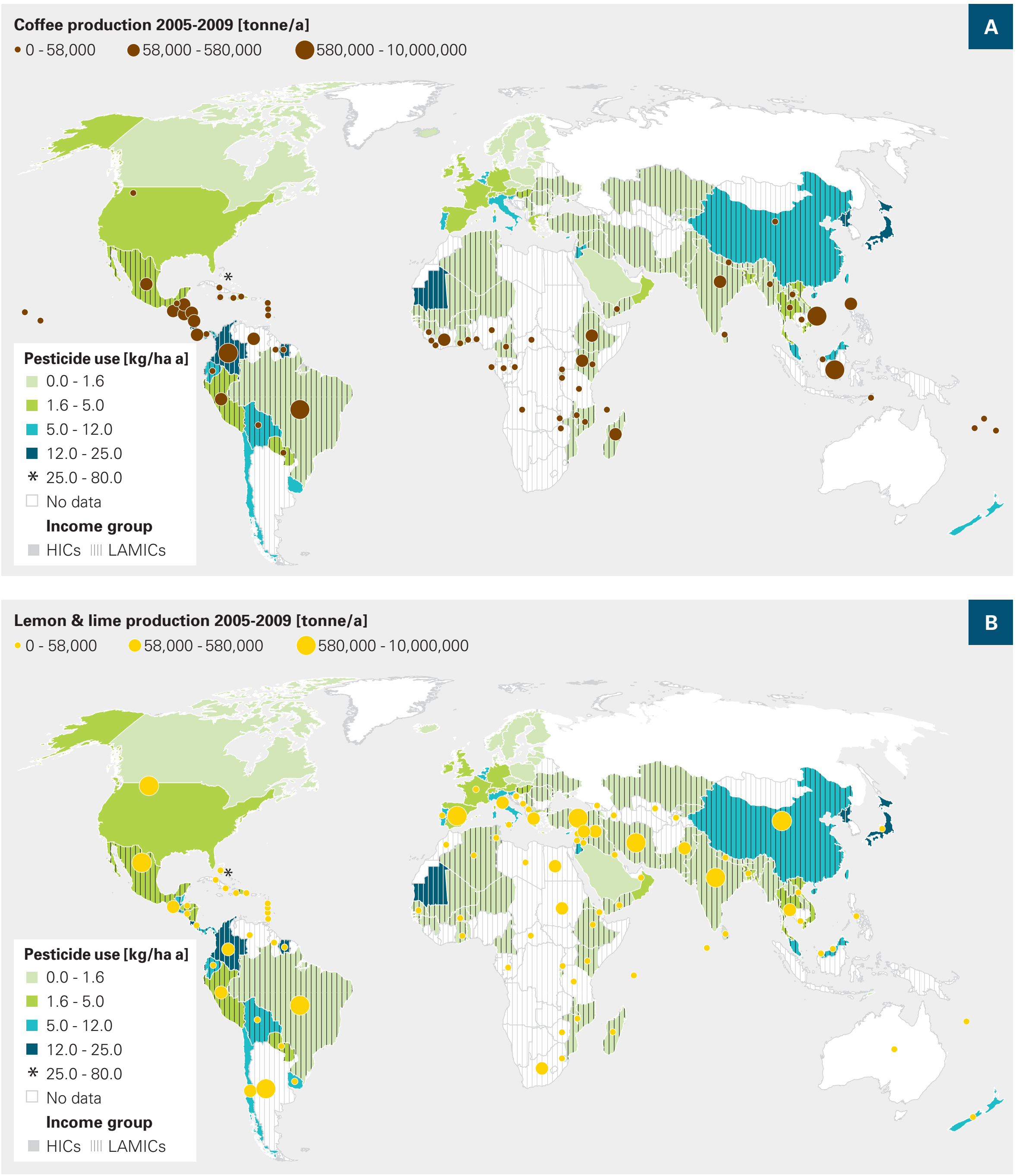
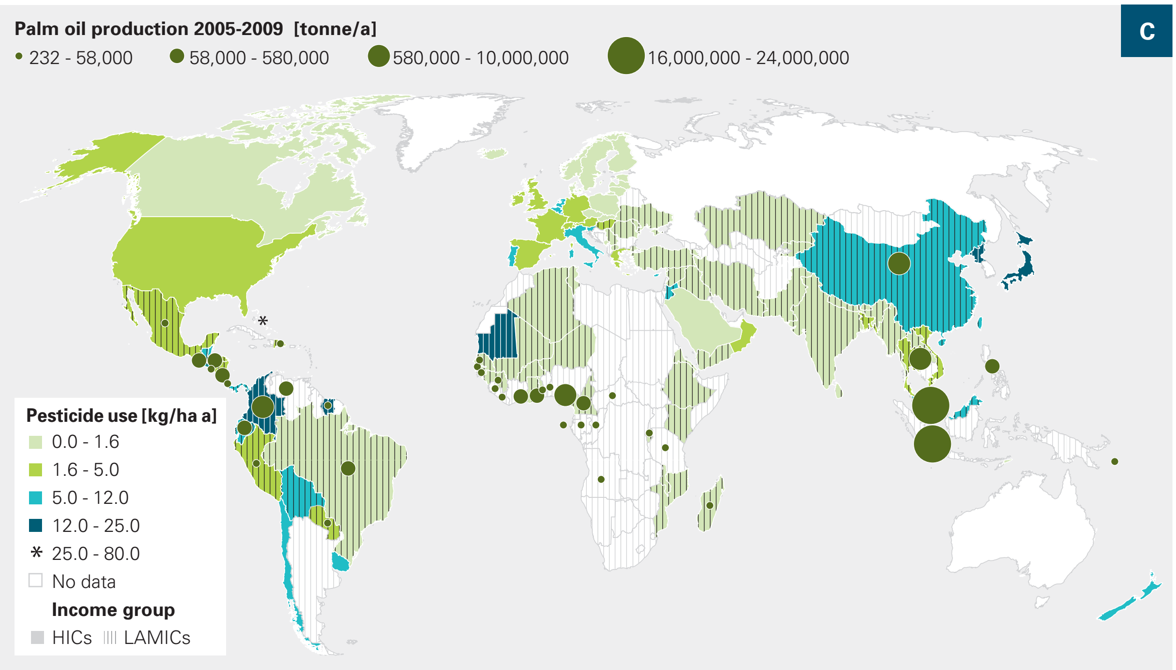
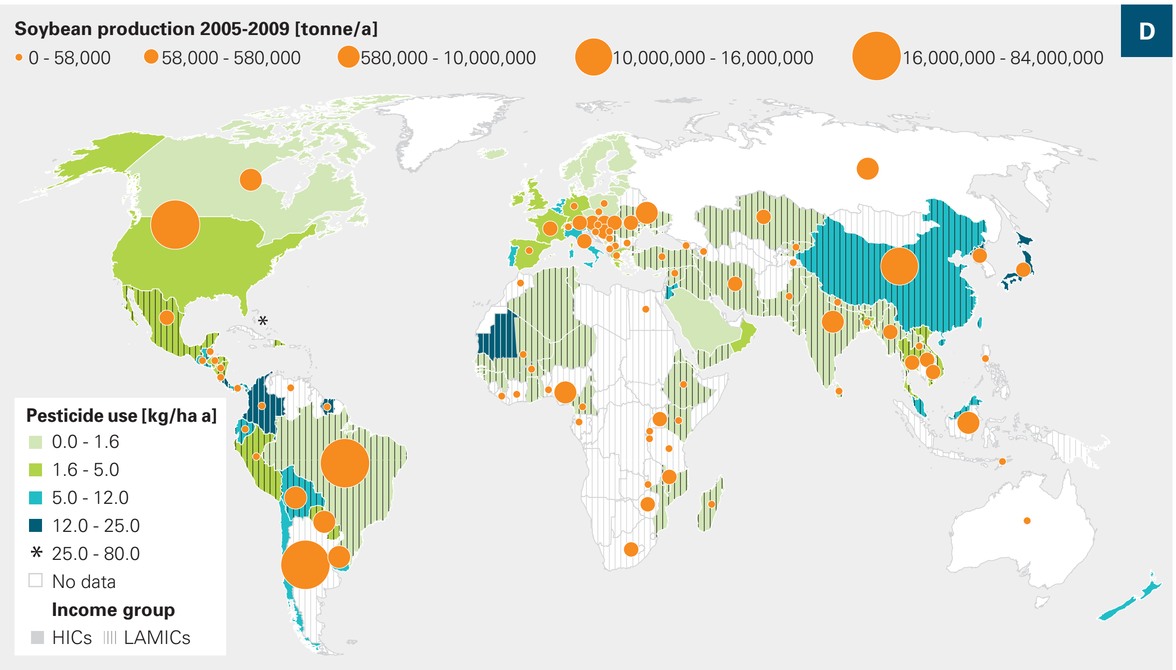


***Figure 7**: Average annual pesticide use in 2001–2010 and the average annual A) coffee, B) lemon and lime, C) palm oil, and D) soybean production. For the period 2005–2009 production ranged from 0 – 84 million tonne (Food and Agriculture Organization, 2013). The shaded areas represent low- and middle-income countries.*

Brazil, between 1992 and 2002, about 123 persons suffered from acute pesticide poisoning. Of these, 46% were intentional self-poisonings and the rest were poisoned as a result of occupational and private incidents. In Brazil as a whole, 5185 people suffer pesticide poisoning annually. Of these, 31.1% are intentional and 68.9% unintentional poisonings (Recena et al., 2006). In the Warangal district in Andhra Pradesh, southern India, more than 1000 pesticide poisoning cases have been observed annually, leading to 200–400 deaths. In 2002, the majority of deaths were caused by the pesticides monocrotophos and endosulfan (Srinivas Rao et al., 2005). A recent headline event covering pesticide poisoning concerned 23 school children who died after eating a school lunch in eastern India. Forensic tests revealed that the meal was contaminated with oil containing residuals of the WHO Class Ib OP, monocrotophos. This is a product that has been banned already in many countries (ABC News Online, 2013).

Besides the observed adverse health impacts to humans, exposure to pesticides can have disastrous consequences for the health of the environment as well. Vertebrates and mammals are often highly susceptible to pesticides. For instance, OCs cause eggshell thinning in birds (Lundholm, 1997). OPs and carbamates are posing high risks to mammals (Kwon et al., 2004) and herpetofauna be-





cause of their high toxicity, their large-scale application in agriculture (Story and Cox, 2001), and, especially, their inhibition of acetylcholinesterase activity. Furthermore, these pesticides and the pyrethroids affect the reproduction of amphibians as well because of their estrogenic activity (Pawar and Katdare, 1984; Kojima et al., 2004). The pyrethroids are less toxic to mammals than the OCs, OPs, and carbamates (Palmquist et al., 2012). Other pesticides act as endocrine disruptors as well. Tests with animals showed that the triazine herbicides can hinder the reproduction of mammals because of their antiandrogenic activity (Stevens et al., 1994; McMullin et al., 2004). Because of their high toxicity, potential to adsorb to organic material, soils, and sediments, or their persistence in water systems, OPs, carbamates, triazines, bipyridylium herbicides, and pyrethroids harm non-targeted invertebrates located close to pesticide treated areas (Fukuto, 1990; Köck-Schulmeyer et al., 2013). At present, there are plenty of publications about other non-target organisms that are affected by exposure to pesticides. For instance, in several regions, honey bee (*Apis mellifera*) populations are endangered. It has been proven that pesticides are causing significant delays in the development of bees. Furthermore, the exposure to pesticides is making bees more susceptible to viral, spore, and bacterial infections and these are showing sub-lethal effects (Wu

Organochlorines cause eggshell thinning in birds; organophosphates, carbamates and pyrethroids affect the reproduction of amphibians because of their estrogenic activity; triazine herbicides can hinder the reproduction of mammals because of their antiandrogenic activity; organophosphates, carbamates, triazines, bipyridylium herbicides, and pyrethroids harm nontargeted invertebrates located close to pesticide treated areas (e.g. honey bees).

Worldwide, 400,000 to 500,000 tonne of obsolete pesticides are stockpiled in low- and middle-income countries.

et al., 2011a). Bees and other pollinators are very important in most terrestrial ecosystems. They guarantee genetic variation in the plant community and flora diversity, specialization, and evolution. The production of seeds, nuts, and fruits relies on pollination; in the absence of bees and other pollinators, many species of plants and animals would not be able to survive (Bradbear, 2009).

Also, other invertebrates are affected adversely by contamination with of pesticides. For instance, the crustacean *Americamysis bahia* and the branchiopoda *Ceriodaphnia dubia* are sensitive to pyrethroids, having a low LC_{50} after 10 days of exposure, ranging from 2 to 140 ng/L. The amphipod crustacean *Hyalella azteca* has a low LC_{50} after 10 days of exposure of from 4 to 110 ng/L (Hladik and Kuivila, 2009). The carbamates, bipyridylium, and triazine herbicides are known to cause inhibition of nucleic acid metabolism and protein syntheses and affect photosynthetic activity (Audus, 1976; Ebert and Dumford, 1976; Moreland, 1980; Ocampo and Barea, 1985; Morais et al., 2012). The non-selective bipyridylium herbicides are known to promote oxidative stress as a result of producing reactive oxygen species (Pasternak et al., 2007) or for destroying plant cell membrane (Fishel, 2014a).

For instance, 0.5 mg/L atrazine completely inhibits the autotrophic growth of *Chlamydomonas reinhardtii* (Helling et al., 1971) and 1 mg/L of atrazine, paraquat, or diquat is able to inhibit photosynthesis and growth or kill the cyanobacteria *Anabaena azollae* after 10 days of exposure (Holst et al., 1982). In addition, although the amounts of atrazine that are affecting the growth of *Chlamydomonas reinhardtii* are quite high, field studies showed that atrazine concentrations of even 50 µg/L or greater were ecologically relevant (Solomon et al., 1996). The primary producers (algae, cyanobacteria, and other plants) are important for sustaining the high quality of the aquatic habitat, which enables other organisms, such as invertebrates and vertebrates, to survive and settle down. Chronic exposure to herbicides may lead to a reduction of primary production which consequently can have adverse effects on the survival, growth, and reproduction of herbivores and predators, leading to disruptions of the food chain (Solomon et al., 1996). According to data obtained by FAO (Food and Agriculture Organization, 2013), the highest risk areas for environmental and human health from exposure to pesticides seem to be in middle America, northern and southern South America, west, central and southeast Africa, and south and east Asia. This assessment is based on the annual amounts of pesticide used (kg per ha of arable land) and the amount of crops produced that require large amounts of pesticides (or highly toxic ones) for their growth.

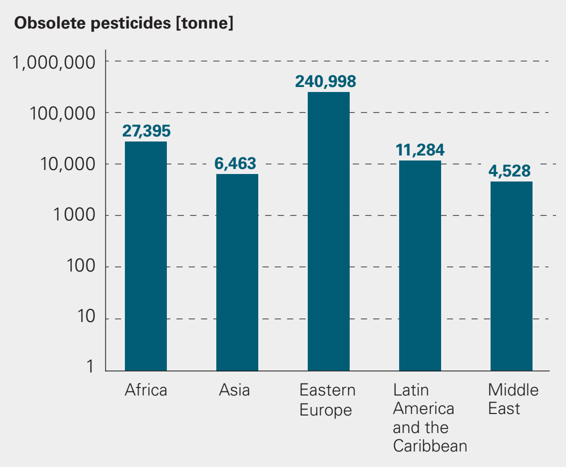


Figure 8: *Volumes of obsolete pesticides stockpiled in different areas of the world (Food and Agriculture Organization, 2015a)*

Issues of special concern

Inadequate storage

The stockpiling of obsolete pesticides is a serious problem in many low- and middle-income countries (Elfvendahl et al., 2004; United Nations Environment Programme, 2013c). After they were banned, their registrations withdrawn, or because of international policy decisions and conventions, several stocks of highly toxic and persistent pesticides, which were being phased out, were transferred from high-income countries and deposited in low- and middle-income ones. For instance, DDT, lindane, aldrin, atrazine, endosulfan, chlordane, heptachlor, metazachlor, and pendimethalin are examples of these obsolete pesticides that have been transferred. Today, these unwanted pesticides are often a severe source of pollution because they are stored under inadequate and unsafe conditions, thus posing high risks to human and environmental health (Elfvendahl et al., 2004). Examples of these stockpiled obsolete pesticides were found in low- and middle-income countries all over the world (García de Llasera and Bernal-González, 2001; Haylamicheal and Dalvie, 2009; Dasgupta et al., 2010). FAO published data about the volumes of pesticides which were disposed of inappropriately and under unsafe conditions (Figure 8). At present, they estimated that, worldwide, 400,000 to 500,000 tonne of obsolete pesticides are stockpiled in low- and middle-income countries (Food and Agriculture Organization, 2001). Of this amount, about 50,000 tonne are found in Africa alone (United Nations Environment Programme, 2003, 2013). Figure 8 shows that the highest amounts of stockpiled pesticides can be found in eastern Europe; Russia, Macedonia, Ukraine, and Uzbekistan have the highest volumes. Africa has the second highest volume with Mali, Tanzania, and Tunisia holding the highest amounts of these pesticide legacies. It is estimated that it would need US$1.25 billion to clean up this amount of obsolete pesticides (Food and Agriculture Organization, 2015a).

Case study of obsolete pesticide stockpiles

One good example of a country with a legacy of obsolete pesticides is Tanzania. There, according to estimates of the Food and Agriculture Organization of the United Nations, about 1500 tonne of obsolete pesticides were stockpiled in the whole country in 2008 (Food and Agriculture Organization, 2015b). In Arusha and Tanga, 470 L of atrazine, 10 kg pirimiphos methyl + permithrin, 11 kg benomyl, 40 tonne DDT, 8 tonne endosulfan and 3000 L dinitro-ortho-cresol were found (Rwazo, 1997). In 1989 in the Co-operative and Rural Development Bank warehouse in Mikocheni, about 11,000 L and 350 kg of the OPs Damfin P (methacrifos) and phosphamidon and the fungicide Thiovat (sulfur) were found. In 1993, according to a survey conducted by the Tanzania-Germany Project on Integrated Pest Management 40,000 L of obsolete pesticides – endosulfan, flumeturon, atrazine, malathion, methidathion, and DDT – were found in Mwanza and Shinyanga in the southern region close to the Lake Victoria. Additionally, 50 tonne of DDT, lindane, aldrin, chlordane, heptachlor, and endrin were located at Vikunge farm (Rwazo, 1997). Today, after removal of the obsolete pesticides at Vikunge farm, there are still high concentrations of pesticides found in this region. Soil samples taken to a depth of from 0 to 5 cm contained 12 to 282 g DDT and 23 to 63 g lindane per kg dry weight. Even after a cleanup of obsolete pesticides, these storage areas are often highly contaminated with pesticide residuals. Tap water at Vikunge farm was contaminated for years after the pesticide cleanup. In 2000, it was showing pesticide concentrations of 0.95 µg/L lindane and 1.7 µg/L DDT. Often only the visible remains of pesticides, the tanks and packages, are removed instead of a systematic removal of the soils within the contaminated areas (Elfvendahl et al., 2004).

Inadequate handling and lack of education

Inadequate handling and inappropriate application of pesticides poses another risk to human and environmental health in low- and middle-income countries (Eddleston et al., 2002; Kesavachandran et al., 2009). Often no personal protective equipment, such as rubber gloves, boots, breathing masks, googles, and coats, are worn because they are too expensive and uncomfortable to wear in the heat and high humidity present in tropical regions. In addition, the agricultural workers are not well educated in handling pesticides. In these countries the level of illiteracy is quite high and farmers are often not able to read or understand the safety precautions printed on the pesticide packages. Up to one-third of agricultural workers in low- and middle-income countries read the safety instructions on the packages, while only 1.5% understand the color coding system that presents information about the toxicity of the pesticide being used (Kesavachandran et al., 2009). These workers are not aware of the consequences resulting from acute or chronic exposure to hazardous pesticides. Often, untrained farmers were blending several hazardous pesticides together trying to increase their effect without knowing if these mixtures are useful or not. A lot of agricultural workers in low- and middle-income countries are continuously exposed to pesticides in several processes, like mixing pesticides (as mentioned previously sometimes pesticides were even blended together by hand), cleaning, and loading spray equipment. They are also exposed through inadequate manual application, by not considering the wind direction when spraying, or by wearing contaminated clothes for days. They are in direct contact with pesticides and they are often not able to wash off pesticide spillages because water is not always available (Eddleston et al., 2002; Kesavachandran et al., 2009; Pesticide Action Network Asia and the Pacific, 2010; United Nations Environment Programme, 2013c). Furthermore, pesticides are stored in their kitchens and living rooms posing risks to human health, especially to children and pregnant women (Pesticide Action Network Asia and the Pacific, 2010). Deliberate self-poisoning through pesticide ingestion is a big problem as well. This comes about because of the easy access to highly toxic pesticides. In the event of contamination, especially in rural regions, there is not much knowledge of how to interpret the symptoms of pesticide poisoning. In addition, there are few or no medical services accessible. In these regions there are too many patients and too few medical facilities, pharmaceuticals, antidotes, and doctors. There is little evidence that people know how to treat poisoned patients properly (Eddleston et al., 2002; Pesticide Action Network Asia and the Pacific, 2010).

A lot of agricultural workers in low- and middle-income countries are continuously exposed to pesticides during mixing of pesticides, cleaning, or loading of spray equipment. Workers are neither aware of the risks nor of the consequences resulting from acute or chronic exposure to hazardous pesticides.

Case study of inadequate pesticide handling

A survey conducted by PANAP (Pesticide Action Network Asia and the Pacific, 2010) in eight Asian countries (Cambodia, India, Sri Lanka, Indonesia, Philippines, Vietnam, Malaysia, and China) showed that farmers and agricultural workers in those regions are often not well educated in the adequate handling of and appropriate application methods for pesticides. The survey showed that mostly the workers are not wearing adequate protective clothing. For instance, in most of the regions surveyed (An Gian, Andhra Pradesh, Digos, Orissa, and Yunnan) only 1–5% of the farmers wore gloves when applying pesticides. In An Gian, Andhra Pradesh, Digos, Orissa, Prey Veng, Sri Lanka, and Yunnan only 0–13% wore overalls and in most of the regions (An Gian, Andhra Pradesh, Orissa, Sri Lanka, and Yunnan) only 0–19% were equipped with masks during pesticide application.

The survey showed that the blending of different hazardous pesticides is another issue. For example in Prey Veng, Cambodia, farmers blended from three to eight different pesticides together. In Hai Van, Vietnam, about three different pesticides were blended together. Often the field workers had no idea which kind of pesticides they were using. Furthermore, the survey revealed that in most of the regions (Andhra Pradesh, Orissa, Nam Dinh, Prey Veng, Sarawak, Sri Lanka, Yunnan) from 77% to 90% of the agricultural workers have never received any training on the pesticides they use in their fields. According to that it would appear that they are often not aware of the toxicity of these pesticides and that they follow bad practices when using pesticides.

Inappropriate regulation and implementation

Another critical point is the inappropriate implementation of government and international regulations and restrictions on pesticides in low- and middle-income countries. In these regions, the governments do not have the resources to enforce and control the availability and the use of pesticides, in part because there is a lack of pesticide registration processes and government infrastructure. Where there are regulations and restrictions governing pesticide use, they often differ markedly between countries. This encourages the illegal import of more toxic, but less expensive pesticides from neighboring countries (Roberts et al., 2003). Strengthening international regulations and initiating additional international conventions, like the Stockholm and Rotterdam ones, would solve this problem. The responsibility for controlling the circulation, safety, and use of hazardous pesticides should rest more on the importers, exporters, manufacturers, and the pesticide industry in general (Eddleston et al., 2002).

Best practices

A more sustainable and secure use of pesticides is required. Currently, there are several government and non-governmental initiatives to control and improve the use of toxic pesticides. Some theoretical approaches as well as some methods that have been implemented already are described below.

Implemented examples

Initiatives and conventions in sound chemical management and consumption

Currently, there are several approaches to achieving more sustainable and ecological agriculture. For instance, the main goal of the Rotterdam Convention is to control and ban the international trade in certain hazardous chemicals, including 32 pesticides. It also seeks to avoid the stockpiling of obsolete pesticides in low- and middle-income countries to prevent environmental and human health hazards. In addition, another objective is to guarantee the sound use of chemicals by giving information about chemical characteristics and labeling toxic chemicals with safety instruction and pictograms (United Nations Environment Programme and Food and Agriculture Organization, 2013). The Stockholm Convention is an international agreement which focuses on abolishing highly persistent, bioaccumulative, and toxic chemical compounds (United Nations Environment Programme, 2013d). In addition there are several non-governmental organizations (NGOs), such as Global Good Agricultural Practices (GlobalGAP) and the PAN organizations, trying to improve or enforce the sound use of pesticides. GlobalGAP is a European non-profit organization that defines voluntary standards for the certification of production processes for agricultural products worldwide. This organization was established to show consumers that agricultural commodities were being produced using sustainable production techniques and smaller amount of pesticides and other agro-chemicals, and to ensure that the working conditions and the animal husbandry practices were fair and safe (GlobalGAP, 2016). PAN is a network, including over 600 participating NGOs, individuals, and institutions, operating in more than 90 countries. Its main objective is to reduce and replace the use of hazardous pesticides with ecologically sound approaches. It has five independent collaborating regional centers located in North America, Latin America, Europe, Africa, and Asia and the Pacific region (Pesticide Action Network International, 2014). For example, PAN Asia and the Pacific conducted a community monitoring study to investigate the effects of pesticides in 12 communities in eight Asian countries. They interviewed 1304 people from the agricultural sector, including vegetable, paddy, and cotton farmers and workers in crop fields and palm oil plantations. They studied which of them used pesticides and which pesticides were the most toxic (paraquat, endosulfan, monocrotophos, etc.). They investigated, if the workers had been educated in the handling, use, and storage of pesticides and if they wore personal protective equipment. Studies like this are helping us to understand and highlight issues in pesticide use and, consequently, to find some solutions to these problems. Furthermore, they are teaching workers how to handle pesticides and what alternative methods could be used for agriculture, for example keeping away unwanted pests by using traps or pheromone traps or predators of the pests (Pesticide Action Network Asia and the Pacific, 2010).

The investigations of Roberts et al. (2003) showed that establishing regulations alone will not always be sufficiently effective to minimize the risks of hazardous pesticides to human and environmental health. For instance, at the beginning of the ban of WHO Class I pesticides in 1995, in Sri Lanka the number of deaths decreased significantly. Three years after this ban, the Class I OPs were substituted with endosulfan and carbamates causing even more deaths than before. This Sri Lankan case indicates that more adjustments and arrangements have to be made than just changing regulations to achieve significant improvements in the long term. Occupational and intended pesticide poisonings could be reduced according to a three step system.

1. eliminate the most hazardous pesticides using regulations and controls and introduce alternative and more sustainable methods to reduce the infestations of pests
2. have people who are trained in the handling of pesticides administer the controls. Only workers who are trained should be allowed to apply pesticides. Pesticides should never be stored at home. They should be stored in community stores with lockers available only to trained individuals. In addition, pesticide exposure should be monitored and controlled regularly
3. personal protective equipment should be used to guarantee safe and healthy working conditions and the medical management of pesticide poisonings needs to be improved to minimize the sequelae of pesticide poisoning (Murray and Taylor, 2000; Roberts et al., 2003).

Extension of data collection

It is important to collect more data about the spatio-temporal distribution of pesticides among the environmental compartments air, water, soil, and biota. This is necessary to obtain more detailed information about the toxicity of pesticides used in the past, present, and future. In future, it will be relevant to investigate the combined effect on environmental and human health of different pesticides or mixtures of pesticides and other anthropogenic agents. Chemicals can be measured directly in soils (Elfvendahl et al., 2004), air, and water (Karlsson et al., 2000) and pesticide residues can be measured indirectly in fruits and vegetables or in animal and human blood samples. For instance, Lehotay et al. (2005) developed a quick, easy, cheap, effective, rugged and safe method based on gas chromatography coupled with mass spectrometry with an ion trap instrument to identify different pesticides in lettuce and oranges. In addition, PAN, together with the European Food Safety Authority and the Swedish Chemicals Agency, are highlighting a selection of endocrine disrupting pesticides found in fruits, vegetables, milk, and eggs (Pesticide Action Network Europe, 2013). Dulaurent et al. (2010) developed a general screening method to determine and quantify pesticides in blood samples. To obtain their measurements they used LC coupled with a single linear ion trap mass spectrometer. With their method it is possible to detect more than 320 different pesticides and metabolites in blood, serum, plasma, and urine samples (Dulaurent et al., 2010).

Low cost approaches

To reduce the number of deaths caused by pesticides in low- and middle-income countries it is important to find cheap and easy methods, which are available in these countries, to monitor pesticide contaminations or for fast diagnosis of poisoning. For instance, the Securetec Detektions-Systeme AG company, Brunnthal, developed, in cooperation with the Bundeswehr Institute of Pharmacology and Toxicology, a rapid and cheap (about €3770 for the applicator and 100 test kits; Mark Johnson (Securetec), personal communication *in vitro* detector which can give information about poisoning by OPs, carbamates, or other nerve agents. Detection is based on the photometric analysis of acetylcholinesterase (AChE) or butyrylcholinesterase (BChE) activity. The inhibition of AChE and BChE is the predominant indicator of poisoning caused by OPs and carbamates. With this tool it is possible to get results within several minutes. The tool is easy to handle and it can be used in the laboratory or in field studies at temperatures ranging from 10° to 50°C (Securetec AG, 2013).

More data and analysis on the spatio-temporal distribution of pesticides and the combined effect on environmental and human health of different pesticides or mixtures of pesticides and other anthropogenic agents is needed.

García-Santos et al. (2011) introduced a low cost method to monitor the drift of airborne pesticides after application using a knapsack sprayer. For their studies, they used a test field of 380 m^2 in Tunja, Columbia. To measure the air born drift of pesticides, highly absorbent papers were fixed at various distances up to 20 m downwind and next to the treated area. Droplet deposition inside the test field and on the applicator was determined as well by installing highly absorbent paper inside the test field and on the applicator. The test solution (for instance water) was sprayed by a farmer under stable weather conditions at low radiation intensity. Afterwards, the distribution and the deposition of potential airborne pesticides in exposed fields next to the test one, inside the test field, and directly at the applicator were determined. This was achieved using a cheap and simple weight method – absorbent papers were weighed directly before and after the application of the test substance. These results were evaluated according to a simple mass balance approximation. In the end, they showed that by using the weight method they were able to explain about 86% of the airborne drift and deposition variance (García-Santos et al., 2011).

Theoretical examples

Improvement of existing regulations

As already mentioned in the chapter "Input pathways of pesticides", internationalizing and generalizing regulations on pesticide use, export, import, and production would help to interrupt the circulation of highly toxic and illegal pesticides. Although there are some international conventions about pesticide use, as a status quo they do not seem to be effective enough. Furthermore, hazardous pesticides, the application of which requires the use of proper and expensive personal protective equipment (overalls and respirators) – especially the majority of the phase I and II pesticides – should be prohibited in low- and middle-income countries, where the appropriate application of the pesticide cannot be guaranteed (Roberts et al., 2003). In addition, there should be more investigation of chronic exposure of humans, animals, and the environment to pesticides. Mostly, the toxicity of pesticides is determined and classified through the investigation of acute animal tests (World Health Organization, 2010b). However, the effects of a long-term exposure of the environment, animals, and humans to pesticides are quite unclear. Moreover, the research on and the use of improved and more specific pesticides, which are potentially less bioaccumulative and toxic, such as most of the pyrethroids, should be promoted and extended. Maybe funding for the use of less toxic pesticides and/or the application of organic agricultural practices could help to reduce the production and the use of pesticides with high toxicity.

More data on the production, application, uses, and distribution of pesticides are required. Often in low- and middle-income countries, monitoring and risk assessment is challenging or impossible because of the scarcity of data and the uncontrolled use of unregistered pesticides. If comprehensive data about

- pesticide use (use rates and concentrations)
- application (application rates and which pesticides are used in which region for each crop)
- crop and pesticide production
- the import and export of pesticides

were available, it might be possible to conduct preliminary risk assessment studies. These would localize high risk areas where further investigation was needed to mitigate the risks to human and environmental health associated with exposure to pesticides.

Veterinary and Human Health Care Pollutants

Chemical characteristics and their potential risks

Introduction

Today, the use of human and veterinary pharmaceuticals for the treatment of diseases is indispensable. There are more than 3000 active pharmaceutical ingredients (APIs) used as analgesics, antibiotics, antivirals, beta-blockers, contraceptives, lipid regulators, sedatives, and impotence drugs (Ternes et al., 2004; Richardson et al., 2005). The persistent application of pharmaceuticals results in a continuous and omnipresent contamination by APIs, in their original form or as transformation products, of aquatic environments and soils particularly (Ferrari et al., 2003; Sarmah et al., 2006; Gros et al., 2007; Larsson et al., 2007). During the last decades, continuous exposure to these substances resulted in relatively new research areas being established – the fields of environmental toxicology and environmental chemistry. These disciplines are driven by the improved ability to measure these micro-pollutants. From the knowledge gained, they have raised awareness that exposure of the environment to pharmaceuticals can adversely affect ecosystems and the environment. It has also been established that these pharmaceuticals are highly active even at very low concentrations (Crane et al., 2006; Hernando et al., 2006; Klavarioti et al., 2009). Even human health might be affected by APIs that are released into the environment, as exemplified by the formation of multi drug-resistant microbial strains (Phillips et al., 2004; Hersher, 2012). In this context, evidence for the development of antibiotic-resistant bacterial strains of tuberculosis (Zager and McNerney, 2008; Hersher, 2012), salmonella (Kingsley et al., 2009), and *Escherichia coli (E.coli;* Rogers et al., 2011), or for the generation of antiviral drug-resistant influenza viruses (de Jong et al., 2005) has been found. To date, the occurrence and fate of pharmaceuticals in the environment have been extensively assessed and documented in high-income countries (Sacher et al., 2001; Heberer, 2002; Kolpin et al., 2002; Ternes et al., 2004; Jones et al., 2005; Togola and Budzinski, 2008; Vulliet and Cren-Olivé, 2011). However, environmental data about APIs in low- and middle-income countries is limited and their risks to environmental health in low- and middle-income countries have been poorly assessed and documented (Richardson et al., 2005; Larsson et al., 2007; Zhao et al., 2010; Rehman et al., 2015). In this context, more investigation of the occurrence and the fate of APIs in low- and middle-income countries is required.

Active pharmaceutical ingredients are omnipresent in aquatic environments and soils, in their original form or as transformation products. Exposure of the environment to pharmaceuticals can adversely affect ecosystems and the environment even at very low concentrations.

Even in low- and middle-income countries, APIs should be considered as significant environmental risk factors.

Main Issues

- The bulk of the pharmaceutical production has and is being relocated from high- to low- and middle-income countries, such as China, India, and Pakistan. These countries are producing large amounts of APIs and the generic forms of the drugs are extensively produced in low- and middle-income countries as well (Pricewaterhouse Coopers, 2012; Rehman et al., 2015). The increased production of APIs in low- and middle-income countries is mainly driven by the lower production costs that are possible in these countries and by the growing demands and markets for APIs in these countries (Rehman et al., 2015)

- Often in low- and middle-income countries the industrial effluents act as a considerable number of point source of micro-pollutants of environmental systems (Larsson et al., 2007) as they are released untreated into the environment (Rehman et al., 2015)

- The consumption of APIs increases in densely populated areas with the availability of cheaper generic drugs and with improving living standards (Zhang and Geißen, 2010; IMS Institute for Healthcare Informatics, 2012)

- Excessive animal livestock farming (aquafarming (Food and Agriculture Organization, 2010) fish, crustacean, mussels or the farming of cattle, chicken and pork (BBC, 2013; Food and Agriculture Organization, 2013; Richard, 2013) is being carried out increasingly in many low- and middle-income countries with veterinary APIs being used intensively and in an uncontrolled manner (Mitema et al., 2001; Sarmah et al., 2006; Ok et al., 2011)

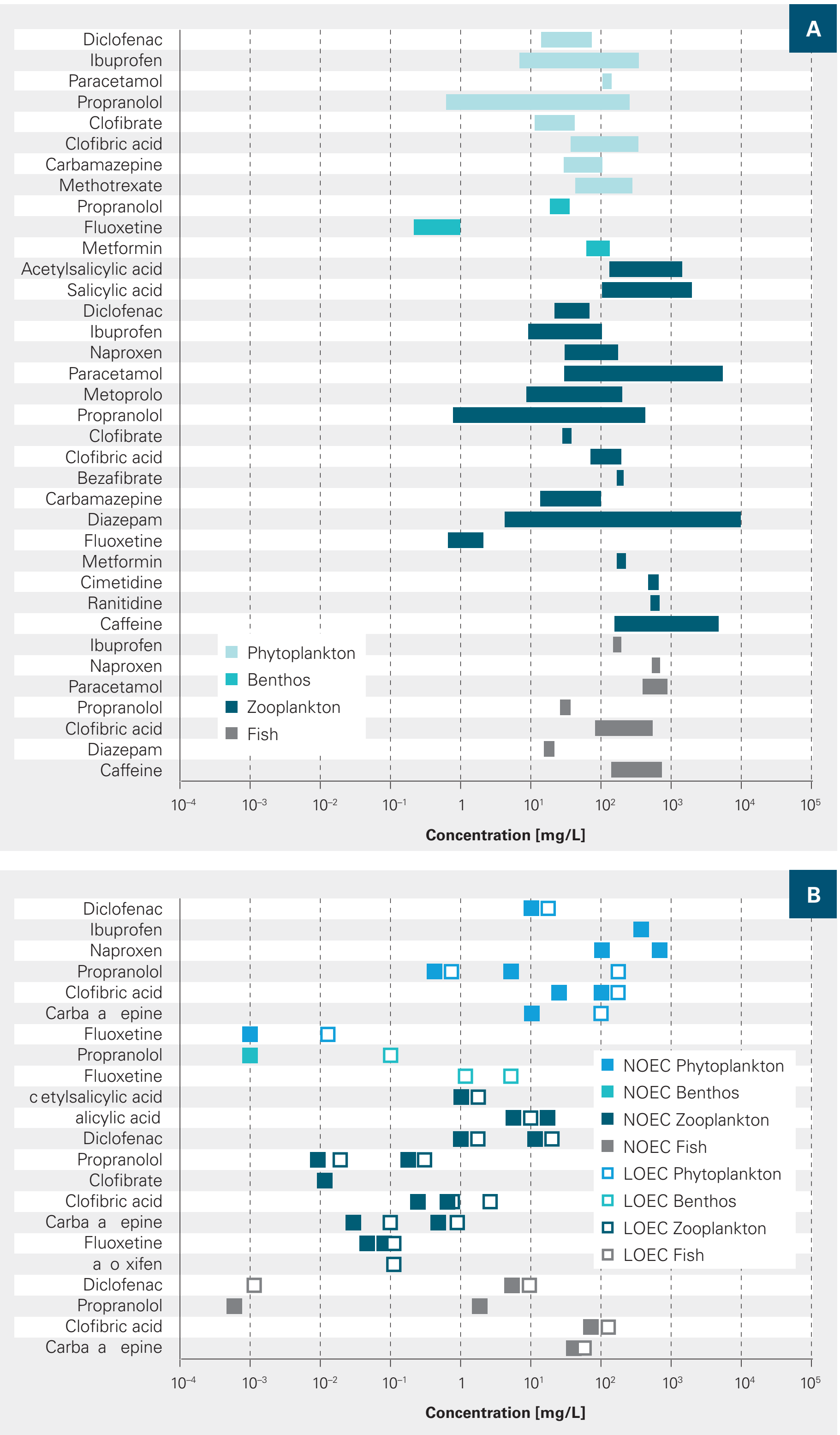


***Figure 9**: Acute (A) and chronic (B) toxicity of individual APIs in different aquatic organisms of different trophic levels (phytoplankton, benthos, zooplankton, and fish). The acute values represent data from different organisms and/or experiments and range over several orders of magnitude for an individual API. The chronic values illustrated are the lowest observed effect concentrations (LOEC) and no observed effect concentrations (NOEC). One data point is referring to one species and/or one experiment (Kümmerer, 2008)*

Toxicological potential

APIs are designed to be persistent and to have a highly bioactive potential even at low environmental concentrations (Heberer, 2002; Fatta-Kassinos et al., 2011; Köck-Schulmeyer et al., 2013). Since their widespread occurrence in the environment (Heberer, 2002; Fent et al., 2006; Fatta-Kassinos et al., 2011), and since they have shown eco-toxicological effects, especially to aquatic systems (Crane et al., 2006; Hernando et al., 2006; Ernst et al., 2012), concern about their effects on the environmental has increased during recent years (Voigt and Bruggemann, 2008; Kümmerer, 2009b). Figure 9 illustrates the high toxic potential of individual APIs on aquatic organisms of different trophic levels. Environmental concentrations of these pharmaceuticals at ng/L and µg/L levels are able to impair considerably the health of water organisms, causing them to show chronic and acute toxic effects (Kümmerer, 2008; Ecotox Centre, 2015). The antidepressant fluoxetine and the beta-blocker propranolol, especially, are acutely toxic to benthos and zooplankton (Figure 9 (A)). Even a chronic exposure of from 0.001 to about 0.0.1 mg/L of the anti-inflammatory drug diclofenac and the antidepressant fluoxetine can cause perceptible adverse effects in fish or phytoplankton (Figure 9B).

The proposals of the quality standards of the Ecotox Centre of Eawag/EPFL (École polytechnique fédérale de Lausanne) also show that even concentrations of several APIs at a level of ng/L can be enough to adversely affect the health of water organisms and to interrupt the interaction. Acute risks to the health of water organisms are assumed when the environmental levels of APIs in surface waters exceed the MAC-EQS and chronic effects to water organisms can be assumed if the environmental water concentrations surpass the AA-EQS (Ecotox Centre, 2015). The proposed MAC-EQS for the antibiotic azithromycin is 90 ng/L, for clarithromycin it is 110 ng/L, and for ciprofloxacin, 363 ng/L. For the hormone preparation and contraceptives 17-ß-ethinylestradiol, 17-ß-estradiol and estrone the AA-EQS are 0.037, 0.4, and 3.6 ng/L, respectively. The analgesic diclofenac has an AA-EQS of 50 ng/L and for the antibiotics erythromycin, clarithromycin, and ciprofloxacin the AA-EQS values of 40, 60 and 89 ng/L, respectively, are determined (Ecotox Centre, 2015).

Physicochemical characteristics

APIs are complex molecules with a molecule weight ranging from 200 to 1000 Dalton and with varying physicochemical and biological properties and functionalities. According to their ionic nature, most of the APIs are polar and consequently remain in aquatic systems (Kümmerer, 2008). Nevertheless some APIs, such as several antibiotics, can have lipophilic characteristics as well (Hamscher et al., 2003; Sarmah et al., 2006; Kümmerer, 2009a) and, therefore, they can adsorb to organic material, such as soil particles, sediments, feces, sewage sludge, and manure. Most of the APIs have a low volatility, which is mainly due to their relatively high molecular weights and their highly hydrophilic characteristics (Hernando et al., 2006).

Consumption

In general, it can be assumed that about several hundred thousand tonnes of pharmaceuticals are consumed worldwide. The annual global consumption of pharmaceuticals per capita is predicted to be of the order of 15 g, while in industrial countries a consumption of pharmaceuticals of between 50 and 150 g per capita per year can be assumed (Ternes and Joss, 2007).

According to our literature search, it can be assumed that more comprehensive data about the consumption and production of pharmaceuticals is not readily available (if at all) to the general public – neither in high- nor in low- and middle-income countries. Since this is the case, it is not possible to compare the consumption and the production of pharmaceuticals in high- and in low- and middle-income countries in more detail. Just the available data on the expenditures of pharmaceutical companies can be used to approximate their production and the consumption in individual countries or lending groups. This is shown in the chapter "Input pathways of pharmaceuticals" and in the following paragraph.

Generally, the production, demand, and consumption of pharmaceuticals is dependent on several factors. The outsourcing of the pharmaceutical manufacturing facilities from Organisation for Economic Development and Cooperation (OECD) to non-OECD countries is driven mainly by the lower production costs in these countries. This, together with the excessive and increased production of generic drugs in low- and middle-income countries, causes a high increase in the production of human and veterinary pharmaceuticals in low- and middle-income countries with fast growing economies, such as China, India, Pakistan, etc. (IMS Institute for Healthcare Informatics, 2012; PricewaterhouseCoopers, 2012; Rehman et al., 2015). Along these lines, PricewaterhouseCoopers (2012) predicts that the 2011 sales of pharmaceuticals in China of US$66.9 billion can increase until 2020 by 163%. In India the US$15.6 billion industry of 2011 can have increased 213% by 2020. In the fast followers (including Argentina, Egypt, Indonesia, Mexico, Pakistan, Poland, Romania, South Africa, Thailand, Turkey, Ukraine, Venezuela, and Vietnam) 2020 can see a growth of 125% in their US$76.6 billion industry. In comparison, in high-income countries the trends in sales of pharmaceuticals will be less pronounced or even decline. For instance, for the USA it is predicted that the sales of US$337 billion will increase by just 26% while in the large EU countries (France, Germany, Italy, Spain, and the UK) the sales of US$205 billion will decrease by 5% from 2011 to 2020 (PricewaterhouseCoopers, 2012). This data are shown in Figure 12 and discussed again in the chapter on "Future trends and hot spots". However, according to these data on the sales of pharmaceuticals the following conclusion can be drawn: In low- and middle-income countries there will be a growing trend in the production of pharmaceuticals during the next years.

In addition, because of future demographic changes, such as improved living standards, the increases in the average life span and the population will be more pronounced in low- and middle-income countries (The World Bank Group, 2014). The demand for pharmaceuticals and the production of lower cost generic drugs, especially in the low- and middle-income countries with strong economies, might increase during the next decades (Kümmerer, 2009b; IMS Institute for Healthcare Informatics, 2012; PricewaterhouseCoopers, 2008; The World Bank Group, 2014). Together, these suggest an increase in demand for and, accordingly, the availability of pharmaceuticals in low- and middle-income countries as well.

For these reasons consumption in low- and middle-income countries with strong economies will be stimulated and will provoke the release of high amounts of pharmaceuticals into the environment. This might give rise to outcomes that impair human health – the formation of multidrug-resistant microbes and to the degradation of aquatic ecosystems – in countries with lower incomes as well (Mitema et al., 2001; Richardson et al., 2005; Zager and McNerney, 2008; Larsson, 2010; Rogers et al., 2011; Zhao et al., 2010; Ok et al., 2011).

Nevertheless, although no comprehensive data about the consumption of pharmaceuticals are available, especially for low- and middle-income countries, some case examples can be found that show that in these countries high quantities of pharmaceuticals are used as well. For instance, Richardson et al. (2005) assumed that in 2004 about 15,770 tonne of antibiotics for human application were used in Hong Kong and the Pearl River Delta region of south China. In the same region, the same amount or even more is used in the agricultural sector as food additives or as veterinary agents for livestock as well. Given the immense number of industrial/pharmaceutical manu-

Production and consumption of human and veterinary pharmaceuticals is rapidly increasing in low- and middle-income countries with fast growing economies, e.g. China, India and Pakistan. This may enhance outcomes that impair human health such as the formation of multidrug-resistant microbes or the degradation of aquatic ecosystems.

facturing facilities in this region, Richardson et al. (2005) suppose that it is possible to find here even higher environmental concentrations of pharmaceuticals and other micro-pollutants with wider distribution than there are in western countries such as Europe, the UK, and the USA. Therefore, overcrowded areas and areas with high agricultural and industrial activities – which is the case in Hong Kong and the Pearl River Delta region – are significant sources of APIs and other industrial chemicals, which pose risks to environmental and human health. This is especially so if there are no, or inadequate or insufficient, wastewater treatment facilities available, which is often the case in low- and middle-income countries (Richardson et al., 2005; Blacksmith Institute and Green Cross, 2012).

In addition, Mitema et al. (2001) identified that in Kenya alone, large volumes – about 14.6 tonne – of active antimicrobials were used in animal food prodution. In 1999, the main antibiotics used in the animal husbandry sector in Kenya were aminoglycosides, ß-lactams, tetracyclines, nitrofurans, quiniolones, and sulfonamides. Between 469 and 39,866 kg were used annually. In general, there is an even greater lack of data on the application of steroids and other growth promoters in the agricultural sector than there is for the human consumption of antibiotics.

A screening for pharmaceuticals of human urine samples from Durban, South Africa, within the scope of the Valorization of Urine Nutrients in Africa (VUNA) project (www.vuna.ch; Etter et al., 2015) shows that APIs, which can cause adverse effects to aquatic environments (Ecotox Centre, 2015), are available, consumed, and excreted as well. The most prominently consumed and excreted APIs of this region are the antibiotics sulfamethoxazole and its metabolite N-acetyl-sulfamethoxazole, trimethoprim, the transformation product of the beta-blocker atenol, atenolol acid, and the analgesic diclofenac (Bischel et al., 2015). Further investigations show that in other countries with low incomes, such as Pakistan, considerable levels of the antibiotics ciprofloxin, oxytetracycline, oflaxacin, and sulfamethoxazole in concentrations of up to 4 µg/L, and the analgesic diclofenac up to a concentration of 8 µg/L, have been measured in domestic wastewater (Rehman et al., 2015).

The groups of APIs of highest eco-toxicological concern, which will play an increasing role in low- and middle-income countries, are highlighted in the following section. For most of these pharmaceutical groups, except antibiotics (Okeke et al., 2005a; Hersher, 2012) and antivirals (Richman et al., 2004; Dilernia et al., 2007; Baggaley et al., 2010), the environmental concentrations in surface waters are generally not supposed to affect human health, therefore the impacts on human health of just the antibiotics and the antivirals are discussed in more detail.

Active pharmaceutical ingredients of environmental concern

A) Analgesics and anti-inflammatory drugs

Paracetamol, acetylsalicylic acid, ibuprofen, fenoprofen, mephenamic acid, naproxen, indomethacin, and diclofenac are common and broadly used as painkillers and anti-inflammatory agents.

Consumption

Worldwide, the annual use of these agents amounts to several kilotonnes (Cleuvers, 2004). Given their low prices and that these agents can be obtained mainly without prescription – they are referred to as over-the-counter-drugs – the pattern of their consumption is relatively incomprehensible (Oaks et al., 2004). The anti-inflammatory drugs ease pain mainly by the inhibition of cyclooxygenase 1 and/or 2 (Vane and Botting, 1998).

Environmental behavior and occurrence

Given the immense consumption of these agents, their persistence, and their high water solubility, several anti-inflammatory drugs or their transformation products can reach considerable environmental concentrations – up to µg/L (Ternes, 1998; Stumpf et al., 1999; Heberer, 2002; Ferrari et al., 2003; Jiménez et al., 2012; Tredoux et al., 2012). This is especially so for the analgesic diclofenac, which is well-known for its high persistence in aquatic environments. Even with state of the art wastewater treatment facilities it is difficult to degrade this API effectively (Zhang et al., 2008). In Côte d'Ivoire, the maximal concentrations of the anti-inflammatory agent diclofenac above 1 µg/L were found in surface water (Weber et al., 2014; Figure 16). In domestic wastewater in Pakistan, diclofenac concentrations up to 8 µg/L were measured (Rehman et al., 2015). In addition, in France (Deblonde et al., 2011) a maximum concentration of diclofenac of 3.1 µg/L was measured in domestic wastewater while in Spain (Gracia-Lor et al., 2012) the value was 1.49 µg/L. Even in groundwater samples in Germany, diclofenac concentrations at a magnitude of ng/L were detected (Sacher et al., 2001; Heberer et al., 2011).

Toxicity

In order to evaluate the eco-toxicological potential of anti-inflammatory drugs in more detail, there is evidence that even low concentrations (0.5 µg/L) of diclofenac showed toxic effects to the organs of a brown trout (*Salmo trutta f. fario*; Hoeger et al., 2005). In addition, the findings of Schwaiger et al. (2004) show that exposure to 5 µg/L of diclofenac is enough to initiate renal lesions and cause adverse effects to the gills of rainbow trout (*Oncorhynchus mykiss*). Moreover, diclofonac is well-known for its alarming eco-toxicological potential, since Oaks et al. (2004) showed that the population of oriental white-backed vultures (*Gyps bengalensis*) in Pakistan had been endangered through eating the carcasses of diclofenac-treated livestock. This ingestion of dead livestock with accumulated residuals of diclofenac by the vultures was leading to renal failure and death. According to the Ecotox Centre, the chronic environmental standard value (AA-EQS) of 0.05 µg/L for diclofenac should not be exceeded in the long term in order to protect aquatic environments. For ibuprofen, the proposed AA-EQS value is 0.3 µg/L and for naproxen it is 1.7 µg/L (Ecotox Centre, 2015).

B) Antibiotics

Active antibiotic substances, such as sulfadimidine, sulfadiazine, cloxacillin, benzylpenicillin, bacitracin, oxytetracycline, and virginiamycin, are used to treat disease and promote the growth of livestock and in aquaculture (Sarmah et al., 2006; Kemper, 2008). Antibiotics like clarithromycin and erythromycin, sulfamethoxazole and trimethoprim are more likely to be used for human treatment (Kemper, 2008; Ernst et al., 2012). Table 2 represents a small collection of antibiotics used for veterinary and human treatments.

Consumption

Worldwide, humans are using approximately 100–200 thousand tonne of antibiotics and the lack of global data about the amount used for veterinary purposes makes it even more difficult to estimate total consumption (Wise, 2002; Sarmah et al., 2006; Rehman et al., 2015). Although the number of studies on the occurrence, fate, and ecotoxicology of antibiotics have increased within the last decades, the processes and the behaviors of these agents in the environment, especially in the long term, are quite unclear (Kümmerer, 2009a).

Environmental behavior and occurrence

Antibiotics can diffuse and accumulate in water systems and soils by having polar and partly apolar properties (Sarmah et al., 2006; Kümmerer, 2009a). This is especially the case if the application of veterinary products is not controlled and regulated and domestic and municipal wastewater and the effluents of hospitals are not treated sufficiently. This is often the case in low- and middle-income countries where antibiotics can be released into the environment through the discharge of untreated industrial wastewaters (Mitema et al., 2001; Larsson et al., 2007; Duong et al., 2008; Ok et al., 2011). For example, the concentration of antibiotics in the effluents of WWTPs in the Pearl River Delta in South China were found to range from 0.009 to 2.054 µg/L (Xu et al., 2007). In untreated hospital wastewaters in Vietnam, the concentrations of fluoroquinolone antibacterial agents were found to be from 1.1 to 44 µg/L for ciprofloxacin and from 0.9 to 17 µg/L for norfloxacin (Duong et al., 2008). Treated wastewater effluents adjacent to an industrial estate near Hyderabad, India, which houses 90 bulk drug manufacturers, contained maximal concentrations of antibiotic-fluoroquinolones of about 31,000 µg/L of ciprofloxacin and 900 µg/L of enrofloxycin (Larsson et al., 2007). In the Poudre River in Colorado, USA, which has urban and agricultural influences, the average concentrations of several tetracyclines and sulfonamides were found to range between 0.05 and 0.17 µg/L (Yang et al., 2004).

Furthermore, antibiotic agents can remain parly in soils as well. Hamscher et al. (2002) found the highest average concentrations of tetracycline (ranging from 86.2 to 198.7 µg/kg) and of chlortetracycline (ranging from 4.6 to 7.3 µg/kg) in soil layers up to 30 cm deep in a field with intensive livestock farming in northern Germany. In another study, they revealed that tylosin, tetracyclines, sulfamethazine, and chloramphenicol, mainly, can be traced in dust samples from a German pig-fattening farm in concentrations of about 12,500 µg/kg dust (Hamscher et al., 2003). These environmental concentrations of antibiotics in water systems and soils indicate that antibiotics have the potential to remain or even accumulate in water and soils.

Anti-inflammatory drugs such as diclofenac are well-known for an alarming ecotoxicological potential. Ingestion of dead livestock with accumulated residuals of diclofenac by vultures has led to widespread renal failure and death in Pakistan.

Toxicity

The eco-toxicological classification of Table 2 shows the maximum measured environmental concentrations of different antibacterial substances found in sewage effluent, surface water, groundwater, or drinking water in Germany. The table also indicates whether the individual substance should be considered as a priority pharmaceutical or not. This prioritization of pharmaceuticals is based on:

- The eco-toxicological effect of concentrations of the pharmaceutical on water organisms
- The occurrence in the aquatic environment
- The consumption rates of APIs between 2002 and 2009.

This prioritization was undertaken by the IWW Water Centre and the German Federal Environmental Agency (GFEA); Bergmann et al., 2011.

However, this classification in Table 2 must be treated with caution, because it is determined by monitoring and measuring environmental concentrations in Germany. What has to be taken into account is that some antibiotics that pose a risk to environmental health, which are not often used in Germany, can be used intensively in low- and middle-income countries and vice versa. Furthermore, it has to be considered that often in lower-income countries water treatment systems are not available or are less effective than the ones in higher-income countries. Even in industrial countries, sewage treatment plants (STPs) have problems in dealing with and eliminating antibiotic agents (Xu et al., 2007; Kümmerer, 2008). In addition, it is suggested that high concentrations of antibiotics in STPs might interrupt the microbiological depletion of pharmaceuticals and other chemical pollutions by inhibiting the proliferation of, or killing, the non-target microbial communities that are required for the biological purification of wastewater (Kümmerer, 2009a). In general, antibiotic agents that are found to pose risks to aquatic systems in industrial countries should not be used in low- and middle-income ones. This suggestion is made because often in these regions there is no monitoring of these compounds and there are probably not enough financial resources available to remediate contaminated sites (Blacksmith Institute and Green Cross, 2011, 2013).

For example, the use of quinolones is restricted in industrial countries because they act as a highly effective group of antibacterial drugs for human infections. They are well-known for their capability to generate cross-resistance and they have the potential to accumulate in sediments because of their low rates of biodegradation. In contrast, in China and Chile these antibiotics are used widely, without any restrictions, in aquaculture (Cabello, 2006).

Table 2: Selection of active antibacterial substances used for veterinary and human purposes (Sarmah et al., 2006; Kemper, 2008; Bergmann et al., 2011)

Class	Compounds	Primary usage	Potential side effects	Eco-toxicological classification [A]
Aminoglycosides				
	Apramycin	Pigs only	Neurotoxic	NA
	Gentamycin	All animals, humans	Nephrotoxic	NA
	Kanamycin	Dogs, pigs, cattle, horses	Ototoxic, nephrotoxic	NA
	Neomycin	All animals		NA
	Sisomycin	Humans only	Ototoxic, nephrotoxic	NA
	Spectinomycin	Pigs, cattle, poultry, sheep		NA
	Streptomycin	Obsolete		NA
ß-Lactams: penicillins				
	Amoxicillin	All animals, humans	Allergic reactions	P 🐟 🐟
	Ampicillin	All animals		NA
	Azlocillin	Humans		NA
	Benzylpenicillin	All animals		NA
	Cloxacillin	Cattle		NA
	Dicloxacillin	Cattle		NA
	Flucloxacillin	Humans		NA
	Methicillin	Humans		NA
	Mezlocillin	Humans		🐟
	Nafcillin	Humans		NA
	Oxacillin	Cattle		NA
	Piperacillin	Humans		NA
	Phenoxymethylcillin	Humans		NA
	Penicillin G	Humans		🐟

Class	Compounds	Primary usage	Potential side effects	Eco-toxicological classification [A]
Cephalosporines				
	Cefalexin	Dogs	Cross allergic reactions to ß-lactams	NA
	Cefalotin	Humans		NA
	Cefazolin	Humans		NA
	Ceftiofur	Cattle, pigs		
	Cefotaxim	Humans		NA
	Cefotiam	Humans		NA
	Cefquinom	Cattle, pigs		NA
Fenicoles				
	Chloramphenicole	Cats, dogs	Anemia	P 🐟🐟
Fluoroquinolones				
	Ciprofloxacin	Humans	Arthropathy in young animals	P 🐟
	Enrofloxacin	All animals, aqua-planting (Holmström et al., 2003)		🐟
	Marbofloxacin	All animals		NA
	Flumequin	Humans, aqua-planting (Cabello, 2006)		NA
	Ofloxacin	Humans		🐟
Lincosamides				
	Clindamycin	Dogs, humans	Gastro-intestinal problems	P 🐟🐟🐟
	Lincomycin	Pigs, cats, dogs, cattle		P 🐟🐟
Macrolides				
	Azithromycin	Humans		🐟🐟
	Clarithromycin	Humans		P 🐟🐟
	Erythromycin	Humans, cattle, chicken		P 🐟🐟🐟
	Roxithromycin	Humans		NA
	Spiramycin	All animals		NA
	Tylosin	Animals only		🐟🐟
	Vancomycin	Humans		NA
Sulfonamides				
	Sulfanilamide	Humans		NA
	Sulfadimethoxine	Cattle, pigs, chicken		P 🐟🐟🐟
	Sulfadimidine	Cattle, sheep, chicken		P 🐟🐟🐟
	Sulfamethoxazole	Humans		P 🐟🐟🐟
	Sulfapyridine	Pigs		NA
	Sulfathiazole	Humans		NA
Trimethoprim		In combination with sulfonamides		🐟🐟
Tetracyclines				
	Chlortetracycline	Cattle, pigs	Hepatotoxic	P 🐟🐟
	Doxycycline	Humans, cats, dogs		P 🐟
	Oxytetracycline	Humans, cattle, sheep, pigs, Aqua-planting (Holmström et al., 2003)		P 🐟🐟🐟
	Tetracycline	Humans, horse, sheep, pigs		P 🐟🐟🐟

A: Declaration if the substance has been assigned to the list of priority substances affecting water organisms as classified by IWW and the GFEA (Bergmann et al., 2011) with
P = high priority substances and
(P) = moderate priority substances.
NA means that these compounds are not prioritized pharmaceuticals or that too little data or no data for prioritization was possible.
MEC_{max} – maximum measured environmental concentration in surface water in Germany, with
🐟🐟🐟 = MEC_{max} > 1 µg/L; 🐟🐟 = MEC_{max} > 0.1 µg/L; 🐟 = MEC_{max} < 0.01 µg/L.

Concerning environmental toxicity, the release of antibiotics into the environment can directly affect organisms because of their acute and chronic toxicity. However, primary organisms, such as bacteria, fungi, and microalgae, seem to be more sensitive to exposure to antibiotics compared to vertebrates and invertebrates, because antibiotics were designed to eliminate microorganisms. High environmental concentrations of antibiotics may lead to an interruption of the food web system.

Antibiotic-resistant bacteria will be most problematic in developing countries where the infectious disease rates are high and newer and more effective antibiotic agents are unaffordable.

The following are examples of the direct toxicity of antibiotics to aquatic organisms. *Vibrio fisheri* showed significant adverse effects to ciprofloxacin at concentrations of 5000 µg/L (Hernando et al., 2007) and the growth of the microalgae *Microcystis aeruginosa* was inhibited at concentrations lower than 100 µg/L (Halling-Sørensen, 2000). After conducting a 7 day experiment with static concentrations of sulfamethoxazole and levofloxacin ranging from 100 to 1000 µg/L, phytotoxic effects were observed in the water plant *Limna gibba* (Brain et al., 2004).

From the environmental prospective, and according to the data of the IWW and the GFEA, the antibiotics amoxicillin, chloramphenicole, chlortetracycline, ciprofloxacin, clindamycin, doxycycline, erythromycin, oxytetracycline, sulfadimidine, sulfamethoxazole, roxithromycin, and tetracycline were found to be the most relevant ones (Bergmann et al., 2011). For instance, according to the Ecotox Centre, the chronic environmental standard (AA-EQS value) of ciproflaxin is 0.089 µg/L, of erythromycin is 0.04 µg/L, and of sulfamethoxazole is 0.6 µg/L (Ecotox Centre, 2015).

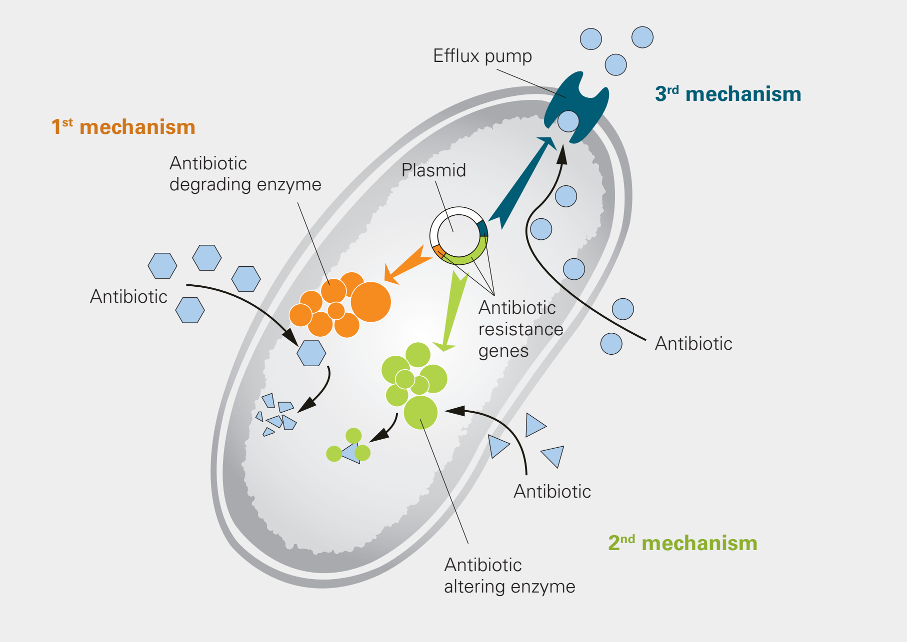


Figure 10: *Three bacterial mechanisms leading to resistance to antibiotics (Byarugaba, 2010)*

Concerning human toxicity, it has been shown that exposure to antibiotics can result in the formation of antibiotic-resistant genes and bacteria strains (Cabello, 2006; Duong et al., 2008; Kümmerer, 2009a; Sosa et al., 2010; Ernst et al., 2012). The formation of antibiotic-resistant bacteria will be most problematic in developing countries where the infectious disease rates are high and people are unable to pay for the newer and more cost intensive antibiotic agents (Kümmerer, 2009a). The formation of antibiotic-resistant bacteria and the interactions between bacterial populations and antibiotics are highly complex processes that are not completely understood (Martinez and Baquero, 2000; Kemper, 2008; Kümmerer, 2008). Nevertheless, it is known that the emergence of antibiotic-resistant bacteria can be induced by different mechanisms. Three of those are presented in Figure 10.

The main mechanisms (the 1st and 2nd mechanism) inducing antibacterial resistance are encoded by plasmids. Plasmids are circular, double stranded DNA molecules including, among other elements, beneficial genetic information that improves the survival of bacteria. This genetic material is transmissible to other bacteria. Expression or suppression of a specific gene *in vivo* can lead to resistance to antibiotics by promoting or inhibiting the production of specific enzymes (Fluit et al., 2001). For instance, for inducing resistance, an enzyme is required that is able to inactivate or degrade the antimicrobial agent by molecular scissioning through hydrolase or other processes (Figure 10, orange pellets, 1st mechanism). In addition, resistance to antibacterial drugs can be prompted by the induction of specific enzymes that are able to either modify and inactivate the antibiotic agent or that inhibit the antimicrobial agent's target receptor (Figure 10, green pellets, 2nd mechanism; Stewart and Costerton, 2001).

Moreover, through changes or inhibition of the bacterial plasma membrane permeability, according to changes in the pore channels or membrane structure, the uptake of antibiotics can be reduced. In addition, antibiotics can be actively pumped out of the cell by transport proteins or so-called efflux pumps (Fluit et al., 2001; Schaechter, 2009; Küster et al., 2013; 3rd mechanism).

In low-income countries, the increased emergence of the resistance of *Salmonella enterica*, subspecies *enterica*, serotype Typhi to the antibacterial agents ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole poses a risk to human health. This formation of multidrug-resistant typhoid strains is causing increased outbreaks of typhus especially in regions where there are no appropriate health care systems and where newer and more expensive antibiotics are less available (Okeke et al., 2005b). The resistance of *Staphylococcus aureus* to vancomycin and methicillin is another prominent example of the antibiotic resistance of bacteria in the medical sector (Sieradzki et al., 1999). Several known antibiotic-resistant zoonotic bacteria that have the potency to transfer infectious diseases from animals to humans and hence pose risks to human health are shown in Table 3 (Kemper, 2008).

Table 3: Resistances in zoonotic bacteria (Kemper, 2008)

Species	Clinical disease in humans	Possible resistance against	Literature
Escherichia coli	Diarrhea, urinary tract infections, septicemia	ß-Lactams Tetracyclines Streptomycin/ spectinomycin Sulfonamides Cimethoprim Chinolones Chloramphenicoles Gentamycin/Kanamycin/ Neomycin	Angulo et al., 2004; Helmuth et al., 2004
Salmonella spp.	Diarrhea	ß-Lactams Tetracyclines Streptomycin/ Spectinomycin Sulfonamides Cimethoprim Chinolones Chloramphenicole Gentamycin/Kanamycin/ Neomycin	Angulo et al., 2004; Hensel and Helmuth, 2005; Davis et al., 2007
Campylobacter spp.	Diarrhea, neural damage as a sequel	Ciprofloxacin Tetracyclines Doxycycline Erythromycin Trimethoprim Sulfamethoxazole	Luber et al., 2003; Angulo et al., 2004; Bae et al., 2005; Senok et al., 2007

C) Antiviral drugs

Oseltamivir, acyclovir, stavudin, and zidovudine are commonly used antiviral agents. Oseltamivir is the main antiviral agent for the treatment and prophylaxis of pandemic influenzas. Acyclovir is broadly used against herpes simplex virus infections and in the treatment of chickenpox. Another field of application of antiviral drugs is as agents used for the treatment of human immunodeficiency virus (HIV). At present, HIV- affected people are treated mainly with a triple combination antiretroviral therapy – highly active antiretroviral therapy (HAART) – by using a mixture of three antiretroviral classes, like protease inhibitors, non-nucleoside reverse transcriptase inhibitors, and nucleoside reverse transcriptase inhibitors (NRTIs). With the help of these mixtures, it is possible to successfully suppress viral replication for long periods and to reduce the potential for the formation of resistant strains (Baggaley et al., 2010; Wu and Musto, 2011).

Consumption

Reliable data about the production and consumption of antiviral drugs that are used to control and treat pandemic influenzas, such as pig and bird flu and other viral diseases, are not available. In low- and middle-income countries, HIV, which is transmitted through unprotected sexual intercourse or the transfusion of contaminated blood and the sharing of contaminated needles, syringes, or other sharp instruments, is still one of the most dangerous and incurable viral diseases. WHO estimates that worldwide there are about 37 million people living with HIV infections, with approximately 95% of these living in low- and middle-income countries (World Health Organization, 2008, 2015b; Baggaley et al., 2010). Of these, about one-third (9.7 million people) have access to antiretroviral therapy and 1.6 million people are dying anually (World Health Organization, 2015b; United Nations Programme on HIV/AIDS (UNAIDS, 2013). In comparison, in 2009, it was documented that the pandemic influenza H1N1 caused about 12,500 deaths in the US (Shresta et al., 2011). The supply of antiretroviral drugs, especially in low- and middle-income countries, is very important and necessary. Nevertheless, the formation of antiviral drug-resistant strains can pose problems of high concern for the health of humans and other animals. Therefore, more investigation of the development of drug-resistant virus strains is required.

Environmental behavior and occurrence

To date, the environmental behavior and occurrence of antiviral drugs has not been studied sufficiently and controversial information about the degradation of these drugs in WWTPs and in the environment can be found. For instance, there are environmental concerns raised regarding the API oseltamivir, which is used for the treatment and prevention of pandemic influenza.

There is evidence that oseltamivir and its stable metabolites, such as oseltamivir carboxylate, are hardly degradable in normal WWTPs and that it is not degraded substantially by ultraviolet light radiation (Fick et al., 2007; Singer et al., 2007). Thus oseltamivir seems to be quite persistent in the environment and it seems to be hardly removable from water systems even through wastewater treatment. Its physicochemical properties include high water solubility and it is not volatile as are most pharmaceuticals, but there is evidence that it can be slightly adsorbed by suspended particles, soils, or organic matter (Kümmerer, 2008; Straub, 2009). This persistence might lead to a release and an enrichment of oseltamivir in aquatic environments and favor the formation of drug-resistant virus strains in the environment (Fick et al., 2007; Singer et al., 2007).

The major concern regarding exposure to antivirals is the emergence of drug-resistant viral strains.

In German surface waters, for example, oseltamivir can be found at concentrations ranging from 0.1 to 1 µg/L (Fick et al., 2007; Kümmerer, 2008). There is evidence that this API is probably not as persistent in surface water as was suspected by Singer et al. (2007) and Fick et al. (2007). Straub (2009) and Bartels and von Tümpling Jr, (2008) revealed that in surface water oseltamivir can be degraded through a combination of indirect photolysis and a microorganism-induced biodegradation. There is evidence for the primary biodegradation of oseltamivir in sediments as well.

In addition, according to a monitoring study investigating the occurrence of antivirals in WWTP effluents and river waters in Germany, oseltamivir and other antivirals, such as acyclovir, abacavir, lamivudine, nevirapine, peniciclovir, ribavirin, stavudine, and zidovudine, were found in raw wastewater as well. Abacavir, acyclovir, lamivudine, peniciclovir, and stavudine concentrations were significantly reduced following wastewater treatment. However, this study did not investigate whether these compounds are degraded biologically by microorganisms or physically removed by adsorption to fecal sludge. In contrast, nevirapine, zidovudine, oseltamivir, and oseltamivir carboxylate concentrations stayed relatively constant, showing similar concentrations in raw wastewater influents and the effluents of WWTPs. So for the latter antivirals, bacterial biodegradation and/or adsorption to fecal sludge seems to be negligible. In river water from Hessian Ried, Germany, maximum concentrations of 0.19 µg/L for acyclovir and 0.17 µg/L for zidovudine were detected (Prasse et al., 2010). In general, knowledge of the environmental behavior, such as the photolytic and biological degradation of antiviral drugs used to treat influenza infections or immune deficiency diseases, are rare. In low- and middle-income countries there is a complete lack of information about the environmental concentrations of antivirals.

Toxicity

To date, the environmental impacts of antivirals on water organisms and aquatic ecosystems have not been comprehensively studied. However, for the API oseltamivir ethylester phosphate, which is available commercially as Tamiflu®, it has been shown that only surface water concentrations at mg/L levels can adversely affect the growth of algae after 96 hours of exposure (*Pseudokirchneriella subcapitata*) and the health of daphnia (*D. magna*) after 48 hours of exposure. A chronic daphnia (*D. magna*) reproduction test of 21 days and a fish early life stage test with *Danio rerio* of 32 days revealed that no toxic effects were observed at the highest tested concentrations (1 mg/L) of oseltamivir ethylester phosphate. Nevertheless, the chronic predicted no-effect concentration of this compound to *D. magna* and *D. rerio* of 0.1 mg/L was investigated (Straub, 2009). There are no proposals yet from the Ecotox Centre for testing other antiviral drugs (Ecotox Centre, 2015), but the chronic environmental standards (AA-EQS) for aquatic environments for the antivirals ribavirin, abacavir, and oseltamivir of 119, 95 and 100 µg/L have been investigated (Straub, 2009; FASS Vårdpersonal, 2014).

The major concern regarding exposure to antivirals is the emergence of drug-resistant viral strains. For example, HIV can replicate very quickly and it has specific mechanisms that are vulnerable to a high rate of mutation. The enzyme responsible for the replication of genetic information in HIV lacks a proofreading mechanism and, in addition, the virus can evolve and recombine at a high rate. These are the reasons why HIV achieves its considerable genetic diversity that enables the formation of strains resistant to antiretrovirals (Baggaley et al., 2010). In addition, the development of resistance to antiviral drugs in general is fostered in regions where there is widespread and unregulated access to antiretroviral medicaments. This is the case in sub-Saharan Africa and other regions that are characterized by war, extreme poverty, and inadequate infrastructure (Harries et al., 2001). Some empirically investigated instances of antiretroviral resistance in several low- and middle-income countries, categorized by drug class and country, are presented in Table 4 (Baggaley et al., 2010). According to this data, the highest resistance to the NRTIs – 11.6 or 12% – was observed in Africa and Thailand. In industrial countries, the occurrence and transmission of antiretroviral drug- resistant virus strains have become a major challenge as well. According to the study of Richman et al. (2004), conducted in the USA, it was estimated that 10 years after access to antiretroviral drugs 76% of the HIV-infected patients carried HIV strains resistant to one or more antiretroviral drugs.

Table 4: Abundance of antiretroviral resistance in low- and middle-income countries (Baggaley et al., 2010)

Region, country	Study	NRTI [%]	PI (primary mutations) [%]	NNRTI [%]
Asia				
India	Hira et al., 2004	6.5	2.5	NI
Korea	Chin et al., 2006	3.8	NI	3.8
China	Jiang et al., 2006	4.2		0
Thailand	Sukasem et al., 2007	12.4	0	0
Africa				
Nigeria	Ojesina et al., 2006	17	NI	NI
Mozambique	Parreira et al., 2006	11.6	NI	NI
Madagascar	Razafindratsimandresy et al., 2006	0	3.5	NI
Burkina Faso	Tebit et al., 2006	2.4	0	4.8
Ethiopia	Kassu et al., 2007	1.1	0	2.2
Latin America				
Brazil	Brindeiro et al., 2003	2.4	2.2	2.1
Argentina	Dilernia et al., 2007	1.4	1.4	2.1
Mexico	Viani et al., 2007	2.5	0	2.5
Russia and Eastern Europe				
Slovenia	Babič et al., 2006	3.9	0	0

NI = no information; NNRTI = non-nucleoside reverse transcriptase inhibitor (antiviral drug Class I);
NRTI = nucleoside reverse transcriptase inhibitor (antiviral drug Class II); PI = protease inhibitor (antiviral drug Class III).

D) Beta-blockers

Betaxolol, carazolol, atenolol metoprolol, propranolol, and nadolol are common beta-blockers that are used worldwide.

Consumption

In general, beta-blockers are used to lower blood pressure for the treatment of hypertension and to prevent further attacks in patients who have suffered from heart attacks. Beta-blockers are competitive inhibitors of the beta-adrenergic receptors. The adrenergic system regulates several physiological functions. For example, it controls oxygen need and beating of the heart and it regulates the vasodilatation mechanisms of blood vessels and bronchodilation (Fent et al., 2006). In general, an increase in cardiovascular disease (CVD) burden is expected even in low- and middle-income countries that will stimulate the production and consumption of beta-blocker as well. In 2012, 17.5 million people died from CVDs worldwide and over three quarters of these deaths took place in low- and middle-income countries (World Health Organization, 2015a).

Environmental behavior and occurrence

It has been observed that beta-blockers, especially atenolol (Fent et al., 2006; Etter et al., 2015; Ecotox Centre, 2015), metoprolol (Fent et al., 2006; Bergmann et al., 2011; Ecotox Centre, 2015), propranolol (Fent et al., 2006; Bergmann et al., 2011), and nadolol (Bergmann et al., 2011), have the potential to accumulate in the environment, posing a risk to environmental health. Although beta-blocker have lipophilic characteristics – they should be able to pass the blood-brain barrier (Fent et al., 2006) – and the excretion rate of unchanged metoprolol and propranolol is quite low (not exceeding 10%; Ternes, 1998), these beta-blockers can be found in surface waters. For example, the metabolite of atenolol, atenolol acid, was found in urine samples in Durban, South Africa at concentrations ranging from 280 to 360 µg/L (unpublished data). In addition, effluents from a treatment plant that is connected to the effluents from around 90 bulk drug manufacturers in Hyderabad, India, showed an alarmingly high concentration of metoprolol of between 800 and 950 µg/L, which is an environmental risk level (Larsson et al., 2007). In hospital effluents from the Hangzhou metropolitan area and Linan County, southeast China, atenolol concentrations ranging from 0.05 to 0.3 µg/L were measured. The environmental concentration in the Qiantang River was determined to be below 0.02 µg/L (Chen et al., 2012).

In German surface water, maximum concentrations of propranolol, bisoprolol, and metoprolol of 0.59, 2.9, and 2.2 µg/L, respectively, were detected. Betaxolol and carazolol were found at lower levels of 0.028 µg/L and 0.11 µg/L (Ternes, 1998). In the Lyon area, France, comparable concentrations of bisoprolol, metoprolol, and propranolol of from 0.05 to 2.94 µg/L were measured as well (Miège et al., 2006).

Toxicity

The acute eco-toxicological effects of beta-blockers have not been extensively studied yet except for propranolol, which is observed to be the most toxic beta-blocker. The exposure of *Ceriodaphnia dubia* and *Daphnia magna* to propranolol showed EC50 (48 hour) values of 0.8 and 1.6 mg/L (Huggett et al., 2002; Ferrari et al., 2004), among phytoplankton. The EC50 (96 hour) of the cyanobacteria *Synechococcus leopolensis* was 668 µg/L (Ferrari et al., 2004). According to the data obtained, zoo- and phytoplankton seemed to be more sensitive to beta-blockers than benthos and fish (Fent et al., 2006). However, a chronic exposure of beta-blockers can cause impairments of reproduction and toxic effects to water organisms at environmentally relevant concentrations. For example, long-term exposure to 100 µg/L and 250 µg/L of propranolol caused significant impairments in reproduction to *Hyalella azteca* and *Ceriodaphnia dubia* (Huggett et al., 2002). To arrive at a conclusion about the eco-toxicity of beta-blockers is not yet possible as there is insufficient information, but their negative impact on environmental health is not negligible. According to the quality standards of the Ecotox Centre (2015), even concentrations of propranolol, metoprolol, and atenolol of about 12, 76, and 330µg/L, respectively, are posing acute risks to aquatic organisms given their proposed MAC-EQS values. Their chronic environmental standards (AA-EQS) are 0.16 µg/L, 64 µg/L, and 150 µg/L, respectively (Ecotox Centre, 2015).

E) Hormone preparations and oral contraceptives

Estrone (E_1), 17-beta-estradiole (E_2), and 17-alpha-ethinylestradiole (EE_2), used directly as active compounds or as the metabolized products of the prodrug mestranol by demethylation, belong to the most frequently found and reported hormone compounds in monitoring studies (Sumpter and Jobling, 1995; Ternes et al., 1999; Duong et al., 2010; Chávez et al., 2011; Ernst et al., 2012).

Consumption

Usually, hormone preparations and contraceptives are prescribed and broadly used as oral contraceptives. In some regions, they may be used as steroids to promote reproduction in or growth of livestock, as well (Fan et al., 2007). Global consumption data for these oral contraceptives has not been determined.

Environmental behavior and occurrence

Because of their occurrence in water samples and their high bioactive potential – they act as endocrine disruptors at concentrations of ng/L (Purdom et al., 1994) – these compounds have received noticeable public attention. Because of that they are partially measured and quantified in water systems, even in low- and middle-income countries. For instance, in influents of an activated sludge wastewater works in Darvill, Pietermaritzburg, South Africa, environmental concentrations (arithmetic mean values) of 84 ng E_1/L, 119 ng E_2/L, and 30 ng EE_2/L were measured. In effluents of a wastewater works in Darvill, concentrations of 23 ng E_1/L, 20 ng E_2/L, and 3 ng EE_2/L were measured. In the Umsunduzi River downstream of this wastewater works, concentrations of 8 ng E_1/L, 10 ng E_2/L, and 2 ng EE_2/L were found. Therefore, within this wastewater works, 72 ± 12% ng of E1, 78 ± 12% ng of E_2. and 90 ± 3% ng of EE_2 were eliminated, mainly through biodegradation, but partly through adsorption processes onto sludge particles (Silva et al., 2012; Manickum and John, 2014). Further investigations in the Tula Valley, Mexico, showed environmental concentrations of E_1 ranging from 10.3 to 77 ng/L and of E_2 from 0.2 to 13.1; the concentrations of EE_2 were below the limit of detection (Chávez et al., 2011). In influents of a Brazilian sewage water treatment plant in Penha, Rio de Janeiro, 40 ng E_1/L and 21 ng/L of and E_2 were determined. Of these, 67 to 83% of E_1 and 92 to 99.9% of E_2 were eliminated through the wastewater treatment (Ternes et al., 1999). In wastewater effluents of WWTPs in Italy and Canada, average concentrations of 9 and 3 ng/L of E_1 were measured, respectively. The E_2 concentration in the WWTP effluents in Italy was 1 ng/L and in Canada, 6 ng/L. An EE_2 concentration of 0.45 ng/L was found in the Italian WWTP effluents while in the Canadian ones it was 9 ng/L (Ying et al., 2002).

Although these oral contraceptives were found in water samples, according to their physicochemical properties they have the potential to adsorb to organic material and particles and for bioaccumulation as well. E_1, E_2, and EE_2 have relatively high log K_{ow} values of 3.42, 3.94, and 4.15, indicating their potential to bind to organic matter (Lai et al., 2000). For example, concentrations of E_1 of 0.17 ng/g, of E_2 ranging from 0.22 to 2.48 ng/g, and of EE_2 ranging from 0.05 to 0.5 ng/g have been found in ocean sediments (Braga et al., 2005).

Toxicity

Within of the scope of the monitoring study of the IWW (Bergmann et al., 2011), EE_2 and E_2 are assigned to the list of high priority substances posing high risks to water organisms because of their high potential as endocrine disruptors (Purdom et al., 1994; Schultz et al., 2003).

These endocrine disruptors are well-known for reducing the fertility and causing feminization of males (Purdom et al., 1994). For example, after treating male rainbow trout with EE_2 concentrations of 10 and 100 ng EE_2/L, embryonic development was impaired by 50% if the sperm of the treated fish was used to fertilize the eggs of untreated rainbow trout. In addition, 1000 ng EE_2/L was deadly for all the test organisms (Schultz et al., 2003). In addition, the laboratory studies of Purdom et al. indicated that low concentrations, of up to 1 ng/L, of EE_2 are able to provoke feminization in male rainbow trout (Purdom et al., 1994). Converse results were found for mollusks. For example, Jobling et al. (2003) found that a 63 day exposure of *Potamopyrgus antipodarum* to about 25 ng EE_2/L stimulated embryo production, while concentrations of about 100 ng/L resulted in inhibiting this stimulation. For *Pimephales promelas*, embryo production was stimulated after the fish was exposed to a concentration of 1 ng EE_2/L and up for 3 weeks. However, exposure to concentrations of 100 ng/L caused spawning to cease. These alterations in reproduction relating to exposure to endocrine disruptive pharmaceuticals are mainly observed in vertebrates and mollusks. They are caused by the disruptors binding to and activating the estrogen receptors (Jobling et al., 2003; Schultz et al., 2003). Additionally, according to the quality values of the Ecotox Centre, chronic exposure to EE_2 of greater than 0.04 ng/L, to E_2 of greater than 0.4 ng/L, and to E_1 of greater than 3.6 ng/L will cause adverse effects to water organisms (Ecotox Centre, 2015).

F) Lipid regulators

The active metabolite clofibrate acid, formed by the transformation of the prodrugs etofibrate, etofyllin clofibrate, and clofibrate, and the active metabolites of the lipid regulators fenofibrate, bezafibrate, and gemifibrozil are found in wastewater, surface water and ground water samples (Fent et al., 2006; Vulliet and Cren-Olivé, 2011).

Consumption

Lipid regulators are applied to reduce cholesterol concentrations in blood plasma. They can be divided into two groups, statins and fibrates. Statins reduce cholesterol synthesis by inhibiting the 3-hydroxymethylglutaril coenzyme A (HMG-CoA) reductase. This decrease in intracellular cholesterol induces the expression of low-density-lipoprotein and consequently leads to resorption of LDL-cholesterol from the blood plasma (Laufs and Liao, 1998). Fibrates are used to decrease the concentrations of cholesterol and triglycerides in blood and they are observed to show anti-inflammatory effects as well (Staels et al., 1998; Fruchart et al., 1999). It is the fibrates that are of particular environmental concern.

Environmental behavior and occurrence

In the surface waters of 18 Brazilian rivers in Rio de Janeiro state, the main metabolites, fenofibric acid and clofibric acid, of the prodrugs fenofibrate, clofibrate, etofibrate, etofyllin clofibrate, and bezafibrate were measured at concentrations of from 0.09 to 0.35 µg/L (Stumpf et al., 1999). Lipid regulators are difficult to remove from wastewater. For instance, with wastewater treatment, from 34 to 51% of clofibric acid and from 46 to 69% of gemifibrozil can be eliminated, thus they have a potential to enrich aquatic environments (Petrovič et al., 2003). In German surface waters, the maximum measured environmental concentration (MEC_{max}) of bezafibrate was above 1 µg/L and the main metabolite (clofibrine acid) of the prodrugs etofibrate, etofyllin clofibrate, and clofibrate was found to be present at a similar level. The $MECs_{max}$ of mecfenobrate and gemifibrozil were likewise measured at the 0.1 µg/L level in German rivers (Bergmann et al., 2011).

Toxicity

In general, data about the toxicity of these lipid regulators are rare. According to the data that were available, the lipid regulator clofibrate seems to show LC_{50} values of from 7.7 to 39.7 mg/L. The fish *Gambusia holbrooki* was affected (LC_{50}) after a 96 hour exposure to 7.7 mg/L of clofibrate (Nunes et al., 2004). According to a water monitoring program for pharmaceuticals in Germany, bezafibrate, a substance classified as having moderate toxic potential for aquatic environments (Bergmann et al., 2011), was found in surface waters with a MEC_{max} above 1 µg/L. The main metabolite (clofibrine acid) of the prodrugs etofibrate, etofyllin clofibrate, and clofibrate was found at similar levels. The $MECs_{max}$ of mecfenobrate and gemifibrozil of 0.1 µg/L were observed in German rivers (Bergmann et al., 2011). Although data about the toxicity of lipid regulators are rare, the proposed acute and chronic quality criteria values of the Ecotox Centre (2015), the MAC-EQS and AA-EQS, of bezafibrate are available. These values indicate that acute exposure to 76 µg/L and chronic exposure to 0.46 µg/L can cause significant adverse effects in water organisms.

G) Sedatives and antidepressants

Venlafaxin, fluoxetine, fluvoxamine, imipramine, and amitriptyline are commonly used antidepressants.

Consumption

Although there is a lack of information about the supply of antidepressants and the treatment of mental disorders in low- and middle-income countries, the amount used for the treatment of neuropsychiatric disorders will increase over time. This is especially so as there are cheaper generic sedatives and antidepressants now available in low- and middle-income countries, so availability and consumption in these countries will rise as well (Patel, 2007). Patel (2007) showed that mental disorders account for 11 % of all the diseases occurring in low- and middle-income countries. The antidepressant fluoxetine, which was found in the environment, is showing its effect by inhibiting the re-uptake of serotonin. As a result of this inhibition, the serotonin level in the pre-synaptic nerve cleft is increasing, causing a reduction of depression (Fent et al., 2006).

Environmental behavior and occurrence

Even in industrial countries, the occurrence of these pharmaceuticals has not been well studied and there is a lack of data about their eco-toxicological relevance and their potential for geo- and bioaccumulation (Brooks et al., 2003).

In low- and middle-income countries, there is even less data available about the environmental concentrations of antidepressants than there is in high-income countries. The effluents of the huge drug manufacturing area in Patancheru, India, (a major production site of generic drugs) contained the globally highest ever measured amounts of pharmaceuticals (the antibiotic-fluoroquinolone) in industrial effluents – up to 31,000 µg/L (Larsson et al., 2007). There, the antidepressant agent citalopram was measured at concentrations ranging from 770 to 840 µg/L. As a result, it has to be considered that drug factories, especially in low- and middle-income countries, can act as relevant pollution sources for pharmaceuticals as well.

In the context of the IWW water monitoring study of German water systems (Bergmann et al., 2011), no measured environmental concentrations were available for several antidepressant agents, such as alprazolam, amitriptyline, citalopram, fluvoxamine, imipramine, etc. Fluoxetine is one of the most commonly used and investigated antidepressants (Reddy et al., 2007). A concentration of 0.0012 µg/L was detected in river water in the USA (Kolpin et al., 2002) and a concentration of 0.099 µg/L was found in river water in Canada (Metcalfe et al., 2003).

Toxicity

It has been found that these selective serotonin re-uptake inhibitors can elicit endocrine effects in vertebrates as well as invertebrates. Studies with zebrafish showed adverse effects on egg viability at test concentrations of the antidepressant mianserin of 250 µg/L after an exposure of 14 days (van der Ven et al., 2006). With invertebrates, fluvoxamine showed contrary effects. For instance, fluvoxamine at concentrations about 0.032 µg/L, lead to a stimulation of spawning in zebra mussels (Fong, 1998). Furthermore, for some organisms fluoxetine seems to be highly acutely toxic; the EC50 values of a concentration of fluoxetine of 24 µg/L for algae was observed by Brooks et al. (2003). According to the proposed chronic environmental quality standards (AA-EQS), the long-term environmental concentration of the sedative fluoxetine should not exceed 0.012 µg/L (Umweltbundesamt, 2012), that for fluvoxamine should not exceed 0.1 µg/L (FASS Vårdpersonal, 2014), and that for venlafaxine should not exceed 4.8 µg/L (FASS Vårdpersonal, 2014).

H) Anticonvulsants

Carbamazepine, diazepam, and promidone are anti-epileptic drugs that are found in the environment worldwide.

Consumption

In 2007, the following predicted sale volumes of carbamazepine in low- and middle-income countries were estimated: India, 115.5 tonne in total or 102 mg per capita; Brazil, 30.4 tonne in total or 160 mg per capita; Pakistan, 24.9 tonne in total or 151 mg per capita; Russia, 21.3 tonne in total or 151 mg per capita; South Africa, 16.2 tonne in total or 368 mg per capita; Egypt, 15.1 tonne in total or 188 mg per capita; Argentina, 11.8 tonne in total or 293 mg per capita; China, 11.8 tonne in total or 8.8 mg per capita; Hungary, 11.7 tonne in total or 1175 mg per capita; and Romania, 10.6 tonne in total or 476 mg per capita. In comparison, in high-income countries the figures were: Germany, 72 tonne in total or 874 mg per capita; UK, 51.2 tonne in total or 842 mg per capita; and France, 31.4 tonne in total of 493 mg per capita (Zhang and Geißen, 2010; Barzel, 2013). Anticonvulsants affect the central nervous system by lowering neuronal activity (Fent et al., 2006). The neuronal activity can be decreased by enhancing γ-aminobutyric acid (GABA)-ergic inhibition (diazepam), by blocking the neuronal and glial uptake of GABA, and by fostering an increase of the synaptic GABA concentration through inhibition of GABA-aminotransferase. It can also be decreased by inhibition of the voltage-dependent calcium ions into neurons (Czapinski et al., 2005; Fent et al., 2006).

Environmental behavior and occurrence

Carbamazepine is one of the most abundant pharmaceuticals found in the effluents of STPs or in surface water, although only 1 or 2% of carbamazepine is excreted unchanged by humans (Ternes, 1998; Ferrari et al., 2003). Nevertheless, carbamazepine occurs broadly in aquatic environments mainly because of its high water solubility (carbamazepine has a water solubility of 112 mg/L (Ferrari et al., 2003) while diazepam has a water solubility of 50 mg/L (Yalkowsky and Dannenfelser, 1992)) and its high resistance to biodegradation. For instance, even in STPs almost no elimination of this pharmaceutical is observed. Results show that sometimes the effluents of STPs contained even more carbamazepine than the influents. This can be explained by the transformation of carbamazepine glucuronides and other conjugates to the parent compound during the enzymatic processes during the wastewater treatment (Gros et al., 2010). Other data showed that less than 10% carbamazepine is eliminated in STPs (Zhang and Geißen, 2010).

In the Pearl River system in China, an MEC_{max} of 43.1 ng/L was found for carbamazepine (Zhao et al., 2010). In Indian river waters, the MEC_{max} of carbamazepine was 128 ng/L (Ramaswamy et al., 2011). In North America (Canada and the USA), the environmental average concentrations of carbamazepine ranged from 2.5 to 166 ng/L, and the MEC_{max} was 1500 ng/L (Cunningham et al., 2010). In Europe, the average carbamazepine concentrations of between 1.1 and 410 ng/L were identified in surface waters and the MEC_{max} was 7100 ng/L (Cunningham et al., 2010).

Toxicity

There is significant evidence that anti-epileptic agents can have adverse effects on water organisms. For instance, Pascoe et al. showed that a concentration of anti-epileptic agents of 0.010 mg/L inhibited polyp regeneration in the cnidarian *Hydra vulgaris* (Pascoe et al., 2003). However, for several other organisms the effect concentrations are outside the range of environmental concentrations. For instance, a motility test of *Daphnia magna* showed EC_{50} (48 hour) values of around 13.8 mg/L after exposure to carbamazepine (Ferrari et al., 2003). Some fish species seem to be relatively sensitive to carbamazepine. It was found that the LC_{50} (24 hour) for *Cyprinus carpio* was 50.70 mg/L (Malarvizhi et al., 2012). In rainbow trout and common carps, a concentration of carbamazepine of 1000 mg/L caused significant adverse effects to the liver, The malfunctions caused by exposure to the pharmaceuticals diclofenac and metoprolol were more pronounced than those caused by carbamazepine and clofibrate (Schwaiger et al., 2004). During a comprehensive sediment study, the midge *Chironomus riparius* was found to be very sensitive to carbamazepine showing EC_{10} values of 0.07–0.21 mg/kg dry weight. In contrast, other species, such as the oligochaete *Lumbriculus variegatus* and the freshwater snail *Potamopyrgus antipodarum*, were not affected at the tested concentrations (0.625–10 mg/kg dry weight *L. variegatus*; 0.4–250 mg/L *P. antipodarum*; Oetken et al., 2005). In summary, apart from some specific organisms, carbamazepine is characterized as low acute toxic to aquatic organisms (Oetken et al., 2005). Along these lines, the proposed acute environmental quality standard (MAC-EQS) of the Ecotox Centre for carbamazepine of 2.550 mg/L is relatively high (Ecotox Centre, 2015). Nevertheless, the exposure of aquatic ecosystems to carbamazepine in the long term can have adverse effects on water organisms as well and this is indicated by the low chronic environmental standard of 0.0005 mg/L.

I) Cytostatic cancer therapeutics

Cyclophosphamide, ifosfamide, methotrexate, cisplatin, 5-fluorouracil, etoposide, doxorubicin, and doxorubicinol are agents often used in the chemotherapy treatment of cancer. These therapeutics work by impairing cell proliferation, particularly of fast growing tumor cells (Fent et al., 2006; Matthies, 2008).

Consumption

Some cytostatics, such as cyclophosphamide and ifosfamide, reduce the growth and inhibit the division of tumor cells and other fast growing cells through the alkylation of DNA. According to the IMS Institute (IMS Institute for Healthcare Informatics, 2012), anticancer drugs lead the market with sales of US$83–88 billion. Since generics of several of these pharmaceuticals are available, the spending on medicines in the so-called 'pharmerging' countries (Russia, Brazil, China, and India) has increased. The IMS Institute (IMS Institute for Healthcare Informatics, 2012) has shown that of 22 new anticancer drugs, between 18% and 46% were available in China, India, Brazil, and Russia (ascending order of availability).

Environmental behavior and occurrence

In aquatic environmental samples, the cytostatics cyclophosfamide, ifosfamid, and methotrexate seem to be the most representative ones. Yin et al. (2010) conducted the first monitoring study of cytostatic drugs in hospital effluents in China (Beijing). They detected the highest concentrations of cyclophosfamide, ifosfamide, and methotrexate – ranging from 4 to 10,647 ng/L – with cyclophosfamide and ifosfamide being found most frequently. Methotrexate, etoposide, and azathioprine were less abundant at maximal measured concentrations of 4689, 380, and 38 ng/L, respectively. They are mostly found in the effluents of hospitals at low levels – between ng/L to µg/L. This was certainly the case in the effluents of German hospitals (Heberer, 2002). In the surface water of a lake in Switzerland, they were found at concentrations ranging from 0.05 to 0.17 ng/L. However, in general, there is a dearth of data about the occurrence of cytostatic agents, especially in surface waters or sediments (Heberer, 2002; Buerge et al., 2006; Zounková et al., 2007; Yin et al., 2010).

According to the investigations of Buerge et al. (2006), cytostatic drugs seem to have persistent characteristics. For example, under dark conditions the half-life of cyclophosphamide was 80 days and that of ifosfamide was 620 days. The transformation of cytostatics by photo-oxidation cannot be excluded, though this process seems to be relevant only in regions of clear, shallow water. Experiments with active sludge revealed that no transformation of cytostatics was observed within 24 hours at test concentrations of about 100 ng/L.

Toxicity

The concentrations measured in the aquatic environment are several orders of magnitude lower than the concentrations posing risk (showing acute toxic effects) to aquatic organisms (Yin et al., 2010). Although they are used as anticancer drugs to treat bronchial, breast, and ovarian cancer, lymphomas and leukemia or to treat auto-immune diseases, they are able to promote cancer at certain concentrations. They are well-known for their mutagenic and embryo-toxic characteristics and for inhibiting cell proliferation (Heberer, 2002; Buerge et al., 2006; Yin et al., 2010). For instance, exposure of the ciliate *Tetrahymena pyriformis* to methotrexate showed an EC_{50} (48 hour) value of 45 mg/L (Henschel et al., 1997). Disorders in fish embryo development were observed at concentrations around 85 mg/L (EC_{50}, 48 hour; Henschel et al., 1997). Zounková et al. (2007) conducted a comprehensive toxicity study using five cytostatics (cyclophosfamide, cisplatin, 5-fluorouracil, doxorubicin, and etoposide). They found that cisplatin and 5-fluorouracil were the most toxic to the bacteria *Pseudomonas putida* and the algae *Pseudokirchneriella subcapitata*, showing LOECs between 0.01 and 1 mg/L. Cyclophosfamide showed values of between 500 and 1000 mg/L (Zounková et al., 2007). Although the concentrations of the cytostatics found in the environment are lower than the concentrations that are causing adverse effects to water organisms, their occurrence and their impact on the environment and on water organism should not be ignored. The use of these agents is still increasing given the constant improvements in living standards and the increase in the number of cancer patients worldwide. These compounds are known to have high bioactive potential and we lack information about their chronic toxicity and the environmental distribution pattern of these agents (Buerge et al., 2006; Zounková et al., 2007; Yin et al., 2010). The chronic environmental standard found for the cytostatic cancer drug doxorubicin is 0.01 mg/L (FASS Vårdpersonal, 2014), that for ifosfamide is 2 mg/L (Bergmann et al., 2011), and that for cyclophosphamide is 20 mg/L (Bergmann et al., 2011).

J) X-ray contrast medium

Iopamidol, iobitridol, iomeprol, iopromide, iohexol, diatrizoate, and ioxithalamic acid are a selection of iodinated x-ray contrast media which are broadly used.

Consumption

These agents are used frequently and with high doses (up to 200 g per person (Steger-Hartmann et al., 1999) as diagnostic agents, especially in hospitals (for computed tomography or x-ray images and magnetic resonance imaging or radiological surgeries). These media improve the contrast between organs or vessels and tissues during x-ray radiography and facilitate visualization and observation of morphological alterations on organ tissues (Steger-Hartmann et al., 1999; Heberer, 2002; Bergmann et al., 2011; Ernst et al., 2012). These agents can be differentiated into ionic (diatrizoate, iothalamic acid, and ioxithalamic acid) and non-ionic (iopamidol, iopromide and iomeproll) contrast media (Ternes and Hirsch, 2000). In all countries with a developed health care system – mainly in emerging and developed countries – the residuals of x-ray contrast media can be found in wastewaters, effluents of STPs, surface water, and ground water.

Environmental behavior and occurrence

X-ray contrast media are specifically designed to be stable against chemical and biological degradation and, because of this, x-ray contrast media are not metabolized after uptake by humans. They are excreted as the parent compound, primarily in urine. This stability of the x-ray contrast media enables it to maintain the efficiency of the diagnostic analysis following application of the x-ray contrast media. Additionally, given their stability, the formation of toxic transformation products is avoided (Ternes and Hirsch, 2000; Kümmerer, 2009b).

Accordingly, these agents are negligibly, or not at all, degraded by bacterial processes or adsorbed to sewage sludge during wastewater treatment or when exposed in surface waters. This is because of their high persistence, high water solubility, and their low lipophilicity (for instance, iopromide has a K_{ow} of $4.7*10^{-3}$; Steger-Hartmann et al., 1999). It has been found in raw domestic wastewater in Atlanta, South Africa, that the maximal concentration of iopromide was 0.09 µg/L. In the VUNA project (Eawag: The Swiss Federal Institute of Aquatic Science and Technology and eThekwini Water and Sanitation (EWS), 2013) a concentration of 97 µg/L iobitridol was found in urine samples in Durban, South Africa. In Gaobeidian, China, effluents of a STP contained about 2 µg/L iopamidol (middle value), 1.5 µg/L diatrizoate, and about 0.2–0.3 µg/L iopromide and iohexol. Analogous values, with magnitudes of µg/L, were found in industrial countries such as Germany and Switzerland (Ternes and Hirsch, 2000; Buerge et al., 2006; Ernst et al., 2012). In addition, in WWTPs in Hesse, Germany, no degradation of x-ray contrast media was observed (Ternes and Hirsch, 2000). Because of that, x-ray contrast media are well-known for their high persistence in aquatic systems (Heberer, 2002; Kümmerer, 2008).

Toxicity

Steger-Hartmann et al. (1999) conducted a comprehensive study on the eco-toxicological behavior of the x-ray contrast medium iopromide. They discovered that iopromide presented no acute toxic effects to the bacteria *Vibrio fisheri*, *Pseudomonas putida*, the algae *Scenedesmus subspicatus*, the crustacean *Daphnia magna*, or the fish *Danio rerio* and *Leuciscus idus* at the highest test concentration of 1 g/L. In addition, *Daphnia magna* showed no chronic toxic effects after long-term exposure to 1 g iopromide/L. Toxicity tests with mammals, which were conducted during the development of the pharmaceutical iopromide, showed no adverse effects on reproduction or any genotoxic effect (Schöbel and Günzel, 1993). According to the environmental risk assessment study of Steger-Hartmann et al. (1999), x-ray contrast media, like iopromide, do not pose any risk to the aquatic environment. Given their high persistence, however, and the lack of knowledge of their ability to cause sublethal effects (Ternes and Hirsch, 2000), environmental assessments are still required. Nevertheless, the chronic environmental standard of 1000 µg/L for the x-ray contrast media iohexol (Bergmann et al., 2011) and iomeprol (FASS Vårdpersonal, 2014) have been proposed.

Input pathways of pharmaceuticals

The possible entry pathways of APIs are outlined in Figure 11. For example, APIs can be released into the environment directly at pharmaceutical production plants, mainly through the release of industrial wastewater effluents. The APIs of pharmaceuticals for veterinary purposes – to treat animal diseases or as food additives to promote growth at aquaculture farms (Cabello, 2006) or animal husbandries – can enter the environment via excretion (Sarmah et al., 2006). In addition, after human uptake, the excreted pharmaceuticals from private households or hospitals can enter the municipal wastewater system via urine or feces, with most of the APIs excreted unchanged (Holm et al., 1995; Hirsch et al., 1999; Duong et al., 2008; Kümmerer, 2009b). If industrial or municipal wastewaters are processed by STPs, the non-degradable APIs are released into the surface water (Gros et al., 2007; Togola and Budzinski, 2008; Voigt and Bruggemann, 2008; Ernst et al., 2012; Köck-Schulmeyer et al., 2013). If no WWTPs are available, which is more likely to be the case in low- and middle-income countries, all the APIs from these wastewaters are directly released into the surface water (Rehman et al., 2015). If sewage sludge or excreta from animals is used as manure in agriculture or the contaminated surface water is used for irrigation, which is often the case in low- and middle-income countries (Heeb et al., 2012; Rehman et al., 2015), APIs can further accumulate in the soil. Alternatively, they can enter surface waters as surface runoff after rain events or they can leach into groundwater aquifers (Rehman et al., 2015). If unused medicaments are flushed down the toilet (this pathway is not presented in Figure 11) they are released into the municipal wastewater system (Kümmerer, 2009b). If expired or unused pharmaceuticals are disposed of as domestic waste in landfills they could leach into groundwater systems as well (Holm et al., 1995; Heberer, 2002).

Given their persistence, their continuous consumption, and the large amounts used, many APIs have the potential to remain and to accumulate in the environment.

As a result, given their persistence (even after wastewater treatment), their continuous consumption, and the large amounts used, many APIs have the potential to remain and to accumulate in the environment (Gros et al., 2007; Togola and Budzinski, 2008; Voigt and Bruggemann, 2008; Zhang et al., 2008; Fatta-Kassinos et al., 2011; Ernst et al., 2012; Kirrolia and Nehra, 2012; Köck-Schulmeyer et al., 2013). In general, the excretion of pharmaceuticals by humans or other animals and the use of contaminated sewage sludge and feces of animals as manure are the main inputs of pharmaceuticals' into the environment. Pharmaceuticals' loads in industrial effluents can be very high as well. However, in general, industrial pollution is very local.

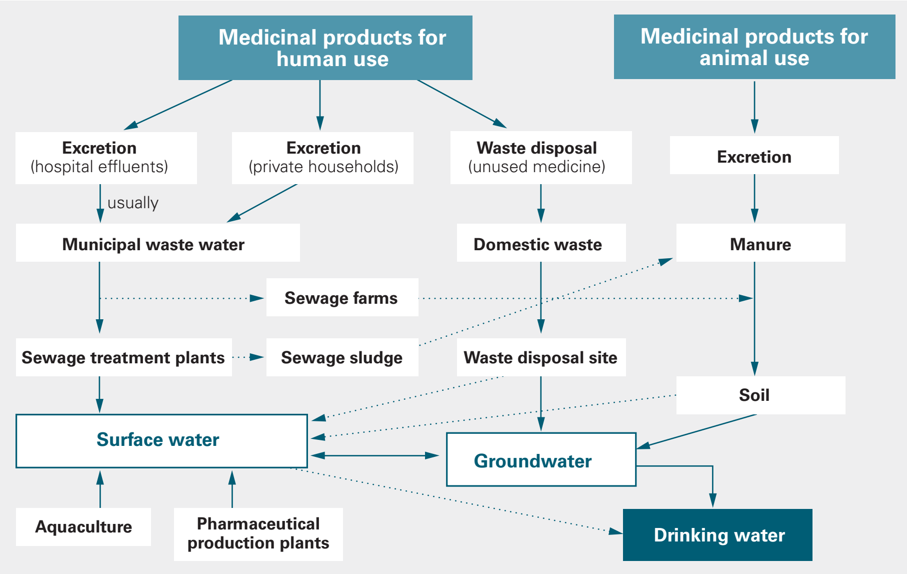


Figure 11: *Entry routes for human and veterinary pharmaceuticals into the aquatic environment (Heberer, 2002)*

Use of pharmaceuticals and pollution trends and impacts

Data availability

Currently, there is a scarcity of data about the production, sales, and consumption of pharmaceuticals. There are almost no comprehensive systematic data available, especially, for the non-OECD countries. Where such data about pharmaceuticals have been compiled using marketing survey studies and industry intelligence, mostly only the urban regions were covered and small-scale and retail enterprises were left out. In addition, there is a lack of transparency about these data and limited public access (Dickens, 2011). The Institute for Healthcare Informatics (IMS Institute), a leading pharmaceutical consulting company, and the consulting company PricewaterhouseCoopers AG (PWC) are focusing on collecting data about pharmaceuticals. They are endeavoring to forecast future behavior changes in pharmaceutical sales and production from a global perspective. But mostly these data are not publicly available or the data about specific pharmaceuticals has to be purchased (IMS Institute for Healthcare Informatics, 2012; PricewaterhouseCoopers, 2012).

Future trends and hot spots

The data introduced by PricewaterhouseCoopers (Figure 12; PricewaterhouseCoopers, 2012; and the IMS Institute (Figure 13) are in accordance with each other. Both are showing an increasing trend in global spending on pharmaceuticals. IMS Institute is showing an increase of from US$658 billion to $1,205 billion from 2006 to 2016, while PWC predicts an increase from US$1,084 billion in 2011 to US$1,571 billion in 2020. Both predict a declining trend for the spending in the EU, while the spending in Canada and Japan will remain almost constant in future. In addition, there will be increased spending on pharmaceuticals in the USA and, especially, in the pharmerging countries – China, Brazil, Russia, and India – and the fast followers – Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan, and Vietnam. According to the IMS Institute, pharmerging countries are defined as those with more than US$1 billion in absolute spending growth between 2012 and 2016 and with a gross domestic product per capita of less than $25,000 at purchasing power parity. These criteria essentially define low- and middle-income countries. Between 2011 and 2016, sales of pharmaceuticals in the pharmerging countries are calculated to increase from US$191 billion to US$362 billion, according to the IMS Institute data. The PWC data indicate a possible increase from

US$205 billion to US$500 billion between 2011 and 2020 (IMS Institute for Healthcare Informatics, 2012; PricewaterhouseCoopers, 2012). These increases in spending will arise for several reasons. Since the economic crisis of 2007, there has been a shift of the industry from high-income countries to low- and middle-income ones (United Nations Environment Programme, 2013c), which will lead to an increase in sales of pharmaceutical products in these countries. Furthermore, PWC and the IMS Institut forecast that the production of generics will increase extensively in pharmerging countries. This process will be stimulated given that the patents of several widely used pharmaceuticals are due to expire. Consequently, there will be a increased manufacture of, and spending on, cheaper generics taking place mainly in low- and middle-income countries. The IMS Institute showed that the increase in spending on pharmaceuticals in pharmerging countries is mainly the result of the increased production of generic drugs. Besides the shift of the pharmaceutical production and the added production of generics in low- and middle-income countries, demographic changes can have effects on the spending on medicines as well. For instance, the global extended life expectancy and the one-child policy in China are promoting the aging population phenomena, leading to an increase in the average age of a population, even in low- and middle-income countries. In addition, the increasing growth rate of the world's population, especially in low- and middle-income countries, will further increase the demand for pharmaceuticals worldwide (The World Bank Group, 2001). Moreover, the middle class will expand worldwide resulting in improved living standards, infrastructure, and development in general. The percentage of the population having an income ranging from US$6000 to US$30,000 purchasing power parity is predicted to further increase (PricewaterhouseCoopers, 2012). The conclusion to be drawn is that this increase in demand, improvement in living standards, and the enhanced production of pharmaceuticals in low- and middle-income countries will improve health care systems. These changes, in turn, will increase the availability of pharmaceuticals in these countries, which will lead to an intensification of the release of pharmaceuticals into the environment though production processes and excretion by humans or animals following their use (IMS Institute for Healthcare Informatics, 2012; PricewaterhouseCoopers, 2012).

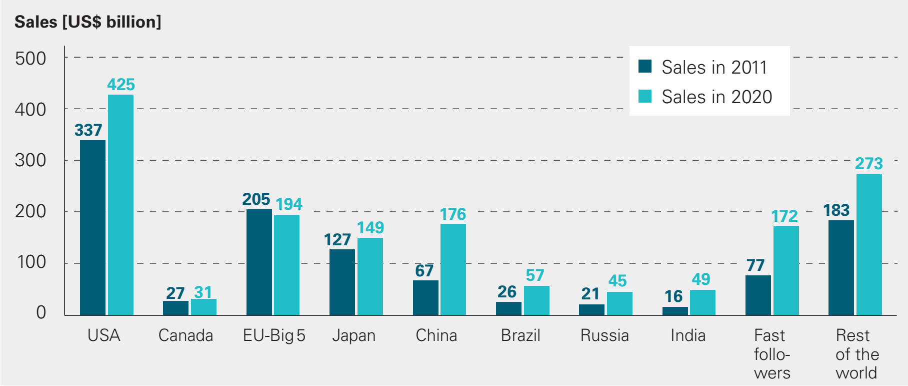


Figure 12: *Sales of pharmaceuticals in US$ billion at constant exchange rates in several countries (PricewaterhouseCoopers, 2012). Total sales in 2011 were US$1,084 billion and in 2020 are predicted to be US$1,571 billion. The EU Big 5 are France, Germany, Italy, Spain, and the UK. The fast followers include Argentina, Egypt, Indonesia, Mexico, Pakistan, Poland, Romania, South Africa, Thailand, Turkey, Ukraine, Venezuela and Vietnam.*

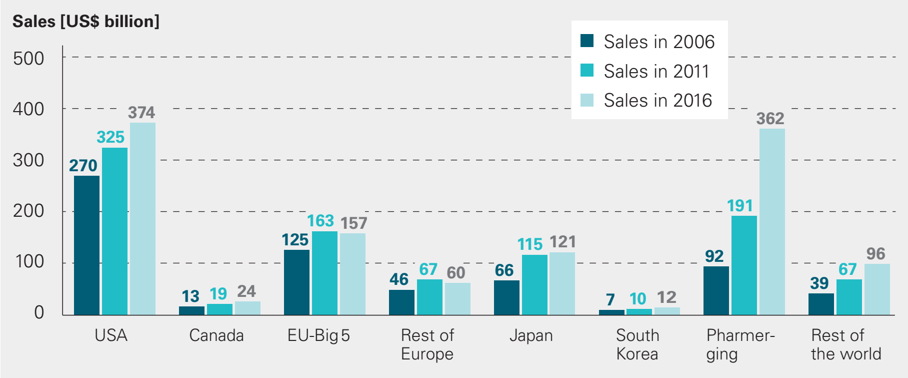


Figure 13: *Sales of pharmaceuticals in US$ billion with variable exchange rates in several countries (IMS Institute for Healthcare Informatics, 2012). Total sales in 2006 were US$658 billion, in 2011 US$956 billion, and in 2016 are predicted to be US$1,205 billion. The EU Big 5 are France, Germany, Italy, Spain and the UK. The pharmerging countries are China, Brazil, Russia, India, Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan, and Vietnam.*

Pharmaceuticals for veterinary treatment

Currently, there is almost no information available about the consumption patterns and amounts of pharmaceuticals – antibiotics, anti-inflammatory drugs, or steroids – used for animal treatment. Nowadays, the use of pharmaceuticals to treat diseases in animal husbandry and aqua-farming is inevitable (Sarmah et al., 2006). Each year, high volumes of these drugs are used in veterinary treatments, especially since these pharmaceuticals are relatively cheap. They are traded worldwide and many of these agents are available as generic drugs. Looking at the volume of chicken, cattle, and pig meat produced in each region may give some indirect insights about those regions where environmental and human health is endangered as a result of the increased exposure to veterinary pharmaceuticals. These agents are released through excretion into the environment without any treatment and leach and accumulate in soils and drinking water reservoirs. According to the data on meat production from FAOSTAT (Food and Agriculture Organization, 2013) and illustrated in Figure 14, the demand for veterinary pharmaceuticals in low- and middle-income countries is highest in China, followed by Brazil, Russia, Mexico, Argentina, Vietnam, and India (in descending order). By considering the tonnes of chicken, cattle, and pig meat produced per 1000 ha of arable land, which is shown in Figure 15, the highest meat production areas in low- and middle-income countries are Djibouti, Malaysia, Lebanon, St. Lucia, Jordan, Colombia, Costa Rica, Seychelles, Jamaica, Kiribati, Occupied Palestinian Territory, Ecuador, Dominican Republic, Samoa, and China (in descending order).

Given the high meat production, especially in these regions, continuous monitoring of the movement of veterinary drugs into the environmental compartments is strongly recommended. However, other regions may be adversely exposed to veterinary pharmaceuticals as well. This cannot be specified more precisely given the data available and with the resolution of the data obtained. One example where environmental health was endangered after exposure of the environment to veterinary pharmaceuticals occurred in two regions, in India and in Pakistan. There, the vulture population declined drastically because of renal failure caused by ingesting the carcasses of diclofenac-treated animals (Oaks et al., 2004).

Moreover, in a cooperative, interdisciplinary project involving the German Federal Environmental Agency, the IWW Water Centre and adelphi (Weber et al., 2014), worldwide data on the maximum environmental concentrations (MEC_{max}) measured were compiled. This

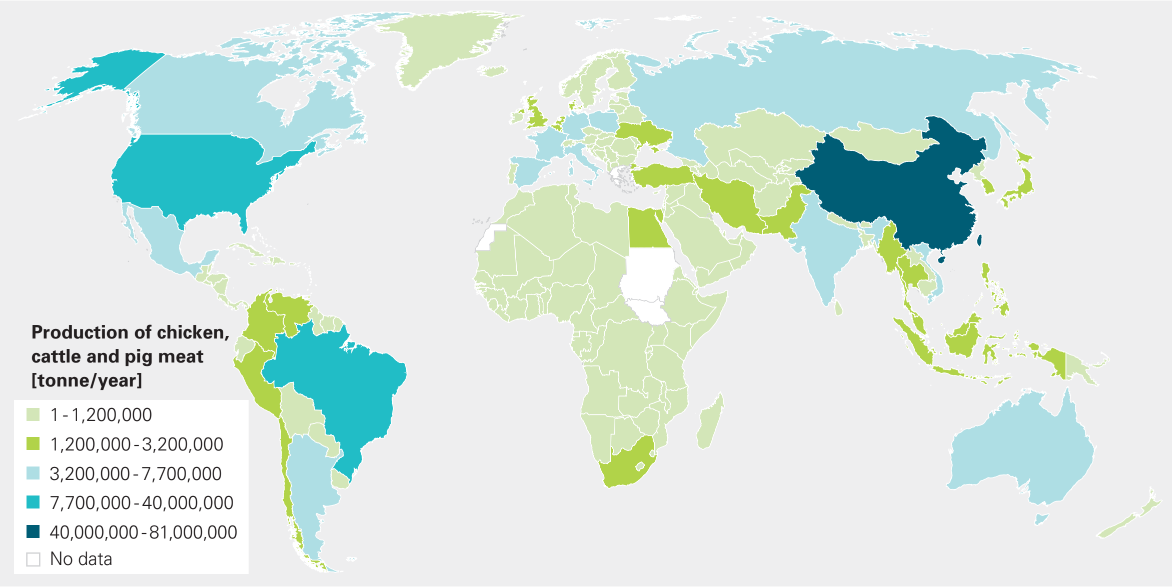


Figure 14: *Summary of the amount of chicken, cattle, and pig meat produced on average between 2006 and 2010. The range is from 1 to 81 million tonne of meat/year (Food and Agriculture Organization, 2013)*

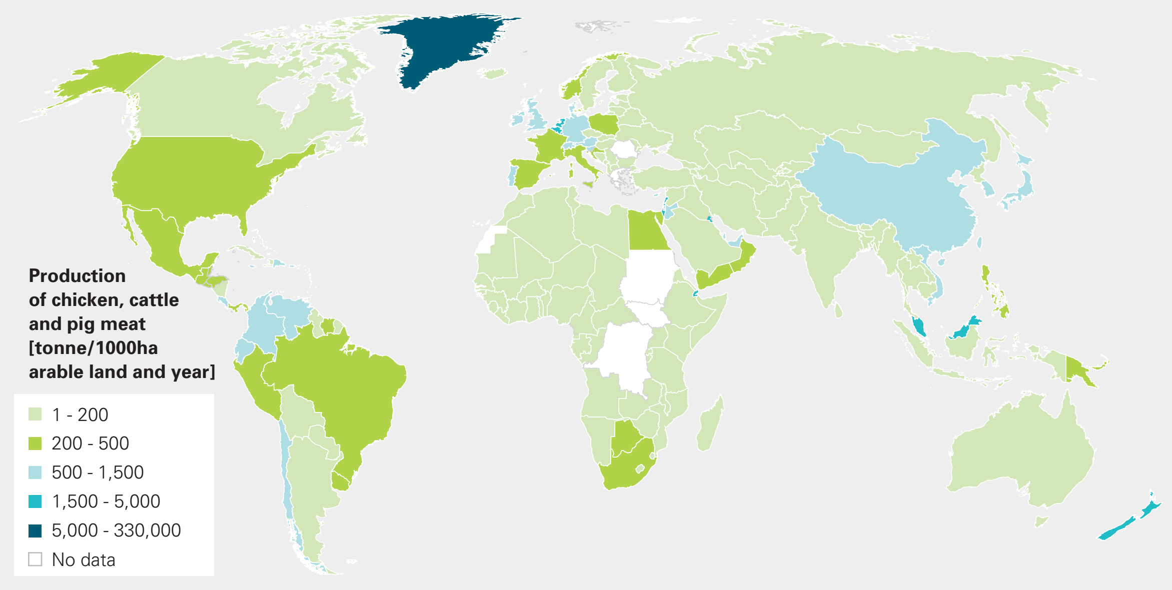


Figure 15: *Summary of the average amount of chicken, cattle, and pig meat produced per 1000 ha of arable land between 2006 and 2010. The range is from 1 to 33 thousand tonne of meat/1000 ha of arable land/year (Food and Agriculture Organization, 2013)*

was undertaken to indicate high risk areas where pharmaceuticals released into the environment may affect human and environmental health. One, not yet finished, example of a collection of measured environmental concentrations is shown in Figure 16 (Weber et al., 2014). According to previous data, the MECs_{max} of diclofenac were measured in low- and middle-income countries like Ukraine, Greece, Pakistan, and Côte d'Ivoire, where concentrations greater than 1 µg/L were detected. In Brazil, Costa Rica, South Africa, Jordan, China, and Malaysia, concentrations ranging from 0.1 to 1 µg/L were found. These values indicate that even in low- and middle-income countries the monitoring of environmental concentrations of pharmaceuticals is highly relevant. This monitoring is relevant, first because of the high concentrations found in these regions and second because of the lack of data on this issue, especially in low- and middle-income countries.

To get a better overview of the global distribution of pharmaceutical industries, the locations of pharmaceutical companies, associations, and pharmaceutical production places were identified using Google Maps and illustrated in Figure 17. These data, although they have to be treated with caution, indicate that high levels of activity are suspected in the low- and middle-income countries of north and west Latin America, west, east and south Africa, India, east and west China, and Indonesia.

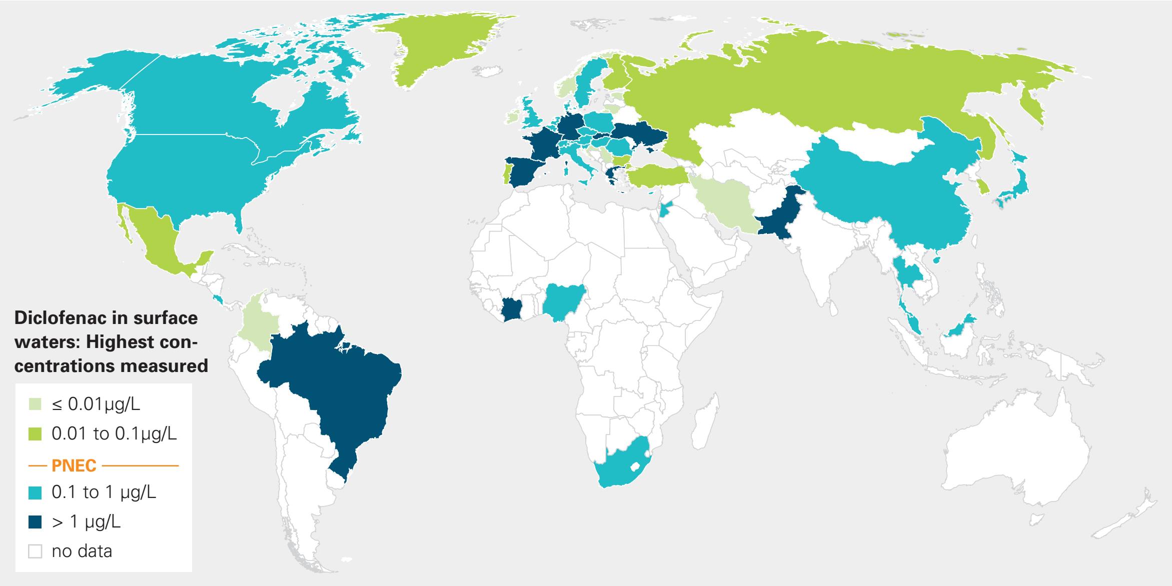


Figure 16: *Environmental concentrations of the analgesic diclofenac in different UN regions; (Weber et al., 2014)*

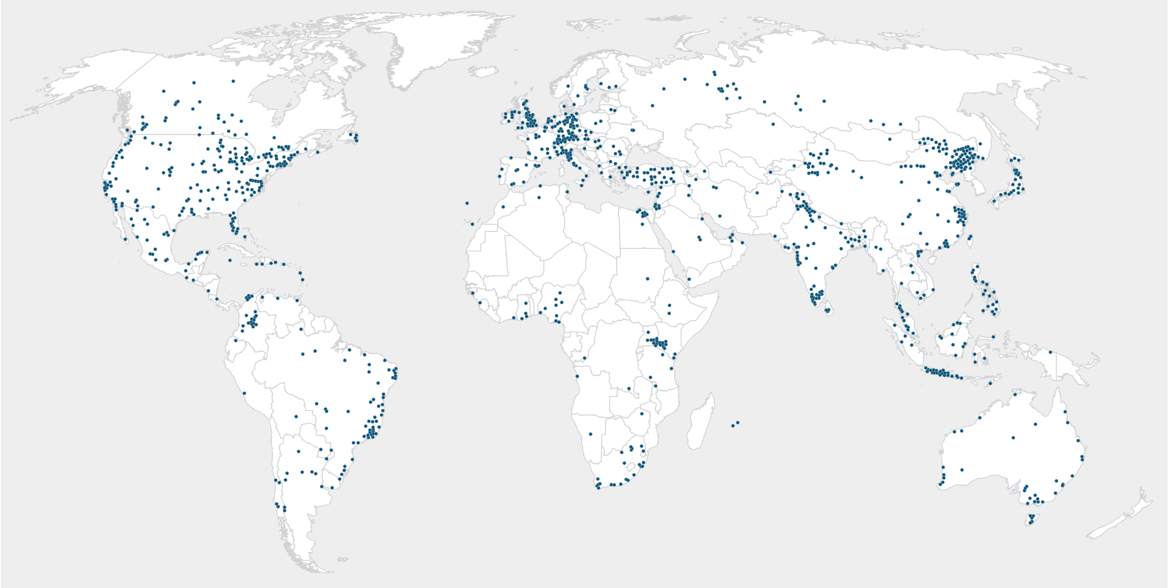


Figure 17: *Google map of places connected with pharmaceuticals and pharmaceutical companies*

Issues of special concern

In general, the excretion of pharmaceuticals used for the treatment of human and veterinary diseases is supposed to be the main pathway for the release of pharmaceuticals into the environment. However, it has to be considered that, especially in low- and middle-income countries the effluents of pharmaceutical manufactories can be relevant point sources of APIs. These latter also show the highest environmental concentrations worldwide. In these regions, there is little or no legislation for sound waste management. There are no regulations governing the maximum concentrations of APIs that are allowed to be present in the effluents of industries and WWTPs. There are no monitoring programs for checking the occurrence of APIs in drinking water and river systems. Often the inspections, if available, are failing and the use of sustainable and environmentally-friendly methods is not guaranteed. The legacies of obsolete, closed factories and the use of landfills for disposal pose risks to environmental and human health. If pharmaceuticals are produced for the global market, as in an example from Brazil, an internationally shared responsibility for producing more environmentally-friendly APIs is necessary.

Diclofenac endangers vulture population in India and Pakistan

As already mentioned in chapters above, one prime example where exposure to pharmaceuticals has had disastrous consequences to environmental health is presented in the Indian and Pakistani regions, where several vulture populations were endangered because of the anti-inflammatory agent diclofenac. Oaks et al. (2004) determined that the renal failure found in vultures was directly correlated with the diclofenac residues found in carcasses of veterinary treated livestock. This indicates that although most of the pharmaceuticals are supposed to be polar and, therefore, should be excreted easily from the body, some of them show the potential for bioaccumulation within the food web system. This results in an enrichment of these compounds per trophic level, posing risk to environmental health, especially to the end consumers of the food web, the raptors and other predators.

Pharmaceutical manufacturing in India

Another example is that pharmaceuticals are not only released into the environment primarily through the excreta of medically treated humans and animals but also by inappropriate disposal of expired medicines – by flushing them down the toilet. In addition, wastewater effluents of manufacturing plants can channel large volumes of pharmaceuticals into aquatic systems. APIs can leach into soils and water aquifers at dumping sites close to production facilities (Larsson, 2010). For instance, Larsson et al. (2007) investigated the effluents of the WWTP in Patancheru near Hyderabad, India. Patancheru Enviro Tech Ltd. (PETL) is posing a risk to environmental and human health. PETL is treating the waste of approximately 90 bulk drug manufacturers. Each day, about 150 trucks of wastewater are delivered to PETL representing a volume of about 1500 m^3. This WWTP is able to deplete about 77% of the organic material contained in the industrial wastewater (measured as the biological and chemical oxygen demands) and about 50% of the total dissolved solids and total suspended solids. The efficiency and the capacity of PETL is not high enough to treat the volume of wastewater received. Larsson et al. (2007) ranked the top 11 APIs found in the effluents of the WWTP. These effluents contained the highest concentrations of APIs measured in any effluent worldwide. For example, the maximum concentrations of the antibiotics ciprofloxacin, and enrofloxycin (fluoroquinolone group) were found to be about 31,000 and 900 µg/L. The beta-blocker metoprolol was measured at concentrations up to 950 µg/L.

The concentrations of ciprofloxacin are so high that the maximum therapeutic dose for humans would be exceeded by ingesting 1 L of this water. The concentration is three to four times higher than that which was toxic to the water plant *Lemna minor* and the cyanobacteria *Microcystis aeruginosa*. An additional problem arises through the inappropriate dumping of untreated wastewater (Gurunadha Rao et al., 2001; Larsson et al., 2007). In two lakes in this area, which are not connected to the effluents of PETL, high amounts of ciprofloxacin – up to 6.5 mg/L – were found. These high concentrations may result from leakages of untreated wastewater from the dumping sites (Larsson, 2010). Many of these APIs (mostly generics), which are produced in Patancheru, are distributed worldwide and included in products sold by other pharmaceutical companies in industrial countries as well. Aside from these findings in India, elevated concentrations of APIs in effluents were found in the effluents of other drug companies in China and Brazil as well (Li et al., 2008a; Deschamps et al., 2012).

Pharmaceutical manufacturing in China

The Shanghai Environmental Department has compiled a blacklist of 721 companies. Of these, 374 companies are not applying approved environmental procedures or are failing inspections. It was found that 159 companies were contravening the water pollution prevention rules (ChinaCSR, 2010). For instance, Li et al. (2008a) found concentrations up to 920 mg/L of oxytetracycline (OTC) in influents and 19.5 mg/L in effluents of a WWTP in North China in Hebei Province. This tetracycline derivate is an antibiotic mainly used for aquaculture and livestock to promote growth. In the surface water of the Xiao River downstream of the WWTP, a maximum concentration of OTC of 712 µg/L was detected. In 2007, about 117 pharmaceutical production plants were forced to close down their facilities until they had improved significantly their facilities and made them more environmentally friendly (China Daily, 2007). According to the Blacksmith Institute's The World's Worst Toxic Pollution Problems: Report 2011, obsolete factories (of both pharmaceutical and other industrial manufacturers) are posing risks to human and environmental health. This is because often, especially in low- and middle-income countries, there is no capacity to remove these legacy structures or nobody feels responsible for their removal (Blacksmith Institute and Green Cross, 2011).

Pharmaceutical manufacturing in Brazil

Deschamps et al. (2012) revealed that pharmaceutical companies in the state of Minas Gerais, Brazil, release their water into the environment without any treatment. At present, there is no legislation in Brazil that controls exposure of the environment to micro-pollutants and pharmaceuticals. (Even in high-income countries there are no critical values implemented for pharmaceuticals in the environment). Moreover, it was brought to light that several companies do not rigorously manage their waste disposal as untreated waste was dumped in landfills and garbage dumps. Primarily, the Brazilian companies are producing commodities for domestic use in contrast to the industrial park area in Patancheru, India, where APIs for the domestic and the global market are produced (Larsson et al., 2007; Deschamps et al., 2012).

Best practices

The impact of pharmaceuticals released into the environment is an emerging issue, especially since general environmental consciousness is rising and better techniques for measuring environmental concentrations have been developed. More attention is being paid to this topic. At the moment, there are several initiatives and programs running with a focus on reducing the emission of pharmaceuticals into the environment and monitoring pharmaceuticals in WWTP effluents, surface water, and drinking water. However, to assess the risks these compounds pose to the environment, especially in low-and middle-income countries, more efforts are required. Examples, some theoretical and others already implemented, of how to reduce the impacts of pharmaceuticals on the environment, which are feasible for low- and middle-income countries, are mentioned below.

Implemented examples

Changes in regulations

Fortunately, during the last decade since the convening of the Johannesburg Plan of Implementation (United Nations, 2002) and Agenda 21 (United Nations, 1992), more commitments to ensure the sound management of chemicals and hazardous wastes have been made. These should enforce more sustainable development and protect human and environmental health. The goal of this implementation is to ensure that, by the year 2020, chemicals are produced and used in ways that minimize significant adverse impacts on environmental and human health, using transparent science-based risk assessment approaches and risk management procedures to support developing countries in strengthening their capacity for sound management of chemicals and hazardous wastes by providing technical and financial assistance (United Nations, 2013). In China, around 100 pharmaceutical production factories were forced to close because of severe pollution issues. To continue operations they must significantly improve the quality of their operations and put more effort into working more sustainably and in a more environmentally-friendly way. In addition, in developing countries, environmental consciousness is slowly growing. In Nigeria and Senegal, industrial wastewaters are starting to be controlled. In most low- and middle-income countries parameters like chemical or biological oxygen demand, heavy metals, pathogens, total suspended solids, pH, conductivity, nutrients, and dissolved oxygen are quantified, but information about the occurrence of pharmaceuticals in wastewaters is lacking (Institut sénégalais de Normalisation (ISN), 2001; Ngwuluka et al., 2011). However, initiatives to assess the state of wastewater management conducted by pharmaceutical industries in Nigeria have been undertaken (Ngwuluka et al., 2011). A survey showed that of 34 pharmaceutical businesses in Nigeria, 31 did poorly in managing the disposal of their waste. About one-third of the pharmaceutical businesses were releasing their wastewaters into the environment without any treatment. Some companies were found to be burying their pharmaceutical wastes near their premises ignoring the fact that these agents can leach into water aquifers or threaten environmental health. Surveys like this are helping to localize weaknesses in regulation or of the authorities. They are helping to identify those regions where the released chemicals are reaching high levels (in the air, soils, and water), and posing risks to environmental and human health. Furthermore, they can help link the pharmaceutical industries with the environmental agencies helping to reduce environmental pollution from industrial facilities that are acting as point sources. This could be beneficial for the industry as well. It will encourage them to develop techniques to further improve their efficiency of production and sustainability. It will help to improve the working conditions of their employees by reducing hazardous emissions in the work place or the occurrence of occupational accidents. In addition, preventing the release of toxicants into the environment is much cheaper than the remediation of contaminated sites (Blacksmith Institute and Green Cross, 2013). Furthermore, such surveys are providing information about which companies require further support and more education in wastewater management. The focus should not be to punish companies with poor results, but, rather, to help them develop strategies and find methods to support the sound production and management of chemicals.

More transparency

As previously mentioned, Larsson and Fick (2009) investigated the origin of pharmaceutical products marketed in Sweden. They came to the conclusion that about one-third of the 242 pharmaceuticals that were available in the Swedish market were produced and delivered from a pharmaceutical production plant in India which releases high amounts of hazardous APIs – mainly antibiotics – into the environment (Larsson et al., 2007). Because of the lack of data about pharmaceutical production and the stages of the supply chain, investigations like these are necessary to obtain more insights into the processes involved in pharmaceutical production and their supply chains. More transparency in the production chain would be helpful in reducing the chemical pollution caused by the pharmaceutical production facilities. Another possibility for assessing the risk pharmaceuticals pose for the environment is to predict the concentrations of APIs in river systems or effluents.

Predictions of pharmaceutical concentrations in sewage treatment plant effluents

Even in high-income countries, there is a dearth of information about the occurrence and biodegradation of several pharmaceuticals in industrial wastewaters (Heberer, 2002), such as antiviral agents (Prasse et al., 2010), sedatives (Brooks et al., 2003), or cytostatic cancer therapeutics (Buerge et al., 2006; Zounková et al., 2007; Yin et al., 2010). Zhang and Geißen (Zhang and Geißen, 2010) modeled the carbamazepine concentration found in the effluents of WWTPs treating human excreta in 68 countries. Although their approximations are a really good approach for calculating concentrations of APIs in wastewater effluents, it has to be considered that for their models, they used values such as:

- Consumption of carbamazepine (represented by the sales volumes of carbamazepine per country in 2007)

- Water consumption

- Disposal rate

- Excretion rate

- Removal efficiency for carbamazepine through wastewater treatment.

These values are not always available for every region and for every substance. Furthermore, the rates of degradation of different groups of APIs and individual pharmaceuticals can vary considerably depending on their physicochemical differences or the different wastewater treatment techniques. This makes it complicated to model the concentrations of APIs in effluents.

Zhang and Geißen estimated that in the low- and middle-income countries – Pakistan, Singapore, Tunisia, Turkey, and South Africa – the predicted concentrations of carbamazepine in WWTP effluents resulting from human excretion ranged from 942 to 1736 ng/L (Zhang and Geißen, 2010). Data like this can help to find risk areas where pharmaceuticals may be released into the environment at high levels, to spot regions where more monitoring would be required, and identify the need for more comprehensive data about toxicants. Consequently, their model is not easily applicable for every substance. For highly persistent chemicals, like carbamazepine, which have elimination rates below 10%, or other substances with stable elimination rates, the concentrations in the effluents can be calculated more accurately (Zhang et al., 2008; Zhang and Geißen, 2010). In contrast, the concentrations of APIs in the effluents of WWTPs cannot be calculated if the efficiency of removal of the WWTPs or the sewage pipes for the different agents vary a lot, it is very difficult to calculate the amount of diclofenac released through WWTPs (or to predict its environmental concentration in surface waters) since its elimination rates range from zero to 70 or 80% in the effluents of STPs (Zhang et al., 2008). Another difficulty is that the production, sales, or consumption data for APIs, especially in low- and middle-income countries, are currently not readily available to the public. Some consulting groups are selling data about sales and production volumes of pharmaceuticals, but these are quite expensive.

Theoretical examples

Changes in legislation

Today, there is less reliable data available about the production and sales of individual pharmaceuticals, particularly for public access (Larsson and Fick, 2009; Zhang and Geißen, 2010). Following the expansion of international trade and the associated complex production chains – covering every step from purchasing raw materials to packaging the end product offered to the consumer – it is even more difficult to obtain information about the real origin of a product. To assess the amount of pharmaceuticals that can be released into the environment and to identify the risks these chemicals pose to environmental and human health, the production and the sales figures need to be more transparent. In addition to more information about the pharmaceuticals for human use, more information about the amounts of veterinary pharmaceuticals produced, sold, and consumed are required as well. This is particularly so if they are used on a large scale – as in livestock and aquaculture for the treatment of diseases or promotion of growth. Production and sales of pharmaceuticals, which are known to show significant adverse effects on water organisms and which are persistent as well, should be reduced wherever comparable and more environmentally-friendly substitutes for these APIs are available. In future, initiatives like the Kiev Protocol on Pollutant Release and Transfer Registers (part of the Aarhus Convention) will help generate more insights about the production and trade of waste and other hazardous material (United Nations Economic Commission for Europe, 2014). The objective of this protocol is to improve public access to information by implementing international pollutant release and transfer registers. It is an open global initiative, so all states can participate in the protocol. At present, apart from Switzerland, Iceland, French Guiana, Ukraine, Georgia, Armenia, Tajikistan, Republic of Moldova, the former Yugoslav Republic of Macedonia, Albania, Montenegro, Bosnia and Herzegovina, and Serbia, mostly EU countries have joined this protocol. Hence, at present there is no information available from most of the low- and middle-income countries. Although there is a change going on and more restrictions and guidelines are being implemented in low- and middle-income countries (China Daily, 2007), the production facilities and the legislation governing waste disposal need to be adapted to the standards of the industrial countries.

More investigations in ecotoxicology

Although there are already a number of investigations on the eco-toxicological potential of pharmaceuticals, the total impact of most of the APIs on the environment and their distribution among biota, water, and soil is still not well understood (Ternes, 1998; Brooks et al., 2003; Oetken et al., 2005; Fent et al., 2006; Kümmerer, 2008). This is especially so for the consequences of chronic emissions of APIs into the environment, the synergetic effect of several APIs (Cleuvers, 2004; Jones et al., 2005; Schwarzenbach et al., 2006), and the exposure of non-target organisms – bacteria, plants, invertebrates (worms and snails), and vertebrates (fish and birds) – which are often unclear (Oetken et al., 2005). Mostly, initiatives were taken to monitor and reduce exposure to pharmaceuticals only after significant adverse effects on environmental and animal health – impairment of reproduction, malformations of mental, physiological, and morphological development, and even species extinction – were noticed (Oaks et al., 2004). Through more detailed investigations of the eco-toxicological potential, the impacts of pharmaceuticals on the environment could be estimated in advance, before the APIs are produced and released into the environment. To achieve that, more comprehensive toxicity tests are required during the development phase of new pharmaceuticals. Often pharmaceuticals are tested in the short term on basic test organisms – zebrafish, daphnia, algae, and rats and mice. But the toxic effects to other plants or invertebrates and vertebrates, like birds, snails, worms, insects, and amphibians, which are essential for ecosystems, remain unclear. In addition, it is important to focus on gaining a better understanding about the presence and impacts of pharmaceuticals in the environment in the long term. This will aid in better understanding the effects within complete ecosystems and the food web. In addition, the implementation of toxicity tests, risk assessments, and modeling approaches are useful tools for predicting the impact of pharmaceuticals on the environment.

Risk assessment

From the risk assessment approaches, valuable information about the toxic potential of different APIs can be investigated. This helps to estimate their risk to the environment. For instance, examination of the toxic potential of APIs on water organisms, expressed as acute quality criterion values (MAC-EQS) and chronic quality criterion values (AA-EQS), delivers information about the acute and chronic concentrations of different APIs that are provoking adverse effects on water organisms (Ecotox Centre, 2015). APIs which are posing a high risk at low chronic concentrations in higher-income countries, for example 17-alpha-ethinylestradiol, 17-betaestradiol, azithromycin, clarithromycin, carbamazepine, and diclofenac (with AA-EQS ranging from 0.037 ng/L to 0.5 µg/L) should be monitored in low- and middle-income countries as well.

More information for physicians, prescribers, and customers

Often the interest groups – the physicians, prescribers, and customers – are well informed about the side effects of pharmaceuticals, but on the packaging or package inserts there is no information available about the ecotoxicological potential and persistence in the environment or about the origin of the APIs. An optional, adequate, and consistent labeling or certification system with pictograms could give information to the provider and the consumer about the ranking of sustainability of the production processes. (For instance, were environmentally-friendly techniques, standards, and controls implemented? Were the APIs produced in domestic or non-domestic facilities? Was the waste disposed of appropriately? Is there information about persistence in the environment and risks to water organisms?) With this information, consumers can make their own decisions; whether they are willing to pay more for a certified environmentally-friendlier product or if they prefer to buy an unlabeled or a cheaper one, which may be produced under less controlled and less environmentally-friendly conditions. Unfortunately at this time, the latter is more often the case in low- and middle-income countries than in higher-income countries (Larsson and Fick, 2009). Larsson and Fick (2009) showed that of 242 pharmaceuticals on the Swedish market, about 123 (51%) products originated from manufacturers located in India. And of these, 74 (31%) were produced in the highly industrial region near Hyderabad, where large amounts of pharmaceutical waste are being dumped into river systems following inefficient wastewater treatment or are being deposited inappropriately in landfills where they could leak into aquifers (Larsson et al., 2007; Larsson, 2010).

More education in the veterinary sector

Besides providing more information for physicians, prescribers, and customers, the farmers involved in raising livestock animals and aquaculture farming in low- and middle-income countries should be better educated about using veterinary medicines as well. This may be of especially high relevance for growing markets like the raising of fish, crustaceans, and mollusks. From 1950 to 2008, fish production through aquaculture increased from less than 1 million tonne to 52.5 million tonne. This represents around 37% of the estimated annual global fish production of 142.3 million tonne (Food and Agriculture Organization, 2010). The production of fish is dominated by the Asian region. Of the 52.5 million tonne of fish produced through aquaculture, 88.8% were produced in Asia (China accounts for 62.3%), while 4.5% was produced in Europe, 3.3% in Latin America, and 1.8% in Africa. Farmers need to be taught about the consequences to the environment that result from using large amounts of pharmaceuticals and how they can reduce the volume of veterinary pharmaceuticals used for animal treatment and growth promotion. They should also be shown that there are alternative therapies available for treating animal diseases and for avoiding parasitic or bacterial infestations of animals. For instance, Romero et al. (2012) introduced some alternative therapies. These included using probiotic microorganisms, essential oils containing antimicrobial components, or bacteriophages as ways of preventing infections by pathogens. One recent headline indicates that more education and stronger legislation and controls are desperately needed in low- and middle-income countries, especially China. There, thousands of dead ducks and the carcasses of around 16,000 pigs were found floating in the Jiapingtang River, which supplies drinking water to the megacity Shanghai. From local reports, it is suspected that the dead animals may have originated from animal husbandries in neighboring Zhejiang province (BBC, 2013; Richard, 2013). The animals probably died of bacterial or viral infections and afterwards they were disposed of inappropriately in the river. Given the large number of dead animals, the question of whether the livestock in this region is kept under tolerable and environmentally-friendly conditions can be raised.

Mining Industry Pollutants

Chemical characteristics and their potential risks

Introduction

The continuous growth of population and increased global consumption of minerals and metals as a result of raised standards of living are increasing the demand for raw material and ores. This is particularly so for the metals and resources used in the high-technology industries, even in low- and middle-income countries (Öko-Institut e.V., 2007; International Council on Mining & Metals, 2012). Given the development of newer and better high-technology products, a broader range of elements are now used. For instance, in the semiconductor industry, 12 elements were used in 1980. By the 21st century, the number of elements used in this sector had increased to 60 (see Appendix Figure 5). This has resulted in an additional rise in demand as well as an increase in pressure on resources (Theis, 2007). Data about the acquisition of primary minerals and metals from mining are difficult to come by. However, in the USA alone, about 85.4 million tonne of primary metals and 294 million tonne of industrial minerals were mined in 2010 (Matos, 2012). Because of these increased demands for raw material, the interest in resource-rich low- and middle-income countries is increasing.

In general, most of the metals and metalloids are used in the industrial sector (in electronics, construction, and in the production of iron), and in the jewelry industry. Because of the increase in demand, the primary exploitation of these essential ores and minerals will further increase over time, while their natural stocks will decline. For instance, the natural stocks of rare earth elements (yttrium, niobium, neodymium, and scandium), the platinum group elements (platinum and palladium), the metalloid germanium, the transition metals (tungsten, cobalt, and molybdenum), the alkali metal lithium, the alkaline earth metal magnesium, and the metals tin and indium have been severely reduced (vbw, 2011). In contrast, the natural stocks of other metals, such as silver, gold, cadmium, manganese, zinc, and iron, have been less exhausted.

Different mining techniques are available for the primary extraction of metals. There are mainly two approaches – surface mining and underground mining. For surface mining, soil and rocks are blasted out of the subsoil or vegetation is removed to create open pits which lay bare the different ores and minerals. For underground mining, tunnel systems are created to exploit the minerals and ores. In general, open-pit mining is used more frequently (two-thirds of the time) than underground mining, because it is cheaper and less dangerous for the employees to work at the surface rather than in narrow underground shafts (Farrell et al., 2004; Blacksmith Institute and Green Cross, 2012).

During the mining, processing, and trade of primary minerals and metals there are four steps. These are ore and mineral exploitation, transportation, extraction, and refining. Several impacts of environmental concern are associated with these processes.

Impact of ore exploitation

The processing of mineral ores produces high volumes of waste. As the more high-grade ore deposits are diminished, lower-grade ones are used and even more waste is produced. For instance, the production of 0.3 mg of gold results in 79 tonne of mine waste. The production of 1 tonne of copper results in 110 tonne of tailings (waste ore) and 200 tonne of waste rocks (Farrell et al., 2004). [Note that the exploitation of mining commodities used as energy resources, such as fossil fuels (gas, oil, and coal) and radioactive uranium ore, and their risks to environmental and human health are not discussed in our report. This does not mean that they are less relevant or of less environmental concern: we did not have the resources to focus on these commodities as well.]

Open-pit mining produces higher amounts of waste than underground mining.

Generally for open-pit mining, higher amounts of waste are produced than from underground mines. This is because open-pit mining can be used to obtain lower-grade sediments and rocks from which the mineral can be extracted (United States Environmental Protection Agency, 1995). Open-pit mining is associated with deforestation and the consequent increased erosion of soil. It is also associated with the use of explosives – mixtures of ammonium nitrate and fuel oil, trinitrotoluene, and nitroglycerine – that may have adverse effects on environmental and human health by polluting vulnerable ecosystems (Brüning et al., 1999; Wihardja, 2010; Swenson et al., 2011; Butler, 2012).

Impact of transportation

In general, the exploited material is stockpiled in heaps or dumps to await further processing. To transport the material, trucks, conveyers, and railways are used. Because of that, hydraulic oils, fuels, lubricants (with such constituents as glycol ethers, benzene, ethylbenzene, toluene, and other hydrocarbons), and batteries (with sulfuric acid, lead, antimony, and arsenic) are needed. Some of these products may be released or dumped into the environment as well (United States Environmental Protection Agency, 1995).

Gold, silver, and platinum are often processed by leaching the heaps with cyanides or by amalgamation. The amalgamation process using mercury is especially of high environmental concern because large quantities of mercury are required and released into the environment during this process.

Impact of ore extraction

Beneficiation methods are used to extract and enrich the compounds of interest. These methods differ for different metals. Commonly, gravity concentration, milling and floating, heap and dump leaching, and magnetic separation are the beneficiation methods used. Gold, silver, and the platinum group elements are often processed by leaching the heaps with cyanides or by amalgamation. The amalgamation process using mercury is especially of high environmental concern because during this process, large quantities of mercury are required and released into the environment. This procedure is widely used in low- and middle-income countries in uncontrolled, small-scale mining operations (Limbong et al., 2003; Farrell et al., 2004; Kippenberg, 2011). For lead, zinc, and copper, milling, flotation, smelting, and leaching with sulfuric or hydrochloric acid are the methods used. Iron is principally extracted by magnetic separation. After extraction, waste rock residues, which may contain toxic extraction chemicals and heavy metals, are disposed of in tailings dams or abandoned as waste rock legacies posing environmental risk (United States Environmental Protection Agency, 1995; International Council on Mining & Metals, 2012). Common chemicals of environmental concern that are used for the processing and extraction of ores and minerals are: hydrochloric acids, sulfuric acid, potassium cyanide and cyanide acids, soda ash, sulfur dioxide, coal tar, and aluminum and zinc sulfates. The quantities of these chemicals used and their risks to human and environmental health are even harder to assess than those of the mineral and metals (United States Environmental Protection Agency, 1995). Even though these pollutants are of environmental concern, in this chapter we focus more on the most hazardous heavy metals, metalloids, and minerals that are released accidentally as side products and that pose risks to the environment.

Impact of ore refining

The pre-treated material is freighted to a smelter where impurities are removed under high temperature to produce the pure raw product, which can be traded and used. During the whole metal production cycle, the smelting of ores consumes the most energy and creates high levels of air pollutants, especially if the smelters or refineries are unregulated and if obsolete methods are used (Farrell et al. 2004; Blacksmith Institute and Green Cross, 2013).

During the processes involved in the exploitation, transport, extraction, and processing of metals and minerals, large amounts of hazardous heavy metals and minerals are unintentionally released into the environment. The minerals and metals of most concern are asbestos and antimony, arsenic, cadmium, chromium, copper, lead, manganese, mercury, and thallium. The products accumulate and remain in the soils next to the mining areas and at the mineral and mining processing facilities (Ayres, 1992; Stoeppler, 1992; Blacksmith Institute and Green Cross, 2012). In general, the accumulation and distribution of these compounds result from such processes as the leaching of heavy metals from tailings and by acid

Main Issues

The main issues associated with mining activities, which especially hold true for low- and middle-income countries, are that:

- Mining (especially open-pit mining) results in the destruction and deforestation of vulnerable natural environments (Farrell et al., 2004; Swenson et al., 2011).
- In mining processes, very large amounts of hazardous extraction chemicals or contaminated waste rocks are released and disposed of into the environment (Farrell et al., 2004; Liu et al., 2005) or abandoned in the mining sites. Acid drainage from the mines can also result (Naicker et al., 2003; Johnson and Hallberg, 2005; Lin et al., 2007; Tutu et al., 2008).
- In low- and middle-income countries particularly, the mine employees often work under poor and insecure conditions and they use obsolete and hazardous extraction methods. Often the legislative framework to manage these issues is missing or not well implemented (van Straaten, 2000; Limbong et al., 2003; Smith, 2011; Blacksmith Institute and Green Cross, 2012).

mine drainage (AMD). Alternatively, these compounds can be distributed as airborne particles and through adsorption onto aerosols as a result of the smelting and industrial processes.

Toxicological potential

In general, it is possible to distinguish between those trace elements that are essential for plant, animal, and human nutrition and those that are not. There are some elements that are required and beneficial for growing, enzymatic processes, and metabolism. A shortage of these essential elements would cause significant deficits in growth, development, metabolic activities, and, consequently, health. There are other elements for which plants, humans, and other animals have no demonstrated biological requirements, but for which exposure is associated with significant toxic effects. The highest concentration or dose of essential and non-essential metals that does not cause statistically significant adverse effects to the exposed population or biota is referred to as the ‘no observed adverse effect level’ (NOAEL). However, for both, essential and non-essential metals, a threshold can be reached where a further increase in concentration or dose does adversely affect the health of plants, animals, and humans and can even lead to death (see Figure 18; Goyer, 1997; Adriano, 2001). The lowest concentration level or dose that causes significant effects to living organisms is referred to as the ‘low observed adverse effect level’ (LOAEL).

Trace metals (and metalloids) such as cobalt, copper, iron, manganese, molybdenum, nickel, selenium, and zinc are essential to plants, humans, and other animals. In contrast, aluminum, antimony, arsenic, beryllium, bismuth, cadmium, gold, lead, mercury, platinum, silver, and tungsten are not essential for plants, humans, and other animals (Adriano, 2001; Luoma and Rainbow, 2008).

Furthermore, it is recognized that metals released into the environment pose one of the most serious pollution problems of today (Chandra Sekhar et al., 2003). This problem results from their specific characteristics. For example, they are non-biodegradable and non-thermo-degradable: heavy metal contamination can last for hundreds and even thousands of years if the contaminants are not physically or chemically immobilized or removed (Bohn et al., 1985; Mapanda et al., 2005). The half-live of cadmium in the soil is from 15 to 1100 years. That of copper is between 310 and 1500 years, while that of lead is between 740 and 5900 years. These wide variations in half-lives depend on the soil type and its physicochemical parameters (Alloway and Ayres, 1993). Consequently, heavy metal concentrations can increase unnoticed over time and reach hazardous or even toxic concentrations (Bohn et al., 1985). In the World’s Worst Pollution Problems 2012 annual report, the Blacksmith Institute and Green Cross estimated that in low- and middle-income countries the health of about 14 million people is at risk as a result of mining and ore processing activities (Blacksmith Institute and Green Cross, 2012).

Metals released into the environment pose one of the most serious pollution problems of today as they are non-biodegradable and non-thermo-degradable and therefore can last for hundreds and even thousands of years if the contaminants are not physically or chemically immobilized or removed.

Generally, comprehensive data about most mining pollutants are not available and this is especially so in low- and middle-income countries. It is next to impossible to assess the consumption, occurrence, and fate of, and risks arising from the use of extraction chemicals such as cyanides (used for extracting precious metals) and sulfuric and hydrochloric acids (used for extracting lead, zinc and copper).

In this section about mining pollutants, the minerals and metals of highest environmental concern and for which the most comprehensive data are available were selected. Similar issues and trends hold true for other hazardous mining commodities, but they are not considered in this report. In this report, the selected pollutants

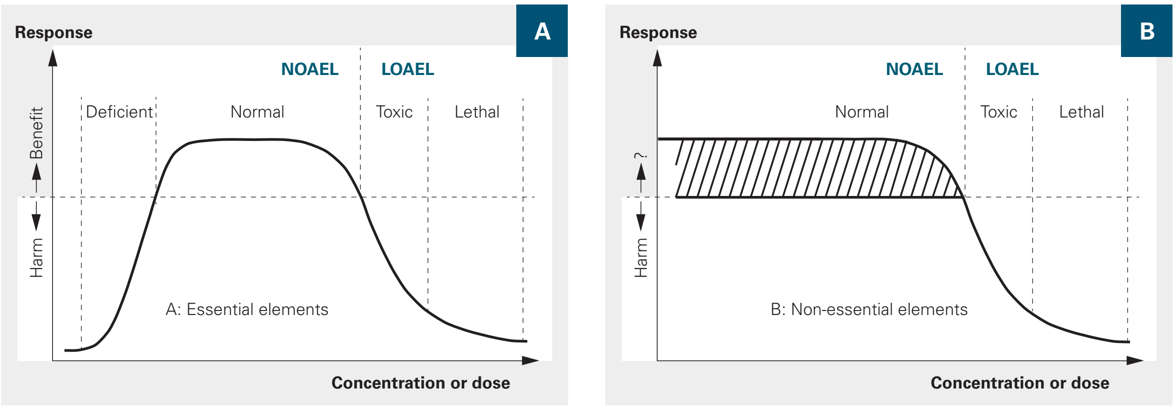


Figure 18: *Dose-response relationship for essential (A) and non-essential (B) elements in plants, humans, and other animals (modified from Adriano, 2001)*

known for being of the highest environmental concern are (Ayres, 1992; Stoeppler, 1992; Blacksmith Institute and Green Cross, 2012):

- The metals (Group A). These include cadmium (Cd), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), mercury (Hg), and thallium (Tl)
- The metalloids (Group B). These include antimony (Sb) and arsenic (As)
- The minerals (Group C). This includes asbestos (ASB)

Considerable amounts of Cd are released into the environment as a by-product of mining production. This is especially the case in the exploitation of Zn and Pb ore fields.

Since the industrialization of the 19th century and the concomitant increase in mining activities, these metals and minerals have become relevant environmental pollutants. This is especially so for Cd, Cr, Cu, and Pb. Given their recent considerable global increases in production; they are of high environmental concern (Barrientos and Soria, 2013; United States Geological Survey, 2013)

Mining pollutants of environmental concern

Group A: Cadmium (Cd)

Introduction

Cadmium is a transition metal that is found mainly in minerals in combination with zinc (Zn), but also in ores together with Cu and Pb (Godt et al., 2006). The sulfide and carbonate minerals – spahlerite/wurzite, smithsonite, boulangerite, tetrahedrite, stannite, and chalcopyrite (in descending order of importance) – are the main ores of Cd with concentrations of the metal ranging from 15 to 50,000 ppm (Vlasov et al., 1966; Brehler et al., 1969; Schwartz, 2000). On average, the Earth's crust contains 0.11 – 0.5 ppm Cd (Fassett, 1975; Salomons and Förstner, 1984; Giuffré de López Camelo et al., 1997).

Given its resistance to corrosion, the demand for cadmium has increased with a corresponding increase in primary production (Fassett, 1975). Generally, Cd is used in electroplating, pigments, plastic stabilizers, and nickel-cadmium batteries (Hutton, 1983). In 1910, the global production of cadmium was 50 tonne, and 17,000 tonne were produced in 1969 (Teworte, 1974). In 2012, world production of Cd stabilized at around 23,000 tonne (United States Geological Survey, 2013).

Considerable amounts of Cd are released into the environment as a byproduct of mining production. This is especially the case in the exploitation of Zn and Pb ore fields (Hutton, 1983; Sanità di Toppi and Gabbrielli, 1999; Benavides et al., 2005). Processes like AMD at orphan mining sites and the leaching of heavy metals into the groundwater and surrounding soils from abandoned waste rock heaps and tailings are further sources from which Cd or other hazardous metals enter into the environment (Farrell et al., 2004; Blacksmith Institute and Green Cross, 2011). The primary and secondary production processes of Cd and Zn, such as thermal smelting and electrolytic extraction, result in the emission of Cd aerosol particles. These precipitate in soils and surface waters near the production facilities, particularly if no aerosol filtering systems are used, obsolete techniques are applied, and insufficient controls are in place. This can be assumed to be the case in several regions in low- and middle-income countries (Díaz-Barriga et al., 1993; Razo et al., 2004). Additional Cd sources apart from mining are the burning of fossil fuels (mainly coal), emissions at power stations, heating systems, metal working industries, urban traffic, and cement and steel production. Contamination with Cd also occurs as a result of the emission or inappropriate disposal of solid wastes or waste incineration. Furthermore, phosphate rocks, used for the production of fertilizer, can contain traces of cadmium and these act as additional Cd sources into the environment (Bertine and Goldberg, 1971; Hutton and Symon, 1986; Jensen and Bro-Rasmussen, 1992; Sanità di Toppi and Gabbrielli, 1999; Godt et al., 2006).

Environmental behavior and occurrence

Cadmium has a relatively high water solubility (Fassett, 1975; Lockwood, 1976; Benavides et al., 2005). This depends on several factors. One of the main factors influencing the solubility in water is pH. At lower pHs, around and below 8, Cd becomes more soluble in water and occurs mainly as Cd^{2+} ions. At higher pHs, Cd has the affinity to precipitate as the predominant Cd salt, $CdCO_3$, or it forms complexes with other ligands. With increasing salinity, the predominant Cd species are chloro-complexes with $CdCl^+$ at lower salinities and $CdCl^2$ at higher salinities (Turner et al., 1981; Comans and van Dijk, 1988). Cd is one of the metals of highest human and environmental concern, because of its relatively high water solubility, its mobility and its toxic effects even at very low concentrations (Benavides et al., 2005).

Cd is one of the metals of highest human and environmental concern, because of its relatively high water solubility, its mobility and its toxic effects even at very low concentrations.

The human uptake of Cd happens mainly through inhalation of Cd-bound airborne particles from burning processes, smoking, and from ingesting contaminated food and water (Godt et al., 2006).

Additionally, it has been shown that plants have an affinity to take up Cd at high rates and that it accumulates in the roots and shoots. This uptake and accumulation process is dependent on the type of soil, the pH, and the nutrient content of the soil. Soils, plants, and drinking water aquifers close to mining sites, smelters, and industrial districts can register higher levels of Cd or other hazardous metals (Benavides et al., 2005; Yang et al., 2006).

In high-income countries (HICs) like Australia, New Zealand, Denmark, Sweden, and the USA, natural mean concentrations ranging from 0.13 to 0.71 µg Cd/g have been measured in agricultural soils (McDowell et al., 2013). A mean dissolved Cd concentration of 0.02 µg/L was measured in two French rivers (Deycard et al., 2014).

In low- and middle-income countries, such as southern China, particularly in the Wu Jiand River basin where untreated mining wastewater is used for irrigation, high mean Cd concentrations of 13.59 µg/g dry weight in paddy soils and 8.21 µg/g dry weight in the roots of rice plants have been found (Yang et al., 2006). In this region, it is estimated that a 60 kg adult ingests about 132 µg of Cd per day. This exceeds the acceptable daily intake (ADI) of 70 µg of Cd (for an average adult weighing 70 kg). This figure of 70 µg/day is obtained from the provisional tolerable weekly intake (PTWI) of 7 µg/kg for a 70 kg adult (Food and Agriculture Organization and World Health Organization, 2003). In soils at mining sites in Zacatecas State, Mexico, elevated Cd concentrations of from 11 to 47 µg/g of air-dried soil were found (Carrillo González and González-Chávez, 2006).

Toxicity

As previously mentioned, the ADI of Cd is 70 µg. The US Environmental Protection Agency's low maximum contaminant level (MCL) is 5 µg Cd/L (Table 5). This is the level that should not be exceeded in drinking water to guarantee public health. These figures indicate the high toxicity of Cd (Food and Agriculture Organization and World Health Organization, 2003; United States Environmental Protection Agency, 2015c). Furthermore, Cd is not an essential element for plants, humans, and other animals (Adriano, 2001; Luoma and Rainbow, 2008). The uptake of Cd-oxides by inhaling tobacco smoke and breathing in occupational pollution causes acute respiratory distress syndromes and pulmonary edema. Long-term exposure leads to renal dysfunction, anemia, osteoporosis, and bone fractures (Friberg et al., 1985; Barbee Jr and Prince, 1999; Godt et al., 2006). In the human body, the kidney is the main target for bioaccumulation. There, the half-life of Cd is about 10 years (Orlowski and Piotrowski, 2003; Godt et al., 2006). In the kidney, chronic uptake leads to tubulus cell necrosis. The International Agency for Research on Cancer (IARC) classifies Cd as a Group I carcinogen for humans (International Agency for Research on Cancer, 1993). From mammalian in vitro experiments, there is evidence that exposure to cadmium salts promotes micronuclei and chromosomal aberrations and DNA strand breaks, and that the salts have a weakly mutagenic potential (Waalkes, 2003). In addition, although cadmium is not redox-active, there is evidence that exposure to Cd enhances the induction of oxidative stress (Shaikh et al., 1999; Ercal et al., 2001) and promotes the inhibition of several DNA-repair mechanisms (Hartwig and Schwerdtle, 2002). In short, Cd reacts with a wide variety of biomolecules, such as DNA, proteins, and membranes, with visible effects (Bertin and Averbeck, 2006). Given its toxicity, in Germany, the acceptable concentration of Cd in the blood of workers is not allowed to exceed 15 µg/L (Godt et al., 2006). In rat glioma cells an EC_{50} (24 hour) of 0.7 µmol/L of Cd has been identified.

Besides its toxic effects on mammals, Cd has negative effects on plant health and development.

Besides its toxic effects on mammals, Cd has negative effects on plant health and development. Among other adverse effects, it reduces the adsorption and transport of nitrates by inhibiting the nitrate reductase activity (Hernandez et al., 1996). It inhibits ATPase activity (Fodor et al., 1995), and disturbs chlorophyll biosynthesis (Stobart et al., 1985). The most visible symptoms of cadmium intoxication in plants are stunting leaf rolls and chlorosis (Das et al., 1997; Benavides et al., 2005).

From an environmental toxicological point of view, 24 hour EC_{50} values of between 180 µg/L *(Paramecium caudatum)* and 2650 µg/L *(Euplotes patella)* have been determined for these different ciliate species (Madoni et al., 1992). The reproduction of the water snail *Potamopyrgus antipodarum* was significantly affected at test concentrations of 25 µg Cd/L after exposure for 28 days (Sieratowicz et al., 2011). From an environmental toxicological point of view, even chronic concentrations of 0.08 to 0.25 µg/L of dissolved Cd can affect the health of aquatic organisms (Table 5; European Parliament and Council of the European Union, 2008).

Group A: Chromium (Cr)

Introduction

Chromium (Cr) is a transition metal and commercially mined as chromite ($FeCr_2O_4$). It occurs relatively frequently in nature. Hence, its average concentration in the Earth's crust is about 100 ppm (Salomons and Förstner, 1984; Barnhart, 1997).

Given its metallurgical properties Cr is used in alloys. For example, the addition of chromium during steel production helps to produce stainless steel which has corrosion and oxidation resistance characteristics. Furthermore, given its resistance to heat, it is used in refractory furnaces and foundry sands. In addition, Cr is used as a pigment for textile dyes, paints, inks, and plastics and in chemicals for leather tanning and preserving wood (Barnhart, 1997; Johnson et al., 2006; Straif et al., 2009; Blacksmith Institute and Green Cross, 2011). It is contained in the raw material used for cement production and as a trace element in phosphorus fertilizers. (Giuffré de López Camelo et al., 1997). Thus chromium has a wide range of applications, which explains why it is one of the most widely used metals (Barnhart, 1997). In 2012, worldwide mining production was about 24 million tonne (United States Geological Survey, 2013).

Chromium is in the waste rocks, slag, and solid wastes of mining processes and in the wastes of refineries and metal and e-waste recycling facilities.

Chromium is released into the environment during mining activities, its extraction and smelting, the burning of fossil fuels (especially coal), and industrial activities (steel production, metal alloy production, the textile industry, and tanneries). It is in the waste rocks, slag, and solid wastes of mining processes and in the wastes of refineries and metal and e-waste recycling facilities (Mukherjee, 1998; Johnson et al., 2006; Li et al., 2008c; Blacksmith Institute and Green Cross, 2011).

Environmental behavior and occurrence

Under environmental conditions, the most stable oxidation states of chromium are Cr(III) and Cr(VI). In aquatic systems, trivalent Cr is more likely to be precipitated as $Cr(OH)_3$, especially at pHs between 6 and 12. Outside these conditions, hexavalent Cr has a much higher water solubility and is, therefore, more transportable in water (Rai et al., 1989; Loyaux-Lawniczak et al., 2001). In the environment, Cr(III) is oxidized mainly by manganese oxides to the more hazardous Cr(VI). Hexavalent Cr is reduced to trivalent Cr by Fe(II), by mineral sulfides containing Fe(II), and by organic matter (Schroeder and Lee, 1975; Rai et al., 1989; Deng et al., 1996; Peterson et al., 1997; Loyaux-Lawniczak et al., 2001). In general, the hexavalent oxidation state of Cr is more stable in an oxidizing alkaline environment whereas trivalent Cr is more stable under reducing acidic conditions (Godgul and Sahu, 1995).

The main routes for hexavalent Cr uptake are through the inhalation of dust, mists, and fumes while working in the ore, metal, textile, and dye processing sectors.

The natural levels of Cr in the surface soils of industrial countries, such as Denmark, Germany, Japan, USA, and Canada, range from 28 to 50 ppm dry weight (Kabata-Pendias and Pendias, 2001). In most of the drinking water sources in California, Cr(VI) concentrations ranged from 5 to 50 µg/L (Pacific Gas and Electric Company Groundwater Remediation Program, 2011).

Large amounts of heavy metals, such as Cr, continuously enter the environment from mining and industrial estates. The ambient air in western India contained chromium concentrations ranging from 0.016 to 0.089 µg Cr/m^3, and drinking water samples contained from 4 to 95 µg Cr/L (Sathawara et al., 2004). In a mining area in southern Togo, elevated levels of Cr between 182 and 1029 ppm were measured (Gnandi and Tobschall, 2002).

Toxicity

The chemical and biochemical reactivity, the toxicity, and the mobility of chromium as Cr(III) and as Cr(VI) are drastically different (Kotaś and Stasicka, 2000; Loyaux-Lawniczak et al., 2001). Cr(III) is an essential metal for animals and humans, but not for plants. For instance, it is crucial for the control of glucose and the lipid metabolism in mammals (Anderson, 1989). In contrast, Cr(VI) provokes several forms of cancer as a consequence of DNA damage and oxidative stress (Norseth, 1981; Gibb et al., 2000; Li et al., 2008c; Straif et al., 2009). According to the US EPA, the MCL of Cr in drinking water is 100 µg/L (Table 5) although Cr(III) is considered essential for animals and humans (Adriano, 2001). According to the IARC, hexavalent Cr is classified as a Group 1 carcinogen for humans (International Agency for Research on Cancer, 2012d). Between 1990 and 1993 in the EU alone, about 800,000 workers were estimated to have been exposed to Cr(VI) (Kauppinen et al., 2000). The Blacksmith Institute estimated that in their area of operation, 5.5 million people located in low- and middle-income countries are at risk from exposure to chromium alone (Blacksmith Institute and Green Cross, 2011). The main routes for hexavalent Cr uptake are through the inhalation of dust, mists, and fumes while working in the ore, metal, textile, and dye processing sectors. Cr(VI) is also absorbed through the skin. Smoking cigarettes is a significant source of Cr(VI) as well (Straif et al., 2009). Occupational exposure to Cr(VI) in the long term can lead to perforation of the nasal septum, asthma, bronchial inflammations, lung cancer, and inflammations of the larynx and liver. Skin contact results in allergies, dermatitis, dermal necrosis, and dermal corrosion (Lee et al., 1989; Straif et al., 2009; Bedi et al., 2013).

From an environmental toxicological perspective, the acute (96 hour) LC_{50} of hexavalent chromium of 41.75 mg/L for the freshwater fish *Channa punctatus* was investigated. Abnormal behavior, like erratic swimming and loss of equilibrium, and histopathological changes in gills and liver have been observed from exposure to 20 mg/L Cr(VI) (Mishra and Mohanty, 2008). Exposure to Cr(VI) causes adverse effects on plant growth and development. For higher plants, concentrations of about 100 µmol/kg dry weight of hexavalent Cr showed toxic effects (Davies Jr et al., 2002). For instance, Cr(VI) reduces the germination of seeds (Rout et al., 2000; Zeid, 2001). Hexavalent Cr hinders the uptake of nutrients and essential metals, such as nitrates, phosphorus, Fe, Mg, and potassium (Turner and Rust, 1971; Adriano, 2001). Additionally, it inhibits the growth of roots (Prasad et al., 2001), stems (Rout et al., 1997), and foliage (Sharma and Sharma, 1993). Furthermore, inhibition of photosynthesis and ATPase activity can be caused after exposure to Cr(VI) (Zaccheo et al., 1982; Vajpayee et al., 1999). For Cr(III) the chronic environmental quality standard (AA-EQS) is 4.7 µg/L and for Cr(VI) it is 3.4 µg/L (Table 5; UK Technical Advisory Group on the Water Framework Directive, 2008). Therefore, to guarantee the health of water organisms within an aquatic system, these concentrations should not be exceeded in the long term.

Group A: Copper (Cu)

Introduction

The transition metal copper (Cu) can be found as native copper and in the form of sulfides (chalcopyrite, bornite, and chalcocite), oxides (cuprit and tenovite), hydroxyl carbonates (malachite and azurite), and silicates (chrysocolla; Kruesi and Frahm, 1982). In the Earth's crust it occurs at an average concentration of 50–55 ppm (Taylor, 1964; Salomons and Förstner, 1984).

Copper has a wide range of uses. It has applications as a construction and building material, being used for water pipes, drain pipes, and plumbing fixtures primarily because of its light weight, its waterproofness, its flexibility, and its natural microbial resistance (Lehtola et al., 2004). Nowadays, plastic water pipes are frequently substituted for copper ones (United States Geological Survey, 2013). Because of the high electrical conductivity of copper even at low temperatures, it is used in the electronics industry in wires and electronic devices (Berman and MacDonald, 1952), and in transport equipment and vehicles (Berman and MacDonald, 1952; Kapur and Graedel, 2006). In addition, it is used as a pigment in ink and in the printing industry (Babler, 1998). It is used also in the metal industry to produce the alloys brass and bronze (Duke, 1944). Copper compounds are applied as wood preservatives (Hingston et al., 2001) and to purify water. Given its properties as an algaecide, fungicide, nematocide, and molluscicide, Cu is used as an antibacterial and antifouling agent (Fraser et al., 1974; Cooney and Tang, 1999; Borkow and Gabbay, 2005; Gabbay et al., 2006). Globally, annual copper production has increased immensely. In 1968, 5.8 million tonne (Förstner and Wittmann, 1979) of Cu was produced, increasing to 8.3 million tonne in 1985 (Bowen, 1985). By 2012, world mining production of copper reached 17 million tonne (United States Geological Survey, 2013).

Copper is introduced into the environment in a large number of ways. Mining and metal processing activities, such as smelters and refineries, brass mills, and bronze production are some such sources. Other sources include the cement industry, its use as an aquatic pesticide against fungi, bacteria, and algae (McKnight et al., 1983; Richardson, 1997), and the disposals of e-waste and construction materials (Flemming and Trevors, 1989).

Environmental behavior and occurrence

Cu has three oxidation states, Cu(0), Cu(I), and Cu(II) (Flemming and Trevors, 1989). At pH values up to 6, Cu(II) occurs in aquatic systems as dissolved Cu^{2+} ions. With increasing pH, Cu(II) species, such as $Cu_2(OH)_2^{2+}$, $CuOH^+$, and $CuCO_3$ are predominant (Sillén and Martell, 1964; Sylva, 1976; Luoma and Rainbow, 2008). Cu(II) is a potent complexing agent and in the positive charged form it has a high tendency towards hydrolysis (Flemming and Trevors, 1989). The Cu levels in solution are regulated by different processes: complexation to inorganic (more predominant in seawater than in freshwater; Leckie and Davis, 1979; Flemming and Trevors, 1989) or organic ligands (in fresh and seawater), precipitation as oxides, hydroxyl carbonates, silicates, and sulfide minerals (Sylva, 1976; Elder and Horne, 1978; Kruesi and Frahm, 1982; Davis, 1984; Coale and Bruland, 1988), and adsorption to biota and organic particles (Ramamoorthy and Kushner, 1975; Ramamoorthy and Rust, 1978; Kuo and Baker, 1980). These processes control the presence of the different Cu species, increase or decrease their mobility within aquifers, and affect their availability, uptake, and further adsorption to biota (Flemming and Trevors, 1989). Because of these interactions, Cu is distributed among three different phases – the aqueous phase (as free ionic and water soluble complexes; Sylva, 1976), the solid phase (as particles, colloids, soils and sediments), and the biological phase (adsorbed and absorbed in biota; Flemming and Trevors, 1989; Luoma and Rainbow, 2008).

Natural Cu concentrations in freshwater range from 0.03 to 5 µg/L (Hodson et al., 1979; Bowen, 1985; Luoma and Rainbow, 2008). In uncontaminated soils, Cu concentrations between 16 and 25 µg/g have been found (Hornberger et al., 2000).

An example of environmental pollution occurs in northern Chile, near the city Chañaral. Here, extensive copper mining had been conducted for more than 60 years. Untreated tailings water was disposed of directly into the sea causing drastic beach degradation and a decrease in biodiversity with a loss of invertebrates and algal species (Castilla, 1996; Medina et al., 2005). Years after this exposure, elevated Cu concentrations of between 34 and 50 µg/L could be measured in the water samples of this coastal region (Castilla, 1996; Medina et al., 2005). Elevated Cu concentrations of between 12 and 43 µg/g were measured in sediments of the River Yamuna in India (Jain, 2004). This contamination is more related to the activities of the textile and printing industries and to the disposal of city waste than to the mining industry (Jain, 2004).

Toxicity

Although Cu is essential for several organisms, low concentrations of Cu can have harmful effects on the ecosystem by affecting bacteria, algae, fungi, plants, fish, and invertebrates, particularly in aquatic systems.

The toxicity of Cu is relatively low for mammals and humans because the MCL of Cu in drinking water is 1.3 mg/L. The MCL of the more toxic cadmium is much lower at 5 µg/L (Table 5; United States Environmental Protection Agency, 2015c). Although copper is an essential human nutrient, concentrations above the MCL cause gastrointestinal upsets such as diarrhea, abdominal cramps, and nausea, especially in children. These symptoms are less life-threatening than those of previously mentioned metals (Knobeloch et al., 1994). As there is no evidence that Cu can promote the formation of cancer, it is not classified by the IARC as carcinogenic to humans. Concentrations of 50 to 250 mg/kg copper sulfate are used as a food additive in the diet of pigs to promote growth. These animals can tolerate quite high levels of Cu in their diets (López Alonso et al., 2000). In addition, Cu is essential for plants and for that reason it is added to several fertilizers (Adriano, 2001; Xiaorong et al., 2007).

The environmental toxicological perspective is different. Even though Cu is essential for several organisms, low concentrations of Cu can have harmful effects on the ecosystem by affecting bacteria, algae, fungi, plants, fish, and invertebrates, particularly in aquatic systems (Castilla, 1996; Erickson et al., 1996; Santore et al., 2001; Li et al., 2008b; Rofkar et al., 2014). Several investigations and the reviews of Flemming and Trevors have shown that cupric copper (Cu^{2+}) in particular, and the $CuOH^{+}$ and $[Cu_2(OH)_2]^{2+}$ complex ions are toxic Cu species (Pagenkopf, 1983; Flemming and Trevors, 1989; United States Environmental Protection Agency, 2008). They can interact negatively with essential proteins, enzymes, and nucleic acids at the cell wall, cell membrane, and within such microorganisms as algae, fungi, and bacteria. In addition, exposure to Cu can affect the regeneration of essential inorganic nutrients, inhibit growth and cell division, and inhibit photosynthesis, particularly for algae, cyanobacteria, and aquatic plants. This can have devastating effects on aquatic ecosystems since microorganisms are important primary decomposers of hazardous compounds that are hostile to life. These microorganisms are important also for their ability to regenerate inorganic nutrients; they are necessary primary producers of essential nutrients and oxygen (McBrien and Hassall, 1967; Swift et al., 1979; Kobayashi and Rittmann, 1982; Stauber and Florence, 1987; Flemming and Trevors, 1989; Chaudhry and Chapalamadugu, 1991; Rofkar et al., 2014). Even a single exposure to 10 µg Cu/L leads to a significant, though reversible, reduction in algal biomass and chlorophyll, with negative consequences for photosynthesis. These impacts were not reversible at a test concentration of 40 µg Cu/L (Elder and Horne, 1978; Flemming and Trevors, 1989). Furthermore, a $Cu(SO)_4$ concentration of 10 µg/L results in a significant decrease in the number of viable bacteria (Effler et al., 1980). The amphipod *Hyalella azteca* showed a LC_{50} of 31 µg/L (Ankley et al., 1993). In addition, for juvenile salmon weighing between 200 mg and 340 mg, the LC_{50} values (24 hour) for concentrations ranging from 3.59 to 29.9 µg/L were investigated. Comparable LC_{50} values (24 hours) from 22.8 to 115.7 µg/L were determined for juvenile rainbow trout weighing 600 mg (Buhl and Hamilton, 1990). In addition, a fish toxicity test was conducted with juvenile white sturgeon at two life stages, 8 days post hatch and 40 days post hatch. The median LC_{50} values ranged from 9 to 25 µg Cu/L (Vardy et al., 2014). These LC_{50} values emphasize that fish are highly susceptible to Cu. In fish and other aquatic vertebrates, copper binds to the gill membranes and can cause damage to and interfere with osmoregulatory processes (United States Environmental Protection Agency, 2008). From an environmental toxicological point of view, a chronic environmental quality standard (AA-EQS) of 1µg Cu/L is recommended (Table 5; UK Technical UK Technical Advisory Group on the Water Framework Directive, 2012).

Group A: Lead (Pb)

Introduction

The main host mineral of lead is galena (PbS), which contains about 86.6% lead. Other relevant minerals containing lead are cerussite ($PbCO_3$) and anglesite ($PbSO_4$) (Shukla and Leland, 1973). Often, Pb is found in ores together with Ag (silver), Zn, and Cu (Commonwealth of Australia, 2015). The average concentration of Pb in the Earth's crust ranges from 13 to 26 ppm. Although this amount is relatively low, Pb is not considered to be a rare element because it is easily extracted from ore and easily refined (Zimdahl et al., 1973; Salomons and Förstner, 1984; World Health Organization, 2011; Thomas Jefferson National Accelerator Facility, 2014).

With its high density, malleability, resistance to corrosion (though it does tarnish when exposed to air), low melting point, ease of fabrication, resistance to acid, and its photovoltaic activities, Pb has a wide variety of applications. In ancient times, it was used for making water pipelines, as a building material, and in glazes on ceramics. It was used for color pigments in paints and cosmetics, for armor, and as weights for fishing nets (Commonwealth of Australia, 2015; United States Geological Survey, 2011). Nowadays, Pb is used mostly in lead–acid batteries for vehicles and in industrial-type batteries (Bode, 1977; World Health Organization, 2011; United States Geological Survey, 2013; Commonwealth of Australia, 2015). In addition, Pb and Pb compounds are used for ammunition, to cover cables, in alloys, as additives in bronze and brass production, in the glass and ceramic industry, and in the construction material in the form of sheet lead. Furthermore, it is a shield for x-rays and is used as a noise control material. Lead compounds are employed as coatings for the paper used in photothermography, as stabilizers in plastic, and as vulcanizing agents in rubber and plastics. A few centuries ago it was used in paints and in plumbing material; now less toxic substitutes are used (Agency for Toxic Substances and Disease Registry, 2007b; National Toxicology Program, 2014b; World Health Organization, 2011). Organic lead compounds, like tetramethyllead and tetraethyllead, were used extensively in gasoline as anti-knocking agents from 1992 until the end of the 19th century, when the user of organic Pb compounds was banned. The addition of organic Pb compounds to gasoline resulted in a significant global increase in Pb emissions from car exhaust fumes into the environment (Nriagu, 1990b; von Storch et al., 2003). In low- and middle-income countries, especially in Africa, the enforcement of the ban on organic lead compounds as an anti-knocking agent was delayed. However now, the use of lead compounds in gasoline has been reduced worldwide (United Nations Environment Programme, 1998b; Phiri, 2006). To meet the constantly growing demand for Pb, 5.2 million tonne of Pb were extracted by mining in 2012. Compared to 2011, the production of lead worldwide increased by nearly 10% (United States Geological Survey, 2013).

Today, the main entry pathways for lead into the environment are waste effluents and aerosols that are released into the environment from lead recycling processes, from lead-acid batteries, and the recycling of other e-waste and scrap. Smelters, foundries, and other industrial processes, such as the production of plastic and rubber, the burning of coal (Tang et al., 2008), weapon and ammunition production, and ceramic and glass manufacturing, can emit high amounts of Pb into the environment as well. This is especially the case if no appropriate filter systems are used during the heating and smelting processes. Other significant sources of Pb are mining activities and the extraction of Pb, Ag, Zn, and Cu ores (Agency for Toxic Substances and Disease Registry, 2007b).

Environmental behavior and occurrence

Pb occurs rarely in its elemental state, Pb(0). It is more likely to be present in its bivalent form, Pb(II) (Agency for Toxic Substances and Disease Registry, 2007b). In general, lead accumulates in plants, algae, invertebrates, and vertebrates (Bowen, 1966; Cox and Rains, 1972; Spehar et al., 1978; Freeman et al., 1992; Namihira et al., 1993; Adriano, 2001; Luoma and Rainbow, 2008). The distribution of lead and other metals and transition metals in the matrices of the environment and its uptake by biota depend on several factors. These include pH, redox potential, concentration of chelating agents, soil composition, chemical composition of the metallic compound, and the hardness of the water (Adriano, 2001). In general, low pH and low redox potential increase the mobility of Pb in water, and its solubility depends on the chemical composition as well (Adriano, 2001). In soils with low pH (from 3 to 5), PbO showed the highest solubility in water; $PbCO_3$ and $PbSO_4$ are less soluble (in descending order of solubility). At pH 7, $PbSO_4$ is the most soluble Pb compound and PbO and $PbCO_3$ become less water soluble (in descending order of solubility; Cao et al., 2008). This solubility promotes the leaching of Pb from tailings and soils. Acid mine drainage contributes as well (Vymazal, 1990). Lead compounds, such as lead acetate, lead nitrate, and lead chloride are soluble or miscible with water. Lead arsenate, lead acids, halogenated lead compounds, lead thiocyanates, lead phosphates, and lead sulfates are Pb compounds with lower solubilities (National Toxicology Program 2014b).

The natural level of lead in freshwater is 3 µg/L and in freshwater sediments it is 40 µg/g. Soils have a background content of about 10 ppm (Vymazal, 1990).

Elevated Pb concentrations of environmental concern, ranging from 71 to 2190 ppm in dry stream sediments have been found at the recent mining site of Villa de la Paz-Matehuala, Mexico (Razo et al., 2004). Lin et al. (2007) investigated the chemical dynamics and environmental toxicity of a river, located in a tributary basin area of the Pearl River in China, affected by AMD. In this instance, the AMD was induced by a flood event which occurs periodically every 100 years. In floodwater samples near the Dabaoshan mine, Pb concentrations of between 0.7 and 7.2 mg/L were measured 3.5 km from the point source. Elevated Pb concentrations up to 0.2 mg/L were measured 16 km from the point source (Lin et al., 2007). In soil samples at the Chenzhou lead/zinc mine, Pb concentrations of up to 1061.54 mg/kg were measured (Liu et al., 2005). In this region, the Pb concentrations were 1.91 ppm in maize, 4.58 ppm in capsicum, and 9.00 ppm in taro. Elevated Pb concentrations of 1.399 mg/L were measured in the Pilcomayo River in Argentina and levels of 2.201 mg/L were found in the Tarapaya River in Bolivia. This contamination originates from the extensive mining in these areas (International Agency for Research on Cancer, 2006b). The results show that although most of the studies about the consequences of AMD and the distribution of heavy metals from tailings were conducted in higher-income countries (USA, Canada, and Europe), considerable concentrations of hazardous compounds and metals from mining are found in low- and middle-income countries as well. This is especially the case where obsolete techniques are used for ore extraction and metal processing and if wastes, tailings, and the closing of mines are poorly managed.

Chronic exposure to higher concentrations of Pb, mainly from occupational exposure or living close to smelters, metal processing and recycling industries, lead–acid battery manufactories, and mining areas, may result in an accumulation of Pb in the liver, lungs, spleen, kidneys, bone marrow, bones, teeth, and even the brain.

Toxicity

Occupational exposure, and the exposure of humans and other animals, to industrial estates and metalworking industries, lead or other metals, remain a seriously disputed issue. This is particularly so in low- and middle-income countries and even in HICs (Staudinger and Roth, 1998; Tong et al., 2000). The IARC lists inorganic Pb compounds in Group 2A as probable human carcinogens. Organic lead compounds were classified in Group 3 as not being carcinogenic to humans (International Agency for Research on Cancer, 2006b). This categorization shows that inorganic Pb compounds have a higher toxicity than organic ones. According to the US EPA, the MCL for drinking water is about 0.015 mg/L (Table 5). The low value of this limit indicates that an exposure to lead compounds in the long term has adverse effects on human health. Children and pregnant women seem to be most susceptible (United States Environmental Protection Agency, 2015c; World Health Organization, 2011). Also, Pb is not beneficial to plants, animals, and humans (Adriano, 2001). Pb can enter the blood stream from the alveoli by inhaling lead dust or fumes and it can enter the intestine by ingesting contaminated food and water. Lead is discharged from the body in urine and feces (Agency for Toxic Substances and Disease Registry, 2007b; World Health Organization, 2011). The circulation of the blood distributes the Pb throughout the whole body (Ong and Lee, 1980; World Health Organization, 2011). Chronic exposure to higher concentrations of Pb, mainly from occupational exposure or living close to smelters, metal processing and recycling industries, lead–acid battery manufactories, and mining areas, may result in an accumulation of Pb in the liver, lungs, spleen, kidneys, bone marrow, bones, teeth, and even the brain (Agency for Toxic Substances and Disease Registry, 2007b). According to several investigations, Pb is suspected to cause the formation of several forms of cancer, especially in the lungs, kidney, and brain, though there are converse results as well (Steenland and Boffetta, 2000; World Health Organization, 2011). Hartwig (1994) showed there is evidence that exposure to Pb in vitro can enhance the mutagenicity of other mutagens by inhibiting the repair of DNA. In addition, increased chromosome aberrations or sister chromatid exchanges were found in exposed workers (Mäki-Paakkanen et al., 1981). Lead has adverse neurological effects on humans and other mammals. Significant behavioral and cognitive deficits, such as malfunctions in activity, adaptability, attention, reduced memory and learning ability, up to irreparable mental retardation, are observed after continuous exposure to Pb (Horn Rummo et al., 1979; Gilbert and Rice, 1987; Schwartz and Otto, 1987). WHO recommends not exceeding an ADI of 250 µg for a 70 kg adult. Globally, the limit for drinking water should not exceed 10 µg/L and that for air should not exceed 0.5 µg/m^3 (World Health Organization, 2010a). Keeping the level of lead in the blood below between 10 and 20 µg/100 ml would prevent lead poisoning or problems in neuropsychological development, especially for children (United Nations Environment Programme, 1998a; Gidlow, 2004).

From an environmental toxicological point of view, Pb affects the health of vertebrates and primary producers as well. For instance, rainbow trout were significantly affected after exposure to dissolved lead. In toxicity tests in hard and soft water, they showed an LC_{50} (96 hour) ranging from 1.17 to 1.47 mg/L. In addition, chronic exposure (6–7 month) to 0.064 mg/L Pb enhanced the formation of physical abnormalities in fingerling rainbow trout (83 mm length). At this concentration, the tail of the tested rainbow trout turned black. A month later, the trout exhibited spinal curvature as a result of dorsal-ventral spinal flexures (lordosis), and/or bi-lateral spinal flexures, described as scoliosis and degeneration of the caudal fin. The formation of these abnormalities can be explained as direct or indirect influences on the central nervous system or biochemical inhibition in the metabolism (Davies et al., 1976).

Plants are capable of taking up and accumulating Pb as well (Deng et al., 2004; Rotkittikhun et al., 2006). In general, the roots are able to accumulate the most Pb, followed by the leaves, stem, inflorescence, and seeds, in descending order. This order can differ between individual plant species (Antosiewicz, 1992). Lead uptake can lead to several adverse effects, such as inhibition of enzymatic activities and photosynthesis, disturbance of the uptake of essential minerals and nutrients, and impairment of membrane permeability. These problems lead to inhibition of root growth, stunted growth of the plant in general, and even chlorosis (Burton et al., 1984; Sharma and Dubey, 2005). For instance, after a 20 day exposure of rice seedlings to 103.6 and 207.2 mg $Pb(NO_3)_2$/L, root growth was inhibited by 22 to 42% and shoot growth was reduced by 25% compared to a control without exposure to Pb (Verma and Dubey, 2003). For the algae (diatom) *Phaeodactylum tricornutum*, short-term exposure to 7.5 mg Pb/L caused complete inhibition of photosynthesis (Woolery and Lewin, 1976). The chlorophyte *Chlamydomonas reinhardii* seemed to be more resistant to exposure to Pb, showing a 47% reduction in growth after exposure for 48 hours to 0.207 mg Pb/L (Irmer, 1985). According to the estimated chronic environmental quality standard, a concentration above 0.0012 mg/L (Table 5) in the long term can impair the health of aquatic organisms (European Parliament and Council of the European Union, 2013).

The uptake of lead can have several adverse effects for plants, leading to inhibition of root growth, stunted growth of the plant in general, and even chlorosis.

Group A: Manganese (Mn)

Introduction

Manganese appears as a whitish-grey metal, mainly in coexistence with iron (Fe). Because of that, they are similar in their chemical behaviors. It has a melting point around 1255°C and it oxidizes in air and rusts under humid conditions. While it is harder than Fe, it is relatively brittle. Principally, it is deposited as manganese nodules on the ocean floor and the floors of freshwater lakes (Post, 1999). It is distributed and deposited in metamorphic, sedimentary, and igneous rocks in tropical, subtropical, and the warmer temperate zones of the Earth (Post, 1999). The main minerals of manganese are oxides, carbonates, and silicates – pyrolusite (MnO_2), rhodochrosite ($MnCO_3$), magnetite ($MnO_3 * H_2O$), hausmannite (Mn_3O_4), braunite ($3Mn_2O_3 * MnSiO_3$), and rhodonite ($MnSiO_3$). Manganese minerals are well distributed around the globe and occur frequently, with an average concentration in the Earth's crust of 1000 ppm (Salomons and Förstner, 1984; Adriano, 2001).

Manganese is used mainly as an additive during steel production. As an alloy, together with metals like chromium, aluminum, and zinc, it acts as an anti-corrosive agent during the production of stainless steel and provides strength, toughness, and hardness (Adriano, 2001; International Manganese Institute, 2014). Given its metallurgical properties, it is used in the production of several alloys of steel, aluminum, and copper. Additionally, Mn is used for non-metallurgical purposes as well. For instance, it is used in the production of alkaline batteries, electronic coils, matches and fireworks, welding rods, as a dye in paints, and in the ceramic or glass industry (as a decolorizer or as a pigment). Furthermore, Mn compounds are found in paints, varnishes, and oils as drying agents. They are used as disinfectants, animal food additives, and as bleaching agents in the textile industry and in the tanning of leather. Manganese oxides and Mn chlorides are used in dry cell batteries and as catalysts. Organic Mn compounds (methylcyclopentadienyl manganese tricarbonyl – MMT) are used as an anti-knock agent in fuels as substitutes for methylated Pb compounds, as fungicides (e.g. maneb and mancozeb), and they are contained in contrast agents used in resonance imaging (Adriano, 2001; Santamaria, 2008; United States Geological Survey, 2013). Manganese is the fourth most widely used metal in the world. For instance in 2011, worldwide production of manganese alloys was 17.7 million tonne (International Manganese Institute, 2014).

Manganese is mainly released into the environment from mining activities, manufacturing and metal processing activities, and as an anti-knock agent in fossil fuels. Its toxicity is less pronounced than that of other metals like Pb, Cd, Hg, and Cr (Santamaria, 2008).

Environmental behavior and occurrence

Overexposure to Mn can have an adverse effect on humans and can affect the health of other animals. Once Mn has passed through the blood–brain barrier, it causes neurodegenerative impairment resulting in syndromes comparable to those of idiopathic Parkinson's disease.

Manganese can be found in oxidation states I, II, III, IV, VI, VII. Generally, in nature, salts with the oxidation states II, IV, VI, and VII are the most stable. MnO, $MnCO_3$, and Mn_2O_3, with lower atomicity (II-III), are alkaline and Mn compounds with higher oxidation states are acidic (Adriano, 2001). The oxidized form Mn(II) is very stable in an acidic milieu and MnO_2 is more stable under basic conditions in the presence of oxygen. Divalent Mn is less likely to form complexes with other ligands, whereas Mn(III) can form complexes with phosphorus compounds and with other organic compounds (Adriano, 2001; Santos-Burgoa et al., 2001; Yakushev et al., 2009).

In general, the biogeochemistry of Mn is quite complex, mainly because of its occurrence in several oxidation states and because Mn oxides can occur in crystalline or pseudocrystalline forms. In addition, the oxides are often coexistent with Fe oxides. Iron and Mn hydroxides show amphoteric characteristics, which means that they can act as a base or as an acid by having the tendency to react with both cations and anions. Microbiological activities and physical and chemical factors control the oxidation-reduction reactions of Mn compounds. For plants, the uptake of Mn(II), organic Mn compounds, Mn oxides, and soluble Mn silicates seems to be of highest relevance. Especially at lower pH values, lower redox potentials, and under reducing (anaerobic) conditions, Mn is more soluble and more available for uptake via roots (Boxma and De Groot, 1985; Brookins, 1988; Patrick and Jugsujinda, 1992; Adriano, 2001).

Mn occurs naturally in soils at levels around 1000 ppm (Salomons and Förstner, 1984; Adriano, 2001). However, elevated Mn contamination can be found in water or soil samples in low- and middle-income countries in areas with high levels of mining activity. For instance, investigations in a Mn mining district in central Mexico showed elevated environmental mean concentrations of 45.34 mg Mn/L (maximum, 240.25 mg Mn/L) in river water samples, 119.25 mg Mn/kg (maximum, 264.00 mg Mn/kg) in soil samples, 39.95 mg Mn/L (maximum, 241.90 mg Mn/L) in well water, and 20.2 mg Mn/ dry kg (maximum, 52.5 mg Mn/ dry kg) in ready to eat food (Santos-Burgoa et al., 2001). In the Lipu manganese mine area in Guangxi, South China, elevated environmental concentrations of Mn and other heavy metals were found as well. There, in an area of bare mining land with tailings, soil concentrations up to 10,000 mg Mn/kg (ppm) were reached. An adjacent region showed elevated concentrations up to 7600 mg Mn/kg (ppm). In an adjacent restored mining area with an artificial chestnut forest and a dense shrub belt, elevated Mn concentrations of around 2000 ppm were measured. In addition, the results indicate that plants are embedding considerable amounts of Mn, particularly in their roots and leaves. In 12 dominant species in the Lipu Mn mine district, concentrations of 17.4 to 816.5 mg Mn/kg (ppm) were found in the roots and levels of from 89.2 to 3280.0 mg Mn/kg (ppm) were measured in the leaves (Li et al., 2007).

Toxicity

For human beings and other animals, the uptake of Mn is essential to guarantee normal development and body function (Keen et al., 2000). Mn binds to enzymes and controls enzymatic reactions. For instance, Mn acts as a fundamental co-factor for arginase, which enables urea production in the liver, and it is involved in enzymatic processes that reduce cellular oxidative stress (Carl et al., 1993; Keen et al., 2000; Crossgrove and Zheng, 2004). However, overexposure to Mn can have an adverse effect on humans and can affect the health of other animals. Once Mn has passed through the blood–brain barrier, it causes neurodegenerative impairment resulting in syndromes comparable to those of idiopathic Parkinson's disease (IPD; Barbeau, 1984; Cowan et al., 2009). Besides these impairments to the central nervous system, there is evidence from human and animal studies that overexposure to Mn can lead to interference with the function of the lungs, cardiac system, and liver. In addition, it can cause impairments to reproduction by decreasing fertility, increasing the formation of fetal abnormalities, and inhibiting fetal development (Crossgrove and Zheng, 2004). The main clinical symptoms of an overexposure to Mn are headaches and insomnia (86%), exaggerated tendon reflexes (83%), memory loss (75%), hyper-myotonia (75%), emotional instability (35%), hand tremor (23%), speech disturbances (6%), and festinating gait (3%; Crossgrove and Zheng, 2004).

The uptake of Mn occurs mainly through inhalation at ore exploiting areas, steel production, smelting, and battery manufacturing sites, or by ingesting contaminated food or water (Santamaria, 2008). Given its toxicity, WHO recommends a limiting value of 0.4 mg Mn/L for drinking water and has set the tolerable daily intake (TDI) at 0.06 mg Mn/kg of body weight. It should be noted that workers have shown significant clinical effects of Mn toxicity following continuous exposure to Mn concentrations higher than 5 mg/m^3 (Whitlock Jr et al., 1966; Cook et al., 1974; World Health Organization, 2004; Santamaria, 2008).

In plants, manganese is an essential micronutrient that is required for several functions. Plant respiration and the metabolizing of organic acids, P, and N depend on the availability of Mn. Furthermore, Mn is involved in the photosynthetic formation of oxygen in chloroplast (Römheld and Marschner, 1991). It is involved in protein synthesis, the control of the carboxylic acid cycle, and the metabolizing of carbohydrates (Adriano, 2001). Although Mn is essential for plants, human beings, and other ani- mals, it is one of the major factors limiting crop production, particularly on acidic soils. About 30% of the crops on the world's total land area are affected by Mn toxicity (Kochian, 2000; Alam et al., 2006). Furthermore, it has been shown that concentrations in plant tissues of from 100 to 500 mg/kg dry weight are enough to cause toxic effects (Jones, 1991; Adriano, 2001). As a consequence of overexposure of Mn, plants exhibit such symptoms as chlorosis, necrosis of leaves, leaf rolling, and inhibited plant growth. From the environmental toxicological point of view, the estimated AA-EQS of Mn was 0.123mg/L (Table 5; UK Technical Advisory Group on the Water Framework Directive, 2012). Therefore, although Mn is essential for all living organisms and it is not considered in many toxicological assessments (for instance, there is no US EPA MCL value for Mn), overexposure can cause significant toxic affects to plants, mammals, and humans.

About 30% of the crops on the world's total land area are affected by Mn toxicity.

Group A: Mercury (Hg)

Introduction

Elemental Hg appears as a silvery white metal and it is the only metal which is liquid at room temperature (Morel et al., 1998). In mining, the sulfide cinnabar (86.2% Hg) is most relevant, and other minerals, like metacinnabar and livingstone are less important exploitation sources for Hg. The average concentration of this transition metal in the Earth's crust ranges from 50 to 80 ppb (Fleischer, 1970; Salomons and Förstner, 1984; Adriano, 2001; Dong et al., 2013).

Mercury is used in many fields. Today, it is used primarily to extract gold and silver using the amalgam process during artisanal and small-scale mining operations (Farrell et al., 2004; Artisanal Gold Council 2015). The Artisanal Gold Council determined that 1620 tonne of Hg were used in artisanal gold mining in 2010 (Artisanal Gold Council 2015). In addition, it is used in high volumes as a catalyst during vinyl chloride monomer production and in the production of chlorine and sodium hydroxide using the chlorine-alkali process. Nowadays, especially in HICs, the more modern diaphragm and membrane method substitutes for the chlorine-alkali process (Pacyna et al., 2006; Swain et al., 2007). Mercury is used in the pulp and paper industry as a slimicide. Furthermore, old fluorescent lamps, batteries, dental amalgam fillings, paints, cosmetic products, antifungal agents for preserving wood, and pesticides can contain mercury. In HICs, the use of mercury has been reduced by finding alternative and equivalent substitutes. For instance, instead of amalgam, plastic and ceramic inlays now are used in dentistry. Fluorescent lamps containing Hg have been replaced by light-emitting diodes using indium or lithium. Nickel–cadmium and zinc–air batteries are substitutes for mercury–zinc ones. Digital thermometers or ones containing new alloys (galistan) are replacing ones containing mercury (United States Geological Survey, 2013). Medical and electronic devices and specific parts of cars (car switches) can contain small quantities of mercury (de Lacerda and Salomons, 1998; Adriano, 2001; United States Geological Survey, 2013). Although the use of mercury has decreased in HICs, it can be assumed that large amounts of mercury are still used in low- and middle-income countries. It has been shown that mercury has a net flow from higher-income to lower-income countries, because in the latter its use in the industrial and the mining sector is less constrained. Also it can be contained in electronic waste which is disposed of inappropriately in low- and middle-income countries (Maxson, 2005; Swain et al., 2007; International Labour Organization, 2012). To meet demand, 1600 tonne of mercury were mined in 2012, while additional mercury is produced from secondary recycling processes (United States Geological Survey, 2013).

Altogether, the highest global anthropogenic release of mercury into the environment is about 1960 t/year. This comes from artisanal gold mining (727 t/year), coal and oil combustion (483.9 t/year), non-ferrous metal production (193 t/year), cement production (173 t/year), large-scale gold production (97.3 t/year), waste disposal (95.6 t/year), emissions from contaminated sites (82.5 t/year), ferrous metal production (45.5 t/year), caustic soda production through chlorine-alkali processes (28.4 t/year), oil refining (16 t/year), and mercury mining production (11.7 t/year; United Nations Environment Programme, 2013a)

Environmental behavior and occurrence

Mercury is an omnipresent environmental pollutant of high concern, having natural and anthropogenic sources.

Mercury is an omnipresent environmental pollutant of high concern.

In the environment, Hg has three different oxidation states. It occurs as elementary Hg(0), as oxidized Hg(I) (mercurous Hg), and as Hg(II) (mercuric Hg; Adriano, 2001). Mercury is remarkable in that it can evaporate directly from water into the atmosphere, mainly as Hg(0). It can sublimate directly from solids and it occurs as inorganic salts, organic complexes, and as methylated compounds.

About 5000 t/year are stored annually in the atmosphere. The land stores about 1 million tonne and about 2.88 million t/year are deposited in the oceans (Swain et al., 2007). Given its physicochemical properties, such as its vapor pressure of 0.163 Pa at 20°C, its low melting point of -38.8 °C, and its water solubility of 60 µg/L (25°C), mercury has little tendency to dissolve in water and it is more likely to evaporate as elemental Hg or to be deposited in sediments, adsorbed to organic particles or absorbed by biota (Morel et al., 1998; Adriano, 2001).

There is evidence that Hg, particularly in the form of methylated Hg compounds, is accumulating among the food chain through biomagnification.

The partition of Hg among the different environmental compartments is quite complex and there are still some gaps in the knowledge. Elemental Hg (Hg(0)) evaporates from water and sediments and it is released into the air mainly from anthropogenic processes, such as artisanal gold mining and the combustion of fossil fuels. Mercury has a residence time in the atmosphere of about 1 year and it is distributed globally. In the atmosphere, Hg is oxidized slowly to Hg(II), with ozone (O_3) acting as the main oxidizer. Once oxidized, Hg(II) is scavenged from the atmosphere through precipitation or through adsorption to aerosol particles. Because of its long residence time in the atmosphere, its global distribution and subsequent precipitation, Hg can reach considerable concentrations in water and biota even in remote regions without any anthropogenic activity or natural deposits (Hall, 1995; Fitzgerald et al., 1998).

In aquatic systems, Hg(II) can be reduced to Hg(0) and evaporate because of such processes as photo-reduction. It can be present marginally as dissolved inorganic salts (chlorides or hydroxides), as organic complexes, or in the sediments. Under anaerobic conditions, it is precipitated as sulfides (HgS) and methyl groups are added according to bacterial or chemical methylation processes to form methyl mercury (MeHg), dimethyl mercury (Me_2Hg), or ethyl mercury (EtHg). The addition of these methyl groups significantly increases Hg's availability to biota; elemental Hg and the inorganic compounds are less bioavailable (Weber, 1993; Morel et al., 1998).

In low- and middle-income countries, Hg is released into the environment in part through the combustion of fossil fuels, but more significantly from its use in artisanal mining. It is used in this activity as a potent and relatively cheap agent for extracting gold via the amalgamation process. For instance, in North Sulawesi, Indonesia, in the Talawaan watershed where there is extensive artisanal gold mining, high concentrations of Hg were found in sediments, water systems, and aquatic species. Water samples of the Talawaan River contained maximum concentrations up to 0.014 mg Hg/L. These values exceed the EPA MCL for mercury in drinking water of 0.002 mg/L (United States Environmental Protection Agency, 2015c) by a factor of 7. In sediments, concentrations up to 22 mg/kg were found (Limbong et al., 2003). At the Wuchuan Hg mining site, Guizhou, China, high concentrations of between 79 and 710 mg Hg/kg were measured in mine wastes. In soils, concentrations ranging from 0.33 to 320 mg Hg/kg were found and water samples contained Hg concentrations up to 360 ng/L. A high average Hg concentration of 0.26 mg/kg was found in the vegetation. This amount exceeds the Hg concentration of 0.02 mg/kg recommended by the Chinese National Standard Agency for food sources (Qiu et al., 2006). In soils all over the world, the average Hg levels range between 0.58 and 1.8 mg/kg (Kabata-Pendias, 2010).

There is a body of evidence that Hg, particularly in the form of methylated Hg compounds, is accumulating among the food chain through biomagnification (Fergusson, 1990; Renzoni et al., 1998; Marrugo-Negrete et al., 2008). It has been shown that there is a positive correlation between increasing Hg concentrations in sediments and the amounts of Hg found in aquatic invertebrates and vertebrates. Generally, methylated Hg compounds accumulate mainly in the liver, kidney, brain, and muscles of benthic and predatory pelagic species. Because of this, these species represent the main sources of methyl Hg for humans (Renzoni et al., 1998). Eating fish and seafood with elevated levels of mercury causes adverse effects to human life (Harada, 1995; Castilhos et al., 2006). In addition, a positive correlation was found between the number of seafood meals eaten and the total mercury levels found in human hair (Harada, 1995; Renzoni et al., 1998; Olivero et al., 2002). According to a human health risk study, mercury concentrations in freshwater fish were investigated in the Tatelu region in Indonesia. In 154 fish of 10 freshwater species, a mean concentration of 0.58 ± 0.44 mg Hg/kg (wet weight) was measured. This is above the WHO guideline (World Health Organization and United Nations Environment Programme, 2008) of 0.5 mg Hg/kg in fish for human consumption (Castilhos et al., 2006). In the Talawaan watershed, nine of 47 fish muscle samples exceeded the safety level set for the international human consumption advisory limit (World Health Organization and United Nations Environment Programme, 2008). The highest concentration measured in fish in this region was 3.2 mg/kg (Limbong et al., 2003). In the Mojana region of Colombia, where gold mining activities are high, elevated concentrations of Hg, ranging from 0.043 to 0.512 mg/kg, were measured in different fish species. This is increasing the risk of mercury poisoning of the regional inhabitants for whom fish is part of their regular diet (Marrugo-Negrete et al., 2008). The elevated levels of mercury in fish indicate the high potency of Hg for bioaccumulation and biomagnification throughout the food chain.

The uptake of mercury into plants is relatively low; usually the natural mercury concentrations in plants are on a parts per billion level. The roots are usually the most predominant part for Hg accumulation, followed by the stems and leaves. According to one study of five arid-land riparian plants, between 2 and 11% of the mercury to which the plants were exposed was accumulated in the roots, between 0.2 and 3.36% in the stem, and between 0.3 and 0.94% in the leaves (Leonard et al., 1998). The level of Hg in the soil ranged from 23.8 to 53.5 mg/kg. It has been shown that plants can act as conduits for the interfacial transport of Hg from the geosphere to the atmosphere as a result of the uptake of Hg by the roots and assimilation of Hg(0) through stomata (Leonard et al., 1998). Additionally, it has been demonstrated that the uptake of organic Hg compounds is more prevalent than the uptake of inorganic ones (Huckabee and Blaylock, 1973).

Toxicity

Since the link was made that methylated mercury compounds were responsible for causing severe neurological disease in human in the Minamata area of Kyushu, the toxicity of mercury has been studied comprehensively (Harada, 1978). Given its high toxicity, the US EPA set the MCL of mercury in drinking water at 2 µg/L (Table 5) to protect public health (United States Environmental Protection Agency, 2015c). Also, mercury is a non-essential trace metal for plants and other biota (Adriano, 2001).

Generally, Hg(0) enters the human body as a result of ingesting pollutants in the workplace. Inorganic and methylated Hg compounds enter the human body as a result of consuming contaminated food and drinking water. After the pulmonary uptake of Hg(0), it is rapidly distributed within the body where it can cross both the placenta and the blood–brain barriers. If it is then oxidized to the mercuric ion, Hg(II), it will remain in the brain or placenta affecting human and fetal health. Non-oxidized Hg can be released from the body through exhalation, urine, sweat, saliva, or feces. The uptake of Hg(0) via the gastrointestinal (GI) tract is negligible, but between 7 and 15% of inorganic mercury compounds and from 90 to 95% of methylated mercury compounds are absorbed via the GI tract (Keating et al., 1997; Wolfe et al., 1998; Adriano, 2001). Inorganic Hg compounds have less of a tendency to pass the placenta and the blood–brain barriers, but methylated mercury compounds can easily pass through them. After gastrointestinal uptake, MeHg compounds bind to glutathione, cysteine, and other sulfhydryl-containing ligands that are secreted in the bile. Then these Hg compounds are reabsorbed in the gut entering the blood cycle. Here 90% are absorbed into the red blood cells and 10% are contained in the plasma. The binding of mercury to ligands with sulfhydryl groups promotes the transfer of MeHg compounds to the brain and throughout the placenta. The biological half-life of MeHg compounds in humans ranges from 44 to 80 days which can cause an accumulation of Hg in the human body. The ingested MeHg can be partly excreted through feces, breast milk, and urine (Adriano, 2001).

In humans and other animals mercury is a neurotoxin. Even at low doses it causes impairment of the nervous system. Typical symptoms of mercury poisoning are malfunctions of peripheral vision, numbness in the hands and feet, impairment of speech, hearing, and walking, mental degradation, and kidney damage. This is particularly the case for children born of mothers who have been exposed to mercury. Such children are very vulnerable and likely to suffer from mercury poisoning diseases, such as ataxia, constriction of the visual field, congenital cerebral palsy, and mental retardation (Agency for Toxic Substances and Disease Registry, 1999).

As well as humans, wildlife and the environment also show adverse effects from exposure to mercury. For instance, dietary concentrations of 4 to 5 ppm MeHg were lethal to small carnivores, like minks and ferrets, within 26 to 58 days (Wren et al., 1986; 1988). In some bird species, uptake by ingesting about 2 to 9 ppm is enough to cause impairments in reproduction. These are manifest as an increase in the number of shell-less eggs laid, decreases in the mean egg weight (Borg et al., 1970), and a decrease in egg production in general (Heinz, 1974). For different freshwater and marine algae species, Hg concentrations at a level of 0.1 ppm cause inhibition of growth. For the algae tested, inorganic mercury compounds seemed to be more toxic than the methylated ones (Hannan and Patouillet, 1972; International Agency for Research on Cancer, 2015). At the moment, no chronic environmental standard (AA-EQS) for aquatic organisms has been proposed.

Plants can act as conduits for the interfacial transport of Hg from the geosphere to the atmosphere.

In humans and other animals mercury is a neurotoxin. Even at low doses it causes impairment of the nervous system.

Group A: Thallium (Tl)

Introduction

Thallium (Tl) is a soft, malleable, bluish-white, non-essential metal. Thallium is contained mainly in potash minerals, in sulfides, in the ores of zinc, copper, and lead, and in coal (Kazantzis, 2000; Peter and Viraraghavan, 2005). The sulfide minerals lorandite and crooksite contain up to 60% Tl. Other sulfide minerals, like carlinite, christite, ellisite, weissbergite, galkhaite, vrbaite, and hutchinsonite, contain Tl as well (Peter and Viraraghavan, 2005). In nature, Tl can coexist with other substances like bromine, chorine, fluorine, and iodine and it can be found in sulfide minerals, which are used in gold (Au), Cu, Pb, Zn, and uranium mining (Twidwell and Williams-Beam, 2002). Thallium is found in the Earth's crust at concentrations ranging from 0.1 to 1.7 ppm (Kazantzis, 2000; Peter and Viraraghavan, 2005). In addition, granite and shale contain high amounts of Tl. This is especially so for shale and coal of the Jurassic period which contain highly elevated Tl concentrations – up to 1000 ppm (Smith and Carson, 1977).

In the past, Tl was used intensively in the agricultural and the medical sectors. Until the beginning of the 20th century, Tl salts were used widely to treat tuberculosis, venereal diseases, such as gonorrhea and syphilis, and malaria (DelValls et al., 1999; Kazantzis, 2000; Cvjetko et al., 2010). In addition, it was used as a depilatory in the treatment of ringworm of the scalp (Felden, 1928; Peter and Viraraghavan, 2005). Now, its use has been almost entirely abandoned in the medical sector because of its high acute toxicity (Léonard and Gerber, 1997). In agriculture and in private households, Tl salts were used extensively as insecticides and as a poison for rodents. Although, today, the use of Tl salts as pesticides (mainly thallium sulfates) has been banned in most countries because of their high acute toxicity, these salts are still in use in several low- and middle-income countries (Nriagu, 1998; Kazantzis, 2000)

Thallium is used mainly in the electronics, high-technology, and optical industries.

Nowadays, Tl is used mainly in the electronics, high-technology, and optical industries. It is used in low-temperature thermometers together with mercury and in scintillation counters, which are used to detect and quantify gamma radiation. It is used (together with Ca, Ba, Cu, and O_2) in electronic devices in the semiconductor and superconductor industries, in laser equipment (for medical imaging), in optical fiberglass, in optical lenses, in photovoltaic cells, and in infrared spectrometers (Zitko, 1975; Switzer, 1986; Galván-Arzate and Santamaría, 1998; Ramsden, 2002; United States Geological Survey, 2013). Moreover, it is used in the production of imitation jewelry, together with lead, zinc, silver, and antimony in alloys as anti-corrosion agents, for catalyzing organic reactions such as in the oxidation of hydrocarbons and olefins, for polymerization and for epoxidation, as a pigment in the dye and glass industries, and for impregnation of wood and leather to inhibit the formation of fungi and bacteria (Peter and Viraraghavan, 2005). Because Tl salts have a high acute human toxicity, and because Tl compounds are odorless and tasteless, Tl has acquired a reputation as an agent for criminal poisoning (Meggs et al., 1994; Rusyniak et al., 2002). In 2012, the global production of Tl by the mining sector was 10 tonne. This represents the smallest exploited amount of the metals of high environmental concern presented in this report (United States Geological Survey, 2013). However, it is estimated that between 2000 and 5000 tonne are circulated through industrial activities (Kazantzis, 2000).

The primary anthropogenic sources releasing Tl into the environment are flue dusts, vapors, and solid wastes emitted or discarded into the environment from brown coal and coal-based power generation plants. Thallium is released by the burning of coal in general, from cement production facilities, from the smelting of lead, copper, and zinc ores, and from steel and iron processing facilities. Many of these activities show an increasing trend. Mining activities, exploiting and extracting mineral sulfide ores, old tailings, and wastes from the electronics industry may act as considerable sources of Tl as well (Smith and Carson, 1977; Dolgner et al., 1983; Asami et al., 1996; Zhang et al., 1998; Kazantzis, 2000; Cheam, 2001; Lis et al., 2003; Nriagu, 2003; Stewart and Lemieux, 2003; Cvjetko et al., 2010).

Occurrence and behavior in the environment

Thallium occurs in two oxidation states – as monovalent Tl(I) and trivalent Tl(III). In the environment, Tl(I) is more stable and more common than Tl(III) (Adriano, 2001). In its chemical behavior, Tl(I) is similar to the alkali metal cation of potassium (K) (Zitko, 1975; Peter and Viraraghavan, 2005). Although these monovalent Tl compounds are relatively stable under certain conditions, Tl(I) salts – Tl(I) carbonates and Tl(I) sulfates – can be dissolved in water, reaching Tl(I) hydroxide concentrations up to 259 g/L. In this form, they become bioavailable to plants and biota (Dean, 1999; Zitko, 1975; Vink, 1993). In its chemical behavior, Tl(III) conforms to aluminum. It shows strong oxidizing properties and, in the environment, it is slowly converted to Tl(I) (DelValls et al., 1999). Tl(I) compounds are suspected of being more soluble and abundant than Tl(III) ones. However, it was found that Tl(III) compounds dominated in samples from a lake in Michigan. Between 68 and 74% of the total dissolved Tl compounds in the samples were Tl(III) ones. The reason for this is that Tl(I) was oxidized to Tl(III) by planktonic bacteria (Lin and Nriagu, 1999; Twining et al., 2003). These results show that there is a dearth of knowledge about the environmental behavior of Tl and that more investigations are required to better understand its distribution into the environment and its toxicity. In general, uncontaminated soils contain Tl concentrations of about 0.33 mg/kg (ppm; Asami et al., 1996). Seawater samples containdissolved Tl, the concentration ranging from 10 to 15 ng/L, and freshwater ones have concentrations of 5 to 10 ng/L (Flegal and Patterson, 1985; Cheam et al., 1995).

At high temperatures, the Tl compounds emitted are volatile. For this reason, they are not held back efficiently by electrostatic precipitators and other conventional filter systems and control facilities. Consequently, large amounts of Tl compounds are released into the environment through the burning of coal, smelting, and cement production processes involving sulfide ores (Ewers, 1988; Kazantzis, 2000). As a consequence, elevated environmental concentrations of Tl between 40 and 124 ppm are found in the Lanmuchang area of southwest Guizhou, China, in soil originating from the mining area (Xiao et al., 2004). Moreover, Tl accumulates in plants and biota. In the Lanmuchang area, China, elevated Tl concentrations in the range of 120 to 495 ppm dry weight (average 338 ppm) were found in green cabbage. In this region other plants, such as carrots, wild herbs, chili, rice, corn, and Chinese cabbage, take up considerable amounts of Tl as well (Xiao et al., 2004). In addition, lake trout from the Great Lakes in Michigan showed elevated average Tl concentrations of 0.141 ppm wet weight. This amount is comparable to the Tl amounts that have accumulated in brook trout, white sucker, and yellow perch in the Adirondack lakes, USA (Lin et al., 2001).

Toxicity

Even in industrial countries, information about the occurrence and the acute and chronic toxicity to humans, animals, and aquatic organisms is quite rare. For this reason, it is extremely difficult to assess the risk this metal poses to humans, other animals, and terrestrial and aquatic organisms in low- and middle-income countries (Peter and Viraraghavan, 2005). Nevertheless, a small number of toxicity studies indicate that Tl is highly toxic and not essential for humans and other mammals. It affects the health of invertebrates and plants as well. According to IARC, Tl has not been classified as a compound which causes cancer in humans. Currently, few toxicity studies are available and no significant link has been found that the uptake of Tl promotes the formation of cancers (International Agency for Research on Cancer, 2015). For mammals, it is suspected that the toxicity of Tl exceeds that of the heavy metals Hg, Cd, Pb, and Cu (Cheam, 2001). Because of that, Tl is on the list of priority pollutants of the US EPA (United States Environmental Protection Agency, 2014c). In addition, EPA defines the MCL as 0.002 mg/L (Table 5; United States Environmental Protection Agency, 2015c). The global limits for Tl concentrations in crops are from 0.03 ppm to 0.3 ppm (dry mass) and those for land plants are 0.008 to 1 ppm (dry mass; Kabata-Pendias, 2010).

The uptake of Tl happens when contaminated food and drinking water is ingested. Thallium aerosols can be taken up by inhalation; Tl can also be absorbed through contact with the skin mucous membranes. This latter ingestion process occurs mainly as a result of occupational exposure. Given its similarity in ionic charge and its ion radius to potassium, Tl, especially Tl(I), can be absorbed and easily distributed throughout the body by mimicking potassium in its movement patterns and intracellular accumulation in mammals. In the body, it accumulates in bones, the renal medulla, and the nervous system. The excretion of Tl occurs mainly through urination. However, it is excreted in breast milk, sweat, and saliva as well (Zitko, 1975; International Programme on Chemical Safety, 1996; Hoffman and Hoffman, 2000; Peter and Viraraghavan, 2005). A dose of between 0.7 and 1.1 g of soluble Tl salts is considered to be the minimum lethal dose for an adult with a body weight of 70 kg (Moeschlin, 1980). The symptoms of acute Tl poisoning are alopecia, nausea, tachycardia, diarrhea, and impairment of the lungs, heart, and gastrointestinal system. Impairment of the nervous system is more likely a result of chronic exposure to Tl, but there is a lack of studies about the regular chronic uptake of low doses of Tl (Saddique and Peterson, 1983; Agency for Toxic Substances and Disease Registry, 2013; Frattini, 2005; Cvjetko et al., 2010). The toxicity of Tl to humans and other mammals is based on the interference of Tl(I) with vital potassium-dependent processes. Since K(I) and Tl(I) have similar ion charges and ion radii, the cell membrane is not able to distinguish between them. For instance, Tl substitutes for potassium in the Na^+/K^+-ATPase. In addition, given its affinity for the sulfhydryl groups of proteins and mitochondrial membranes, Tl inhibits a range of enzyme reactions causing adverse effects and poisoning (Ramsden, 2002). Furthermore, Tl is able to pass the blood–brain and placenta barriers, affecting the nervous system and causing impairments in the growth and development of fetuses (Hoffman and Hoffman, 2000; Tsai et al., 2006).

Reliable data about the toxicity of Tl to organisms of environmental relevance are quite rare. Nevertheless, investigations show that the acute toxicity of fish to Tl is comparable to that of copper.

Reliable data about the toxicity of Tl to organisms of environmental relevance are quite rare. Nevertheless, investigations show that the acute toxicity of fish to Tl is comparable to that of copper. According to this, concentrations ranging from 0.03 to 60 mg/L are lethal for different fish species. For aquatic invertebrates, like daphnia and gammarus, lethal concentrations of 2 to 4 mg/L were found. For mice, an LD_{50} dose of between 16 and 27 ppm (effective dose) was reviewed in a paper by Zitko (1975). According to the chronic environmental standard (AA-EQS), it is estimated that concentrations above 0.013 µg Tl/L can adversely affect the health of water organisms (Staatscourant, 2010).

Group B: Antimony (Sb)

Introduction

Antimony (Sb) is a bluish-white, brittle, and glossy metalloid (Fowler and Goering, 1991). Antimony can be found in the environment as sulfides and complex Cu-Sb, Pb-Sb, and Hg-Sb sulfides and oxides. The sulfides stibnite and antimonite and the oxide valentinite are the most important commercially used ores. In addition, coal and petroleum contain relevant amounts of Sb (Adriano, 2001; Filella et al., 2002). In the Earth's crust, Sb occurs in concentrations of around 0.2 and 0.3 ppm (Fowler and Goering, 1991).

Antimony is used in semiconductors and is contained in detectors, diodes, and Hall-effect devices – used for measuring magnetic fields – batteries, small arms and tracer bullets, cable sheathings, antifriction alloys, and in alloys to increase the hardness and the mechanical strength of lead. It is used also in car brakes (Filella et al., 2002; Iijima et al., 2007, 2008). The Sb oxide Sb_2O_3 is used in large amounts as a flame retarding additive in textiles, papers, and plastics. It is a component of some adhesives. Also, it is used as a pigment in paints, as a catalyst, as a mordant, and in the ceramic and glass industry (Filella et al., 2002; United States Geological Survey, 2013). In addition, Sb_4O_8 is used commonly as an oxidation catalyst for the oxidative dehydrogenation of olefins (Filella et al., 2002). Antimony is used in medicaments for the treatment of tropical protozoan diseases like leishmaniasis, schistosomiasis, ascariasis, and trypanosomasis (Filella et al., 2002). According to the data of the US geological survey, 180,000 tonne of antimony were mined in 2012 (United States Geological Survey, 2013).

There is evidence that exposure to Sb compounds from anthropogenic causes exceeds that from natural sources. The primary sources of Sb are smelting and refining facilities, energy producing plants that burn fossil fuels, waste incineration plants, mining, and vehicles. In the latter, Sb is present in abrasion materials from tires, brakes, and motor bearings (Fowler and Goering, 1991; Newton et al., 1994). Data from 1988 to 1990 show that, annually, about 3500 tonne of Sb originated from anthropogenic sources, while 2600 tonne were emitted through natural sources, such as volcanic activities, salty sea spray, and forest fires. However, since then, primary Sb production has increased from 138,000 to 180,000 tonne, which may have lead to higher anthropogenic emissions of Sb aerosols (Nriagu and Pacyna, 1988; Nriagu, 1989, 1990a; Maeda, 1994).

Occurrence and behavior in the environment

In the environment, Sb occurs mainly in the oxidation states III and V. In soils, background concentrations of around 1 to 10 ppm have been measured (Shacklette and Boerngen, 1984; Hammel et al., 2000; Reimann et al., 2010). In unpolluted freshwater systems, it can be found at concentrations of less than 1.0 µg/L (Reimann et al., 2010), and the oceans contain even smaller amounts of Sb, concentrations below 200 ng/L being reported (Filella et al., 2002). Although Sb is widely used in large quantities, little attention has been drawn to this metalloid. Accordingly, there is little information available about the transformation and distribution processes of Sb and its different compounds among the different environmental compartments. However, as far as it is known, Sb occurs mainly as sulfides and sulfidic complexes, oxides, and hydroxides. It also occurs in the environment as the more volatile methylated species (Filella et al., 2002; Wilson et al., 2010). Since 1990, the obligatory implementation of filter systems for incineration plants, smelters, metal refining facilities, and energy generating plants has led to a decrease in the amount of organic and inorganic pollutants emitted, especially in HICs. However, since these filter systems are not mandatorily applied in all low- and middle-income countries, and large quantities of Sb are still mined there, the emissions of Sb and other metalloids or heavy metals in these regions are reaching levels of environmental concern. For instance, samples collected from Prestea, a gold mining town in West Ghana, showed elevated Sb concentrations in water ranging from 0.09 to 0.75 mg/L and in soils ranging from 8.5 to 90.4 ppm (Serfor-Armah et al., 2006).

In the Abaróa Sb mine area in southern Bolivia, heavy rainfalls have caused severe erosion of tailings dumps, releasing large amounts of inorganic pollutants, such as Pb, Zn, and Sb, into the Rio Chilco-Rio Tupiza drainage system. There, sediments between the Rio Abaróa and the Rio Machocuya, contained an average 341.9 mg Sb/kg (ppm) and the sediments of the adjacent floodplains had Sb concentrations of about 37.40 ppm (Villarroel et al., 2006). In addition, soils at one of the world biggest Sb mining and smelting areas in Hunan, China, had elevated Sb concentrations of up to 5045 ppm (He, 2007).

There is evidence that Sb is bioavailable for plants. However, these results differ a lot from each other and for different plant species. For instance, the leaves and shoots of endive, corn salad, spinach, biennial parsley, and carrot leaves accumulated from just 0.6 to 1% of Sb from the surrounding soil. The soil originates from a historical mining site and contains Sb concentrations of 54.4 to 67.0 ppm (Hammel et al., 2000). In contrast, the leaves of radish plants at a mining site and in the vicinity of smelting facilities accumulated up to 10.8% Sb (the soil concentration was measured at 852 mg Sb/kg (ppm; He, 2007). These differences indicate that knowledge about the uptake of Sb compounds is still raising questions. Most of the studies do not discriminate between the uptake via roots or the adsorption of Sb aerosols onto the epicuticular waxes on the plant surfaces. Therefore, it is difficult to predict the uptake of Sb by the roots (Ainsworth et al., 1990a; He, 2007; Tschan et al., 2009). Tschan et al. investigated by exposing different plant species to 25 µmol/L $KSb(OH)_6$ solutions. It was found that the shoots of sunflowers take up and accumulate Sb to about 24 ppm dry weight, those of perennial ryegrass 17 ppm dry weight, those of wheat 16 ppm dry weight, and those of maize 3 ppm dry weight (Tschan et al., 2009). These results show that plants are able to take up Sb compounds via their roots, although the uptake varies by an order of a magnitude among the different plant species. Under these experimental conditions, the bioavailability of less water-soluble Sb species, such as Sb sulfides and Sb oxides, would be less pronounced than the uptake of the more water soluble Sb hydroxides and KSbO tartrates (Hammel et al., 2000). In contrast, Ainsworth et al. reported that the contamination of vegetation is more likely related to continuing atmospheric deposition than to uptake from the soil (Ainsworth et al., 1990a).

In general, Sb shows a low or no tendency for bioconcentration throughout the food chain (Filella et al., 2002). Although in fish samples near the Sb mining area in Hunan, China, Sb concentrations of up to 218 ppb were measured (Fu et al., 2010), there is evidence that Sb concentrations in ground-living invertebrates are lower than the concentrations in their diets. There is evidence also that the Sb content in the tissue of small mammals is less than that of their dietary intake (Ainsworth et al., 1990b).

Toxicity

Although Sb apparently does not accumulate in the food chain, there is evidence that it has a high toxic potential and that it is not essential for plants, humans, and animals (Adriano, 2001). The IARC has classified antimony trioxide as a Group 2b compound possibly carcinogenic to humans. Antimony trisulfide has not been classified as to its carcinogenicity to humans (International Agency for Research on Cancer, 2015). According to the US EPA, Sb and Sb compounds are considered as priority pollutants and its drinking water standard, called MCL, is 6 µg Sb/L (Table 5; United States Environmental Protection Agency, 2014c, 2015c). In addition to the other metals and metalloids of environmental concern in this report – As, Cd, Pb, Hg, Tl, hexavalent Cr, and Cu compounds – Sb is listed as a hazardous substance because of the Basel Convention restriction on its transfer across borders (United Nations Environment Programme, 2014). In general, organoantimonials, like methylated Sb compounds, are the least toxic. Pentavalent Sb compounds are increasingly so and trivalent Sb compounds show the highest toxic potential (particularly Sb_2O_3; Gebel, 1997; He and Yang, 1999; Krachler et al., 2001). For mammals, there is evidence that trivalent compounds have a clastogenic, but not mutagenic, activity. Rats were exposed through inhalation to 45 mg/m^3 of Sb_2O_3 and Sb ore concentrate. While the male rats were not affected, 27 (25%) of the females developed lung neoplasms (Groth et al., 1986). However, controversial results are found as well. For instance, the findings of Elliott et al. did not confirm that exposing rats to Sb_2O_3 caused genotoxic or clastogenic effects (Elliott et al., 1998). Thus, there is still not sufficient evidence available to determine whether Sb compounds have carcinogenic effects on humans or not (Gebel, 1997). Nevertheless, the Occupational Safety and Health Administration (OSHA) defined the permissible exposure limit at 0.5 mg Sb/m^3 as a time-weighted average concentration over an eight hour working shift (National Institute for Occupational Safety and Health, 1988a).

In plants, an exposure to 30 mg/L caused significant inhibition in root growth in maize and wheat compared to the control. In addition, exposure to just 3 mg Sb/L led to an inhibition, though not significant, in shoot biomass (Tschan et al., 2009). According to the AA-EQS, chronic aquatic concentrations above 7.2 µg/L can adversely affect the health of water organisms (Marion Junghans (Ecotox Centre); personal communication).

Group B: Arsenic (As)

Introduction

Arsenic (As) is a brittle, steel-grey, crystalline metalloid. Like Sb, it is found primarily in sulfide deposits as arsenides, sulfides, and sulfosalts, often together with Ag, Pb, Cu, Ni, Sb, Co, Fe, Zn, and Au (Adriano, 2001; International Agency for Research on Cancer, 2012b). The most prevalent As-containing minerals are arsenian pyrite ($Fe(S,As)_2$), arsenopyrite (FeAsS), löllingite ($FeAs_2$), realgar (AsS), orpiment (As_2S_3), cobaltite (CoAsS), niccolite (NiAs), and scorodite ($FeAsO_4$ x $2H_2O$; Wang and Mulligan, 2006; Smedley and Kinniburgh, 2013). In the Earth's crust it occurs at concentrations between 1.5 and 2 ppm (Salomons and Förstner, 1984; Luoma and Rainbow, 2008).

Historically, inorganic and organic arsenic compounds were used as pesticides, insecticides, fungicides, and soil sterilizers. They were used also as medicaments to treat several spirochetal and protozoal diseases and parasites, and other diseases, such as leukemia, psoriasis, and chronic bronchial asthma. Until now, several As compounds were used in the veterinary sector to treat animals infected with parasites. Arsenic compounds are used also as wood preservatives in non-residential areas (Adriano, 2001; Wang and Mulligan, 2006; Agency for Toxic Substances and Disease Registry, 2007a; International Agency for Research on Cancer, 2012b). However, today, most arsenic-based agricultural and pharmaceutical agents are being phased out because of restrictions related to their high toxic potential (Adriano, 2001; United States Environmental Protection Agency, 2009). Arsenic compounds are used as pigments in the ceramic, tanning, and glass industries and the metal form is used as an additive in lead and copper alloys, ammunition, the grids of lead–acid storage batteries, optical, and infrared devices. Gallium arsenide semiconductors are used in the electronics industry in solar cells, space research, and telecommunication (Adriano, 2001; Bissen and Frimmel, 2003; United States Geological Survey, 2013). In 2012, around 44,000 tonne of arsenic trioxide (AS_2O_3) was produced worldwide. This is the main arsenic compound that enters end-product manufacturing (Adriano, 2001; United States Geological Survey, 2013).

The primary man-made sources of As contamination of the environment are the combustion of coal and oil containing traces of arsenic, orphan mining sites, inappropriately-closed mines, and residual tailings. Waste incineration, disposal of e-waste, and ore refining and smelting processes (especially lead and copper ores) are other significant point sources of arsenic (World Health Organization, 2001; Wang and Mulligan, 2006; International Agency for Research on Cancer, 2012b; United States Geological Survey, 2013).

Occurrence and behavior in the environment

Since arsenic contamination of groundwater has been reported worldwide, anxieties concerning arsenic-related problems have increased (Mukherjee and Bhattacharya, 2001; Wang and Mulligan, 2006; Centeno et al., 2007; Amini et al., 2008). Accordingly, natural contamination by As, through the weathering, leaching, and erosion processes of arsenic-containing rocks and soils, volcanic activity, and natural fires, is of high environmental concern. Within the scope of our report, we focus more on anthropogenic arsenic contamination.

Natural arsenic concentrations in surface waters, such as rivers and lakes, barely exceed 0.01 mg. The oceans and groundwater have average As concentrations around 1 to 0.002 mg and the background concentrations in soils are about 5 mg/kg (World Health Organization, 2001).

Elevated As concentrations, ranging from 3.6 to 295.1 mg/kg, have been found in soil samples in the mining and smelting area of Hunan, China, and concentrations of 942 to 10,200 mg/kg have been found near the gold mining town of Prestea, Ghana, (Serfor-Armah et al., 2006; He, 2007). In Hunan, As concentrations up to 0.0113 mg were detected in water samples and in Prestea the concentrations in the water samples measured 8.25 mg/L (Serfor-Armah et al., 2006; Fu et al., 2010).

The physicochemical properties of As are comparable to those of Sb, but arsenic compounds are much more toxic and more easily bioavailable to plants and invertebrates (Gebel, 1997; Tschan et al., 2009; Fu et al., 2010; Wilson et al., 2010). Similarly to Sb, As occurs mainly in two oxidation states – as trivalent (arsenite) and pentavalent (arsenate) arsenic compounds in the environment. The reduced trivalent compounds are more likely to occur under anaerobic conditions and the pentavalent ones under aerobic ones (International Agency for Research on Cancer, 2012b). Organic arsenic compounds, such as arsines and methylarsines, mostly are unstable in air if they are not absorbed and accumulated by plants and other biota or adsorbed to organic matter (Adriano, 2001; Centeno et al., 2007; Tschan et al., 2009).

In general, adsorption processes to soil and the leaching processes of As compounds from soils depend on several biogeochemical factors, such as particle size, soil composition, organic matter content, nature of constituent minerals, pH, water hardness, redox potential, oxygen, calcareous content, and the number of competing ions (Goldberg and Glaubig, 1988; Masscheleyn et al., 1991; Jones et al., 2000; Adriano, 2001; Smith et al., 2002; Yamaguchi et al., 2011). Generally, it can be said that As(III) is less strongly adsorbed to soil than As(V). Thus, trivalent As compounds are more mobile and, thus, more toxic than As(V) compounds. This increased mobility of As is enhanced because of the reduction of arsenate to arsenite (Masscheleyn et al., 1991; Chiu and Hering, 2000).

There is still a lack of knowledge related to the sorption and mobilization processes of As compounds. There is evidence that in each case they can be mobilized under reducing or oxidizing conditions. On the one hand, under anaerobic aquatic conditions, As(III) is more likely to be mobilized because of reductive dissolution. It has to be said that, in the presence of higher sulfate concentrations, the release of As is hindered, mainly because of microbial-dependent sulfate reduction or surface arsenic adsorption, resulting in the precipitation or incorporation of arsenic compounds in sulfides (Bostick and Fendorf, 2003; Rowland et al., 2006; Amini et al., 2008). On the other hand, under aerobic environmental conditions in arid and semi-arid regions with high evaporation rates and resulting higher salinity, arsenate (AsO_4^{3-}) and other anions are less strongly adsorbed to mineral surfaces and, therefore, are more water soluble (Amini et al., 2008; Smedley and Kinniburgh, 2013).

After the mobilization of As into aquatic media, As compounds can be taken up by plants and other biota. Naturally, plants and aquatic organisms do not incorporate enough As to be toxic to humans, so it seems that As does not accumulate in the food chain. Often, before reaching internal As concentrations that are toxic to humans, the plants suffer from phytotoxic effects leading to inhibition of growth or crop failure. Also it seems that As negligibly bioaccumulates in fish (National Academy of Sciences, 1977; Eisler, 1994; Adriano, 2001; Jones, 2007).

However, contradictory evidence has been found as well. For instance, in areas with extremely high As contaminations, such as near smelting and waste incineration facilities and in areas with a high level of mining activity, As may indeed have the potency to accumulate throughout the food chain (Tamaki and Frankenberger Jr, 1992; Wang and Mulligan, 2006; Agency for Toxic Substances and Disease Registry, 2007a). In addition, the investigations of Tschan et al. show that plants are accumulating arsenic (around three times more easily than Sb). In the shoots of plant seedlings of perennial ryegrass, As concentrations of 58 mg/kg dry weight have been measured after exposure to 1.9 mg As/L for one week. The corresponding value for wheat is 43 mg/kg dry weight, for sunflowers, 36 mg/kg dry weight, and for maize 4 mg/kg dry weight (Tschan et al., 2009). In addition, rice grains collected from mine-affected areas in Hunan, China, had levels of inorganic As up to 624 µg/kg, which is four times higher than that of the vast majority of rice grains on the rice market (Zhu et al., 2008). In barley, wheat and rice, As concentrations of the order of 100 µg/kg up to 10.2 g/kg have been measured. For rice, the amount of As transferred and accumulated in the shoots is even higher (1.5 to 20.6 g/kg) than the amount of As found in the soil (5 to 10 g/kg), indicating that rice is able to bioaccumulate As (Williams et al., 2007). In fish near the mining area in Hunan, elevated As concentrations of up to 152 µg/kg wet weight have been measured (Fu et al., 2010). In addition, considerable concentrations of As in the range of µg/kg to g/kg have been found in food samples (National Academy of Sciences, 1977; Jones, 2007). Whether accumulating through the food chain or not, arsenic poses a risk to environmental and human health because of its high acute toxicity even at low concentrations.

Toxicity

Similarly to Sb compounds, the toxicities of arsenic compounds conform to the following order, from least to highest: organoarsenicals (methylated species), arsenates (pentavalent As), and arsenites (trivalent As; Nriagu, 1994). IARC has listed inorganic As compounds as Group I carcinogens for humans, while organic As compounds are classified in Group III, not carcinogenic for humans (International Agency for Research on Cancer, 2015). The MCL, which represents the highest level of the contaminant that is allowed in drinking water, as determined by the US EPA, is 0.01 mg (Table 5; United States Environmental Protection Agency, 2015c). The uptake of As occurs mainly from eating contaminated food and drinking contaminated water. It can also occur from occupational exposure through the inhalation of pollutants at coal-fired power plants, mining areas, waste incineration, smelting, and battery assembly facilities. It can also be taken up via the mucous membrane and percutaneously (Eisler, 1994; Agency for Toxic Substances and Disease Registry, 2007a; International Agency for Research on Cancer, 2012b). The acute minimal lethal dose of inorganic As is estimated to be between 70 and 200 mg (Caravati, 2004). The symptoms of acute As poisoning are stomach ache, nausea,

The uptake of As occurs mainly from eating contaminated food and drinking contaminated water. Chronic ingestion of As-contaminated drinking water has resulted in significant negative consequences for human health.

vomiting, and diarrhea. Furthermore, acute uptake of As can cause a decrease in the production of red and white blood cells, cardiac arrhythmias, and blood-vessel damage resulting in bruising, and impaired nerve function (Agency for Toxic Substances and Disease Registry, 2007a). With their high acute toxicity and their being odorless, colorless, and tasteless, As salts have been used historically as suicidal and homicidal agents, particularly during the Middle Ages (Smith, 2013). In the long term, a daily chronic exposure to 0.02 mg/kg by ingestion can lead to adverse health effects in sensitive humans (Ontario Ministry of the Environment, 2001). In addition, chronic (20 years) ingestion of As-contaminated drinking water with a concentration of 0.13 mg As/L, has resulted in significant negative consequences for human health (Lerda, 1994). Chronic poisoning symptoms are peripheral neuritis, gastritis, enteritis, liver and kidney failure, cardiac dysfunctions, melanosis, depigmentation, hyperkeratosis, and several forms of cancer (Niu et al., 1997; Mazumder, 2000; Adriano, 2001; Mead, 2005). After uptake, arsenic compounds are effectively assimilated via the gastrointestinal (GI) tract. For instance, in the GI tract 60% of the ingested As(V), 80% of the As(III), and 100% of organoarsenicals are adsorbed after ingestion (Zielhuis and Wibowo, 1984; Gebel, 1997). In short, the toxic effects of inorganic As are a result of their affinity for and ability to bind with sulfhydryl groups, such as glutathione and metallothionein. The results of this binding are alterations of the protein structures, which consequently cause disruptions of metabolic processes. Following the bonding to sulfhydryl groups, metabolic processes, such as cellular glucose uptake, fatty acid oxidation, and production of glutathione, can be affected (Gochfeld, 1997). Arsenic compounds are not directly mutagenic; however, they do behave clastogenically, which means that they give rise to or induce disruptions in or breakages of chromosomes (Jha et al., 1992; Lerda, 1994). In this context, As does not directly interact with DNA: its genotoxic effects are induced indirectly through alterations of gene expression by impairment of DNA methylation, induction of oxidative stress, and changes in the regulation of signal transduction pathways (Gebel, 1997; Kitchin and Ahmad, 2003).

From an environmental perspective, As compounds, such as monosodium methylarsonate, disodium methylarsonate, and dimethylarsinic acid, are known for their phytotoxic effects. Consequently, they have been broadly used as herbicides (Bissen and Frimmel, 2003). In general, for most plants a depression in crop yield results after exposure to soils having concentrations of water soluble As from 3 to 28 mg/L and total arsenic concentrations from 25 to 85 mg/kg (Furlong, 1978; Eisler, 1994). In addition, after exposure of 1.9 mg As/L, wheat, maize, perennial ryegrass, and sunflower seedlings have suffered a significant reduction in biomass, ranging from 48 to 20%. (Tschan et al., 2009). The investigations of Eisler revealed that for aquatic invertebrates, concentrations of 0.019 to 0.049 mg As/L in water for invertebrates, concentrations of 120 mg As/kg in diets, and for algae, concentrations of 1.3 to 5 mg As/kg fresh weight in tissues, provoke significant health-damaging effects and, therefore, pose a risk to environmental health (Eisler, 1994). From an environmental perspective and according to the proposed chronic environmental quality standard (AA-EQS), the concentration of As in aquatic systems should not exceed 0.05 mg/L in the long term to guarantee the welfare of water organisms (UK Technical Advisory Group on the Water Framework Directive, 2008).

Group C: Asbestos

Introduction

Asbestos is the commercially used collective noun for a group of naturally occurring silicate minerals with fibers that are long, thin, and flexible when separated (Stayner et al., 2013). Asbestos minerals can be separated into two groups. These are serpentine minerals, classified as sheet minerals because the silicate (SiO_4) tetrahedrons are serialized as sheets, and amphibole minerals, classified as chain silicates because the SiO_4 tetrahedrons are organized as a double chain of two rows (International Agency for Research on Cancer, 2012c; Stayner et al., 2013). The most abundant chrysotile asbestos is an asbestos mineral belonging to the serpentine group found as veins in serpentine rocks. The asbestos minerals actinolite, amosite, anthophyllite, crocidolite, and tremolite are characteristic amphibole minerals (International Agency for Research on Cancer, 2012c). In ambient air, asbestos compounds are naturally found in concentrations ranging from 0.00001 to 0.0001 fibers/mL (Agency for Toxic Substances and Disease Registry, 2008).

With their physicochemical characteristics of high tensile strength, flexibility, resistance to chemical and thermal degradation, and high electrical resistance, asbestos minerals are useful for a wide range of industrial applications (National Toxicology Program, 2014a; International Agency for Research on Cancer, 2012c; United States Geological Survey, 2013).

Asbestos fibers can be used in the textile industry. With their heat resistance and high insulating properties, they are used in packing materials for steam glands on high-temperature machines and insulation for boilers, steam pipes, and electrical wiring. Asbestos fibers are used in fireproof paints, for suits and blankets, in fireproof construction materials for walls, floors, and roofs, and as additives in asphalt road surfaces. Asbestos-cement is used in the mass production of cheap, fireproof building materials and asbestos-cement pipes are widely used as water and waste pipes. Furthermore, they are used in the automobile industry in brakes, clutch components, and engine gaskets, in the millboard industry, and in filters. The decreased level of production of asbestos in the 1990s is attributable to the finding that exposure to asbestos is associated with the occurrence of lung cancer (Selikoff and Lee, 1978; Tomatis et al., 1978; Agency for Toxic Substances and Disease Registry, 2001; Virta, 2006; International Agency for Research on Cancer, 2012c).

In 2003, the use of asbestos was banned or restricted in 16 countries – Argentina, Austria, Belgium, Chile, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Poland, Saudi Arabia, Sweden, Switzerland, and the United Kingdom. By 2005, the use of asbestos was almost completely banned within the European Union. Until now, the use of asbestos has been restricted or banned in 57 countries (Virta, 2006; International Ban Asbestos Secretariat, 2015). Nevertheless, although asbestos minerals are banned in several countries, the world mining production of 2 million tonne/year indicates that asbestos is still in use. For instance, the US EPA has generated a list of products containing asbestos that are still produced (United States Geological Survey, 2013; United States Environmental Protection Agency, 2015d). In addition, there is evidence that the use of asbestos, especially in many developing countries, is increasing (Stayner et al., 2013).

The modern industrial use of asbestos started around 1880 and peaked in 1975 with an estimated world production of 5.09 million tonne. However, during the last decades worldwide mining production of asbestos has declined and reached a plateau at around 2 million tonne (International Agency for Research on Cancer, 2012c; United States Geological Survey, 2013).

Asbestos fibers, clumps of asbestos and asbestos dust enter the air, aquatic, and terrestrial environments naturally as a consequence of the weathering and erosion of natural deposits and asbestos-bearing rocks. The primary source of asbestos mineral pollution is a result of anthropogenic activities. Open-pit mining operations, crushing, screening, milling of ore, and all the processes involved in extracting, processing, and manufacturing asbestos are man-made sources of asbestos fibers. Furthermore, inappropriate disposal of waste material containing asbestos, corrosion of asbestos-cement pipes, other asbestos materials used in the construction sector, and the abrasion of asbestos from asphalt or vehicle brakes, clutches, and engine gaskets are additional sources releasing asbestos fibers into the environment (Selikoff et al., 1972; Millette et al., 1980; Williams and Muhlbaier, 1982; Cheng and O'Kelly, 1986; Agency for Toxic Substances and Disease Registry, 2001; Abratt et al., 2004).

Although asbestos minerals are banned in several countries, the world mining production of 2 million tonne/year indicates that asbestos is still in use.

Occurrence and behavior in the environment

At the moment, data about environmental asbestos and non-occupational concentrations are quite limited. Nevertheless, there is evidence that significantly elevated concentrations of asbestos can be found in water supplies. Concentrations above 1 million fibers/L have been found in the drinking water of 18% of the 406 cities tested in Puerto Rico and the District of Columbia (Millette et al., 1980). In the Castro Valley Bay area, California, USA, asbestos concentrations of up to 319 million fibers/L have been measured in runoff samples. Creek sediments contained asbestos concentrations up to 230 million fibers/L and street surface particles had concentrations of up to 1300 million fibers/L (Pitt, 1988). In 2012, in the USA alone, 7300 tonne of friable asbestos were reported to have been released by 41 facilities, according to data of the Toxics Release Inventory (TRI) program (United States Environmental Protection Agency, 2012). Data about the release of asbestos in low- and middle-income countries is in short supply (Stayner et al., 2013). However, in these countries, occupational exposure to asbestos minerals is still a big issue, especially when obsolete techniques for mining and processing asbestos minerals are used and if the handling of asbestos products takes place without proper precautions (Ramanathan and Subramanian, 2001). For example, in an asbestos processing mill in Andhra Pradesh, India, maximal asbestos concentrations of up to 488,050 fibers/L were measured. This despite the legal level allowed for asbestos production in this region being set below 2000 fibers/L (Ramanathan and Subramanian, 2001).

Toxicity

All asbestos minerals cause cancer and are potentially toxic. The primary uptake routes for asbestos in humans are by ingesting contaminated food and water and by inhaling asbestos aerosol particles during handling (repacking of asbestos containers, transport, and disposal), processing (dry cutting, milling, and production of construction material), and the use of asbestos-containing raw materials and products. Uptake via the respiratory system seems to be the most hazardous and relevant one. In addition,

All asbestos minerals cause cancer and are potentially toxic. The primary uptake routes for asbestos in humans are by ingesting contaminated food and water and by inhaling asbestos aerosol particles.

people who are living in the vicinity of asbestos mining sites and manufactories, and people living in houses containing asbestos products in the floors, roofs, and walls are taking up elevated amounts of the material and posing risks to their health (World Health Organization, 2006; International Agency for Research on Cancer, 2012c).

The uptake of the acerous, sharp asbestos fibers causes a range of diseases, such as asbestosis (fibrosis of the lungs), mesothelioma, and several other forms of cancer of the pharynx, larynx, esophagus, lungs, stomach, and colorectum, and the thickening of pleural plaques and effusions. These diseases have a long latency (Selikoff et al., 1964; Doll and Peto, 1985; International Programme on Chemical Safety, 1985; Enterline et al., 1987; Selikoff and Seidman, 1991; World Health Organization, 2014; Landrigan et al., 1999; National Research Council, 2006; World Health Organization, 2006; International Agency for Research on Cancer, 2012c). Thus, if the use of asbestos is eliminated right now, the number of asbestos-related deaths will decrease only after a few decades (World Health Organization, 2006).

It is estimated that globally around 125 million people are exposed to asbestos in their occupations. Of these, 90,000 people are estimated to die annually from asbestos-related diseases (World Health Organization, 2006). Given their high toxicity, all asbestos minerals are classified by the IARC as Group I carcinogens for humans. For drinking water, the limiting value of asbestos contamination, referred to as MCL, is 7 million fibers/L (Table 5; United States Environmental Protection Agency, 2015c). In occupational settings, the permissible limits for asbestos range between 100 fibers/L and 2000 fibers/L as a time-weighted average for a normal eight hour workday and a 40 hour week (National Institute for Occupational Safety and Health, 1988b; International Agency for Research on Cancer, 2012c). Nevertheless, it seems that in several regions, especially in low- and middle-income countries, regulations controlling and monitoring human and environmental exposure to asbestos are lacking, posing risks to human and environmental health (Giannasi and Thébaud-Mony, 1997; Joshi and Gupta, 2003; Virta, 2006; LaDou et al., 2010). According to the literature, it is feared that the continuous use of asbestos in low- and middle-income countries will trigger an epidemic of asbestos-related diseases, such as mesothelioma and lung cancer in the near future (Joshi and Gupta, 2004; LaDou et al., 2010; Stayner et al., 2013).

From an environmental toxicological point of view, there have been few investigations of the negative impacts of asbestos on aquatic and terrestrial animals following exposure to anthropogenically released asbestos minerals. However, histological examinations of blue mussels, exposed to waste products containing 10 mg/L of asbestos for five days, indicated that asbestos particles can be taken up and afterwards remain in the gastrointestinal tract causing significant tissue injuries (Halsband, 1974). Further investigations showed that vertebrates – lake trout – incorporate asbestos fibers particularly into their kidneys and, less pronouncedly, into their muscle tissue. In contrast, other fish species, such as catfish, brook trout, and Arctic char, showed a lower potential to incorporate asbestos minerals. The proposed hypothesis to explain this was that the uptake of asbestos minerals is more dependent on eating behavior and the food intake than on uptake via the gill system (Batterman and Cook, 1981). In addition, although asbestos minerals can be incorporated into fish, they seem not to accumulate in the food chain because the asbestos concentration in muscle tissue is half the external water concentration (Batterman and Cook, 1981). Exposure tests on Coho salmon and green sunfish showed that asbestos concentrations of about 1.5 million to 3.0 million fibers/L are enough to cause behavioral stress effects, like impairments in rheotaxic position and balance. Although a destructive effect of asbestos on lateral line histology was observed – this is responsible for the loss of rheotaxic position – the mortality did not increase significantly after exposure to asbestos at the concentrations tested (Belanger et al., 1986). There is evidence that the release of asbestos can affect environmental health. According to the most recent status report, environmental risk assessment is not possible, especially in low- and middle-income countries, where almost no data about environmental asbestos concentrations are published. Nevertheless, a chronic environmental standard (AA-EQS) of 7 million fibers/L was proposed (United States Environmental Protection Agency, 1999).

Table 5: Data about hazardous heavy metals, metalloids, and minerals from the mining industry

Name[A]	Primary production [tonne] (United States Geological Survey, 2013)	Most toxic species	Potentially toxic to (Adriano, 2001)	Maximum Contaminant Level (MCL) (United States Environmental Protection Agency, 2015c) [mg/L]	Environmental quality standard AA-EQS/MAC-EQS [µg/L][B]
Metals					
Cadmium →	23,000 with 54% produced in low- and middle-income countries	Cd(II) (Adriano, 2001)	Plants, animals, humans	0.005	Class 1: 0.08/0.45 Class 2: 0.09/0.6 Class 3: 0.15/0.9 Class 4: 0.25/1.5[C] (European Parliament and Council of the European Union, 2008)
Chromium →	24 million with 94% produced in low- and middle-income countries	Cr(VI) (International Agency for Research on Cancer, 2012d)	Plants, humans, animals (Mishra and Mohanty, 2008)	0.1	Cr(III): 4.7/32 Cr(VI): 3.4/NA (UK Technical Advisory Group on the Water Framework Directive, 2008)
Copper ↑	17 million with 42% produced in low- and middle-income countries	Cu(II), CuOH$^+$, $[Cu_2(OH)_2]^{2+}$ (Flemming and Trevors, 1989)	Plants, animals (aquatic organisms) (Richardson, 1997; Borkow and Gabbay, 2005; United States Environmental Protection Agency, 2008; Vardy et al., 2014)	1.3	1/NA (based on the bioavailable concentration) (UK Technical Advisory Group on the Water Framework Directive, 2012)
Lead ↑	5.2 million with 67% produced in low- and middle-income countries	Pb(II) (Agency for Toxic Substances and Disease Registry, 2007b)	Plants, animals, humans	0.015	1.2 (based on the bioavailable concentration)/14 (European Parliament and Council of the European Union, 2013)
Manganese ↑	16 million with 76% produced in low- and middle-income countries	Mn(VII)O_4^- (Young et al., 1996), Mn(II, III) oxides, Mn(II)SO_4, Mn(II)Cl_2 (United States Environmental Protection Agency, 2010)	Plants	NA (WHO limiting value 0.4) (World Health Organization, 2004)	123/NA (UK Technical Advisory Group on the Water Framework Directive, 2012)
Mercury ↓	1,600 with 92% produced in low- and middle-income countries	MeHg, Me_2Hg (Weber, 1993; Morel et al., 1998; Wolfe et al., 1998)	Animals, humans	0.002	NA (but biota standard is 20 µg/kg wet weight)/0.07 (European Parliament and Council of the European Union, 2013)
Thallium →	10 (proportion produced in low- and middle-income countries not definable)	Tl(I), $Tl(I)_2SO_4$, $Tl(I)_2CO_3$ (Zitko, 1975; International Programme on Chemical Safety, 1996; Hoffman and Hoffman, 2000; Cheam, 2001; Peter and Viraraghavan, 2005)	Plants, animals, humans	0.002	0.013/0.8 (van Vlaardingen and Verbruggen, 2009)
Metalloids					
Antimony →	180,000 with 97% produced in low- and middle-income countries	Sb(III); $Sb(III)_2O_3$, Sb(V) (Gebel, 1997; He and Yang, 1999; Krachler et al., 2001; International Agency for Research on Cancer, 2015)	Animals, humans	0.006	7.2/NA (Marion Junghans (Ecotox Centre; personal communication)
Arsenic ↓	44,000 with 73% produced in low- and middle-income countries	As(III), As(V) (Nriagu, 1994)	Plants, animals, humans	0.01	50/NA (UK Technical Advisory Group on the Water Framework Directive, 2008)
Minerals					
Asbestos ↓	2 million with 48% produced in low-and middle-income countries	Fibers (Agency for Toxic Substances and Disease Registry, 2001)	Animals, humans	7 million fibers/L	7 million fibers/L (United States Environmental Protection Agency, 1999)

A: *● Decreasing use trend; ● Use trend is unsure – approximation is difficult; ● Increasing use trend (United States Geological Survey, 2013; Barrientos and Soria, 2013).*

B: *The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.*

C: *AA-EQS and MAC-EQS of cadmium are dependent on water hardness classes: Class 1: < 40 mg $CaCO_3$/L; Class 2: 40 to 50 mg $CaCO_3$/L; Class 3: 50 to 100 mg $CaCO_3$/L; Class 4: 100 to 200 mg $CaCO_3$/L.*

Input pathways of mining pollutants

The lifetime of a mine depends on the main material being mined and the stocks of the ores and minerals of interest. Thus the lifetime can be several years or several decades, even as long as a few centuries (International Council on Mining & Metals, 2012). Uneconomical mines can be closed inappropriately, especially in low- and middle-income countries, with nobody assuming responsibility for the orphan mining sites. Often the authorities do not have the capacity to remediate contaminated regions. At abandoned mining sites, the chemical or bacterial oxidation of iron pyrite or other sulfidic minerals results in acidified mine water effluents, causing acid mine drainage (AMD). These acidified mining effluents contain high concentrations of dissolved heavy metals and metalloids, of which arsenic, cadmium, copper, and lead are of the highest concern. These effluents endanger water resources and the environment. AMD occurs particularly in flooded mining sites, waste rock dumps, tailings, and piled heaps of proceeded material (Johnson and Hallberg, 2003, 2005; Farrell et al., 2004).

Acidified mining effluents contain high concentrations of dissolved heavy metals and metalloids, of which arsenic, cadmium, copper, and lead are of the highest concern.

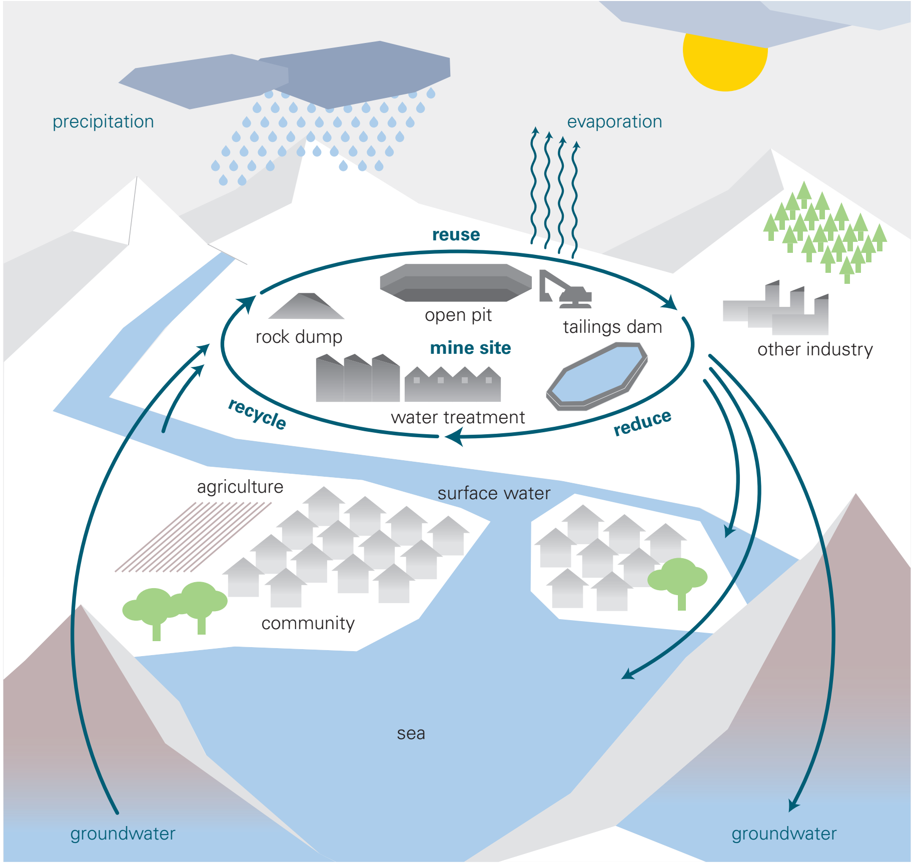


Figure 19: *Mining-related water cycle (International Council on Mining & Metals, 2012)*

AMDs and other untreated mining wastewater, slag, solid waste, and tailings can be discarded inappropriately into surface waters or left uncovered next to the mining site (Blacksmith Institute and Green Cross, 2012). These abandoned mining wastes, with their high contents of acids and toxic heavy metals, pose risks to environmental and human health. From these mining wastes, toxic compounds can leach into groundwater aquifers, lakes, and river systems through surface runoff. In low- and middle-income countries, these contaminated water sources are often used for irrigation, thus degrading valuable and fertile agricultural land (He, 2007; Figure 19).

In addition, during ore exploitation, transport, and extraction, and the processing and refining of ores and minerals, hazardous pollutants and metals can be released into the environment.

Social impacts of mining

Since the Industrial Revolution, and as a result of the further developments and progress made in the technical industrial sector, the extraction of metals, metalloids, and minerals has been indispensable for meeting resource needs. The mining industry is a viable way for achieving a rapid and profitable economic revival in the short term (International Institute for Environment and Development, 2002; Low, 2012).

To date, the mining sector has made little contribution in terms of sustainable development (International Institute for Environment and Development, 2002). In addition, although this sector is associated with social and economic benefits, it is known for its ruthless approaches that cause environmental destruction and disadvantage society (Farrell et al., 2004). Today, the mining industry is under pressure to improve its environmental and social performance. From this perspective, the social impacts of mining are emphasized in this report (Miranda et al., 2003).

On the one hand, as already mentioned, there are some social benefits that result from mining (Table 6). The extraction of resources can lead to a rapid and temporary economic boom, result in an increase of gross domestic product, and create new jobs. Furthermore, mining is often associated with the setting up or improvement of infrastructure, such as roads, hospitals, living quarters, telecommunication systems, and water supplies. These are needed to enable the transport and refining of the exploited raw materials and to accommodate and supply the mine workers (Miranda et al., 2003; Farrell et al., 2004)

On the other hand, mining comes with a list of disadvantages and negative social impacts (Table 6). The mining sector is a heavy user of energy and water. Indeed, the mining sector is one of the most energy-intensive of all industries. It consumes approximately 7 to 10% of global energy production each year. In addition, while it is common knowledge that mining requires a lot of water during the exploitation, extraction, and refining processes, the global volume of water that flows through this industry has not been estimated yet (Farrell et al., 2004). Also, mining can cause the destruction of valuable living environments for humans and wildlife. Mining activities are often associated with deforestation, the dredging of huge pits, the disposal of waste rocks, acids, and ores, and the possible formation of AMD. In this sense, one-quarter of the World Heritage Sites are at risk from the extractive industries, including mining and oil and gas extraction. Deforestation can have secondary consequences, such as increasing surface runoff and the erosion of sediments, which result in suspended sediment loads in surface waters and floods of increasing frequency (Miranda et al., 2003; Farrell et al., 2004). Additionally, mining often causes severe pollution of soils or water bodies, groundwater, and other drinking water sources.

> **The mining sector is a heavy user of energy and water.**

> **Mining activities are often associated with deforestation, the dredging of huge pits, the disposal of waste rocks, acids, and ores, and the possible formation of Acid Mine Drainage.**

These events contribute to the degradation of agricultural land and drinking water resources. Previously established and longstanding traditional businesses, such as agriculture and fisheries, which are indispensable to the lives of local people, are often affected as well. An increasing shortage of water and the degradation of arable land provoke tensions between farmers, miners, and other local inhabitants by increasing their competitiveness. Furthermore, the local people often lack accurate information about the effects of mining. Moreover, there is evidence that mining is responsible for the displacement and resettlement of local inhabitants. This can provoke riots and violence, causing a general public discomfort or even civil wars (Downing, 2002; Terminski, 2012).

There are several international initiatives to promote more environmentally-friendly and ethically reasonable mining. These initiatives include the World Summit on Sustainable Development (WSSD), the Mining, Minerals and Sustainable Development (MMSD) project, the Extractive Industries Review of the World Bank, and the International Council on Mining and Metals (ICMM). They involve implementing best practices in those regions, mostly in low- and middle-income countries, where regulations are poorly implemented. Informal artisanal and small-scale businesses seem to be of particularly high relevance (Miranda et al., 2003; Swenson et al., 2011; Low, 2012). In these regions, there are less controls and monitoring studies of the hazardous toxicants that are released into the environment by the mining and other sectors. Often, poor approaches to waste management and waste and protective clothing are other problems, related to mining. In low- and middle-income countries the frequency of occupational accidents far exceeds that in higher-income ones (Miranda et al., 2003; Farrell et al., 2004).

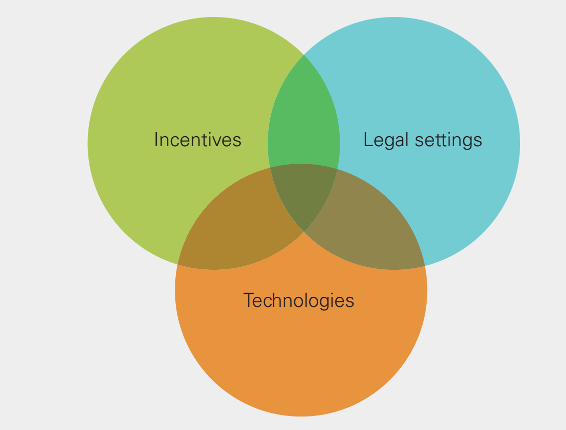


Figure 20: *Venn diagram of the basic modules enabling more environmentally-friendly mining*

In general, viable economic incentives from government, consultants, and NGOs, acceptable legal settings from politicians, decision makers, and local authorities, and proper technologies need to be applied in the mining industry to enable the more sustainable, environmentally-friendly, and ethically reasonable exploitation and processing of metals, metalloids, and minerals (Figure 20).

Table 6: Short overview of the social benefits and detriments of mining activities (Miranda et al., 2003; Farrell et al., 2004)

Social benefits	Social detriments (not best practices approaches [A])
• Temporary economic boom • Setting up and/or improvement of infrastructure	• High consumption of energy and water by the mining sector • Destruction of valuable living environments for humans and wildlife • Severe pollution of soils and water bodies, groundwater, and and other drinking water sources, affecting human and environmental health. Previously established and longstanding traditional economic sectors, such as agriculture and fisheries, which are indispensable to the lives of local people, are often affected • Displacement of local people, causing general public discomfort

A: Efforts, initiatives, and best practices are implemented to reduce the negative social impacts which tend to accompany mining activities. Nevertheless, there is evidence that such best practice approaches are not yet available and feasible worldwide, which leads to the significant list of social detriments mentioned here

Production and pollution trends of hazardous metals, metalloids, and minerals

Data availability

At present there are two comprehensive public databases available that address the primary production of metals, metalloids, and minerals. One is a compendium of world mining data from the 'Austrian 'Federal Ministry of Economy, Family and Youth' and the 'International Organizing Committee for the World Mining Congresses' (Reichl et al., 2013). The other is the data from the 'Mineral Commodity Summaries, 2013' (United States Geological Survey, 2013), developed by the United States Geological Survey (USGS). For this report, the USGS data were used because they are used and mentioned more frequently in scientific literature and have been compiled since 1996.

Future trends and hot spots

According to the USGS data presented in Table 5, it can be seen that the primary production of copper, lead and manganese has increased until the last few years. The exploitation of cadmium, chromium, thallium, and antimony through mining has plateaued while the primary production of mercury, arsenic, while asbestos has decreased during the last years.

Figure 21 shows the sum of the mined metals, metalloids, and minerals of highest concern to environmental and human health that are discussed in this report – antimony, arsenic, asbestos, cadmium, chromium, copper, lead, manganese, and mercury. The primary production of gold is also included because often large quantities of mercury are still used for gold extraction as can be seen in Figure 23. For thallium, no comprehensive data were available (Castilhos et al., 2006; Artisanal Gold Council, 2015; Barrientos and Soria, 2013; United States Geological Survey, 2013). Figure 21 shows the areas of potential risk in low- and middle-income countries. These are the places where the highest amounts of hazardous metals, metalloids, and minerals are mined. They include South Africa, China, Kazakhstan, India, Brazil, Gabon, Peru, Indonesia, Zambia, where Mexico and production volumes range from 670,000 to 14 million tonne.

For a broader perspective, Figure 22 shows the sums of the primary production of minerals and/or ores:

(A) Used for industrial purposes. These include asbestos, barite, boron, diamonds, diatomite, feldspar, fluorspar, graphite, kaolin, magnesite, perlite, phosphates, potash, salt, sulfur, talc, vermiculite, and zircon

(B) Iron and ferro-alloy metals. These include iron, chromium, cobalt, manganese, molybdenum, nickel, tantalum, titanium, tungsten, and vanadium

(C) Non-ferrous metals. These include aluminum, antimony, arsenic, bauxite, bismuth, cadmium, copper, gallium, germanium, lead, lithium, mercury, rare earth minerals, tellurium, tin, and zinc.

The latest available data for each commodity for the period 2010–2012 are used (Soria, 2013; United States Geological Survey, 2013).

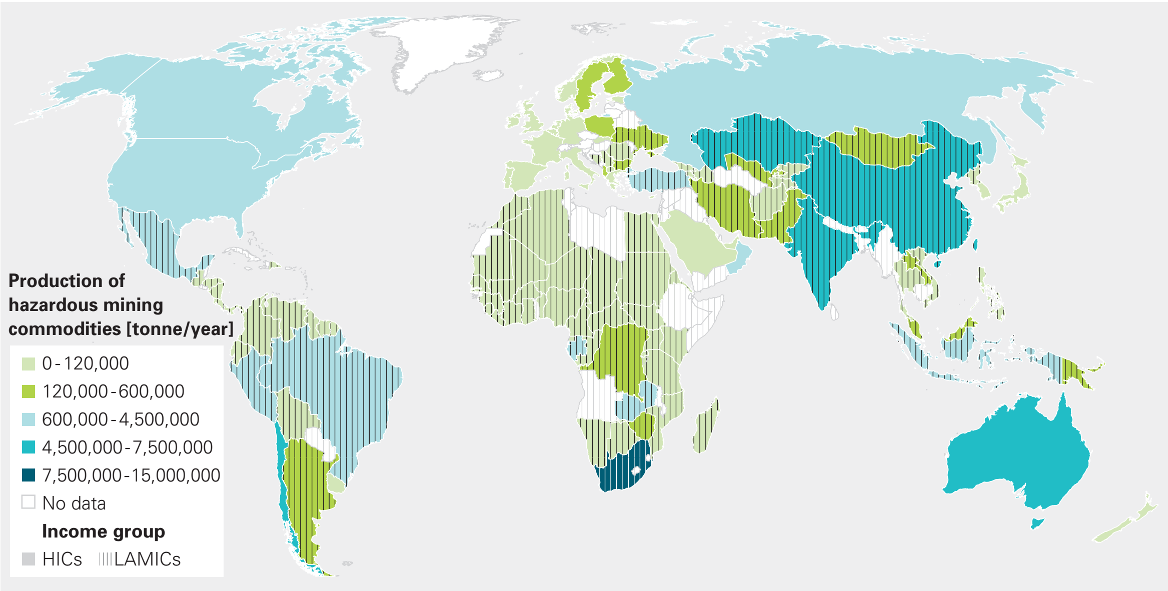


__Figure 21__: World primary production (tonne/year) of heavy metals, metalloids, and minerals of highest concern to environmental and human health. These include antimony, arsenic, asbestos, cadmium, copper, chromium, gold, lead, manganese, and mercury (Barrientos and Soria, 2013; United States Geological Survey, 2013)

These data show that in low- and middle-income countries, such as China, Morocco, India, Brazil, Iran, Mexico, Egypt, Turkey, and Chile, the largest amounts of industrial commodities are produced by primary production. The countries are listed in descending order of production. Primary production ranges from 12 million to 210 million tonne. Iron and ferro-alloy metals, in particular, are mined in low- and middle-income countries like China, Brazil, India, South Africa, Ukraine, Kazakhstan, and Iran. Production volumes range from 13 to 330 million tonne. China, Brazil, and India mined the highest amounts of commodities used in the non-ferrous metal industry; outputs ranged from 20 to 69 million tonne.

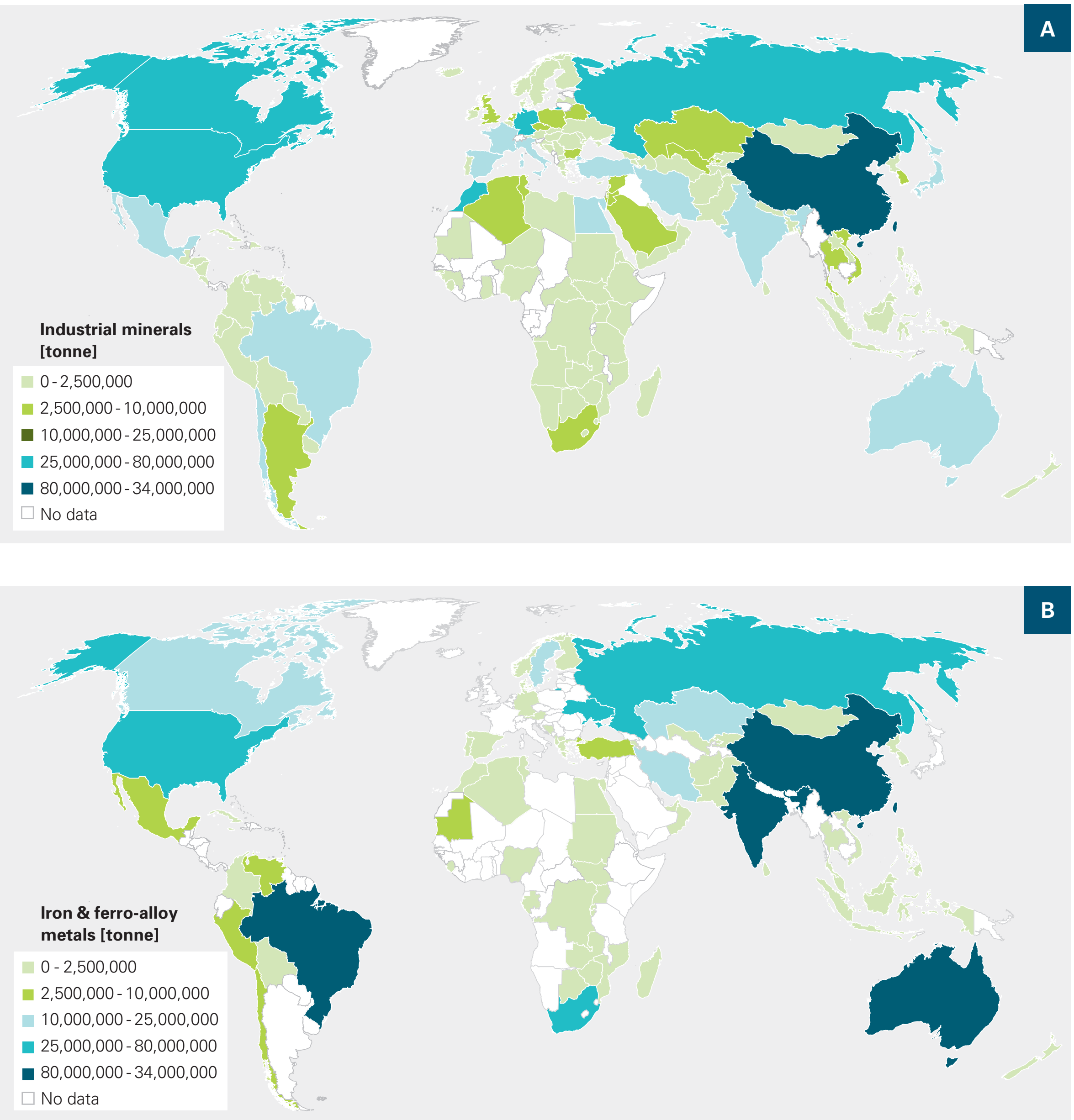


***Figure 22**: Extraction [tonne] of industrial minerals (Barrientos and Soria, 2013; United States Geological Survey, 2013)*

A: Asbestos, barite, boron, diamonds, diatomite, feldspar, fluorspar, graphite, kaolin, magnesite, perlite, phosphates, potash, salt, sulfur, talc, vermiculite, and zircon

B: Iron, chromium, cobalt, manganese, molybdenum, nickel, tantalum, titanium, tungsten, and vanadium

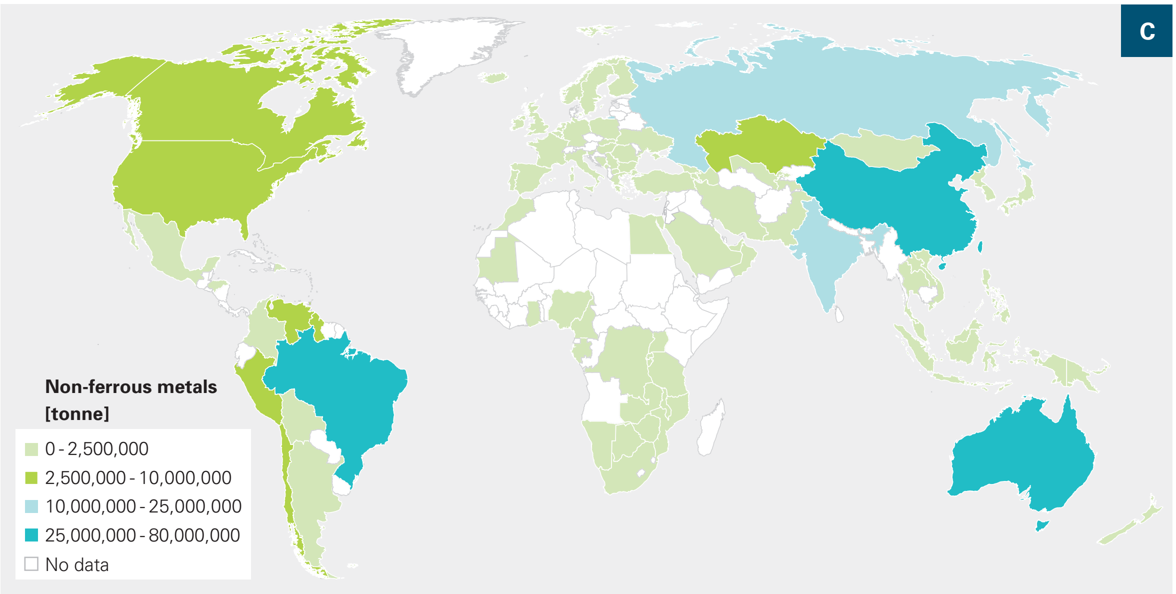


Figure 22: *Extraction [tonne] of industrial minerals (Barrientos and Soria, 2013; United States Geological Survey, 2013)*

C: Aluminum, antimony, arsenic, bauxite, bismuth, cadmium, copper, gallium, germanium, lead, lithium, mercury, rare earth minerals, tellurium, tin, and zinc

Issues of special concern

Artisanal small-scale mining

One of the biggest environmental problems related to mining in low- and middle-income countries is that of informal artisanal and small-scale mining (ASM). ASM activities are known for their large-scale risks (Farrell et al., 2004; Artisanal Gold Council, 2015). Given the informal nature of this business, a reliable assessment of annual gold production through ASM is not possible. However, it has been estimated that about 10–15 million people are engaged in ASM and that about 12–30% of the gold on the world market comes from ASM activities (Farrell et al., 2004; United Nations Environment Programme, 2008; Telmer and Veiga, 2009). ASM, in the main, uses obsolete production methods including the amalgamation technique. In this technique, large amounts of mercury are used to extract the gold. (To extract one unit of gold, three units of mercury are required (Telmer, 2011). Often, these miners are poor. They have few resources to invest in pollution control devices. They are poorly educated in mining and they have little awareness of the hazards of mercury or the other chemical agents used for the extraction of metals from ores (United Nations Environment Programme, 2008). Commonly, these miners are organized in small collectives or they work with their families to extract gold and other precious metals. In the latter case, the women and children are at highest risk because often the amalgamation is done by them at home while the men dig for ores. There is evidence that the mercury used for extraction is handled with bare hands and normal cooking equipment is used (Farrell et al., 2004; Low, 2012). Furthermore, the unregulated disposal of mercury pollutes soils and water (Malm, 1998; van Straaten, 2000; Limbong et al., 2003; Telmer and Veiga, 2009). In addition to the potential for environmental pollution, ASM has acquired a bad reputation for its support of child labor (Kippenberg, 2011). In several regions, parents send their children to work in the mines, risking their lives to increase the family income. Moreover, often the artisanal and small-scale miners are paid very little for the gold extracted; it is the traders and local officials who make the big profits (Kippenberg, 2011).

Figure 23 shows that artisanal and small-scale gold mining pose a large-scale risk. For instance, in the low- and middle-income countries of Mongolia, Guyana, Venezuela, Democratic Republic of the Congo, Burkina Faso, Tanzania, Brazil, Ecuador, Peru, Philippines, Colombia, Indonesia, and China, from 10 to 445 tonne (mean values) of mercury are released each year by artisanal gold mining activities (Artisanal Gold Council, 2015).

Acid mine drainage at abandoned mining sites

In active and, more likely, in abandoned open-pit mines, open underground shafts, and at sites where tailings have been dumped, the formation of acid mine drainage (AMD) is a very serious environmental pollution problem (Naicker et al., 2003; Kalin et al., 2006). AMD is mainly the result of sulfide rocks (mainly pyrite and marcasite) and sulfide rich tailings being exposed to oxygen and water (moisture in the air, rainwater, surface water, and groundwater) and several abiotic and biotic oxidation processes (Johnson and Hallberg, 2003; Kalin et al., 2006). Whereas in active mines, the groundwater is pumped out in order

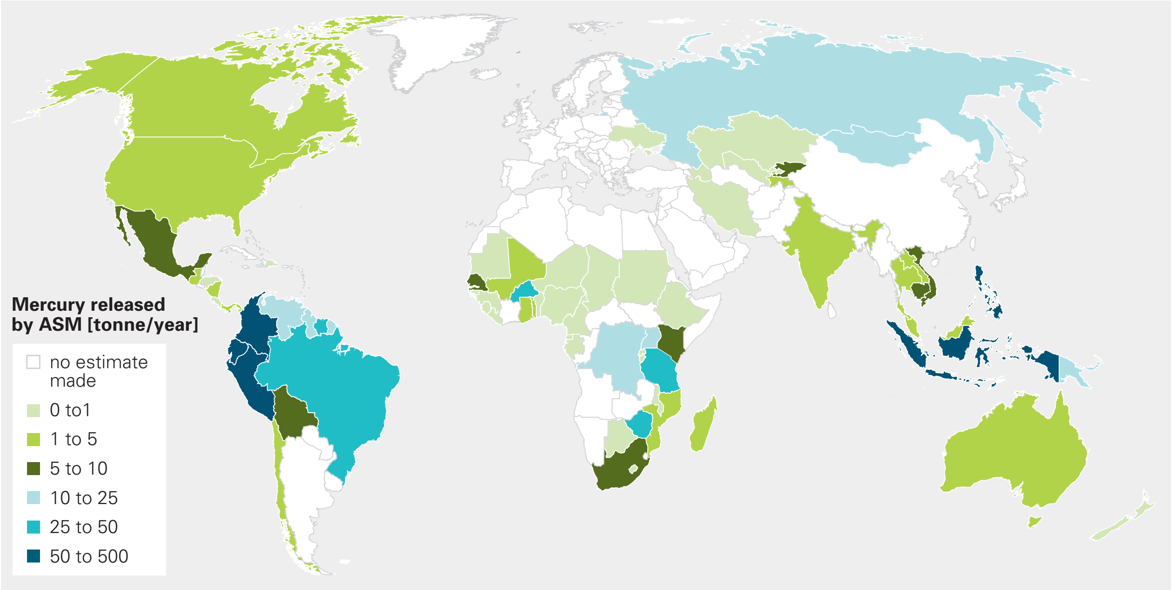


***Figure 23**: Amount (tonne) of mercury released by artisanal gold mining (mean values) (Artisanal Gold Council, 2015)*

to mine the ores, in abandoned mines, when the pumps are turned off, the water table rises. This, in the presence of oxygen and of sulfide rocks, results in AMD (Johnson and Hallberg, 2005). If these sulfides are oxidized in the presence of water, sulfuric acid is produced. These acidic drainages (AMDs) leach into the soil and migrate with surface and groundwater streams. With their low pH they provoke the release of several heavy metals and metalloids associated with sulfide rocks. These include antimony, arsenic, cadmium, copper, iron, mercury, manganese, lead, thallium, and zinc (Schwartz, 2000; Adriano, 2001; Filella et al., 2002; Naicker et al., 2003; Peter and Viraraghavan, 2005). The chemical processes involved in the formation of AMD are:

1. The oxidation of iron sulfide
2. Ferrous iron (Fe^{2+}) oxidation
3. Ferric iron (Fe^{3+}) hydrolysis
4. The enhanced oxidation of ferric sulfide ions.

$$FeS_2 + {}^{7}/_{2}O_2 + H_2O \longrightarrow Fe^{2+} + 2SO_4^{2-} + 2H^+ \quad (1)$$

$$Fe^{2+} + {}^{1}/_{4}O_2 + H^+ \longrightarrow Fe^{3+} + {}^{1}/_{2}H_2O \quad (2)$$

$$Fe^{3+} + 3H_2O \longrightarrow Fe(OH)_3(s) + 3H^+ \quad (3)$$

$$FeS_2 + 14Fe^{3+} + 8H_2O \longrightarrow 15Fe^{2+} + 2SO_4^{2-} + 16H^+ \quad (4)$$

This oxidation of ferrous iron (Fe^{2+}) to ferric iron (Fe^{3+}) and the production of sulfuric acid, and thus the formation of AMDs, can be accelerated by acidophilic bacteria and archaea (Johnson and Hallberg, 2003). Today, especially in low- and middle-income countries, the remediation techniques for AMD polluted sites are still too costly and labor intensive. If untreated, AMD can pose an environmental burden for thousands of years (Farell et. al., 2004).

Investigations in the Witwatersrand region of South Africa, which is famous for its gold mining, have measured highly elevated levels of heavy metals and metalloids in surface water, groundwater, and soil samples near abandoned tailings. As a result of AMD, concentrations in the order of mg/L have been found for chromium, zinc, cadmium, lead, copper, iron, manganese, cobalt, nickel, sodium, and calcium, and in the order of µg/L for arsenic, mercury, and selenium (Naicker et al., 2003). At this mining site, acidified and heavy metal contaminated groundwater and seepage waters with even lower pHs have resulted from AMD, causing high levels of environmental pollution. Although not mentioned in the literature cited before, in the same region, the leaching of uranium from soils through AMD causes environmental damage of high concern (Winde and de Villiers, 2002; Winde and Sandham, 2004; Tutu et al., 2008). In the Natalspruit River, downstream from the mining area, the river beds were coated with a layer of orange colored limonite that has been deposited over decades. The result is that this river is no longer a habitat for animal life; and only a minimal amount of aquatic vegetation can be found in this region (da Silveira et al., 2009). Examples of AMD like this can be found worldwide. However, in low- and middle-income countries, it is those regions with few environmental controls, restrictions, regulations, and resources for remediation, and where abandoned mines and tailings are left in unsafe conditions that are affected the most (Djenchuraev, 1999; McKinnon, 2002; Lin et al., 2007; Blacksmith Institute and Green Cross, 2013).

Working conditions and occupational incidents

In higher-income countries, the mining and ore refining industries have made considerable progress in providing safer work environments and in using more environmentally-friendly methods (Blacksmith Institute and Green Cross, 2012). In low- and middle-income countries, some progress has been made as a result of initiatives of the 'Strategic Approach to International Chemicals Management' (SAICM) policy framework and the 'International Council on Mining and Metals' (ICMM). However, inadequate enforcement of environmental legislation and lack of environmental restrictions and controls result in the release of toxicants into the environment. Besides the adverse effects caused to the environment, the health of the employees in the mining and ore refining sectors is endangered as well. According to the report 'The World's Worst Pollution Problems, 2012', in lower-income countries, the health of 2.5 million people engaged in the lead smelting industry and of 14 million people involved in the mining and ore processing industries is at risk (Blacksmith Institute and Green Cross, 2012).

For instance, there is evidence that bad working conditions have been found in Chinese-run copper mines located in Zambia (Smith, 2011). There, employees are working under poor, unhealthy, and unsafe conditions (inadequate ventilation and insufficient protective clothing). The workers are put under continuous pressure and exploited, having labor shifts of 12 to 18 hours. From medical examinations of and personal interviews with the workers, there is evidence that the employees suffer considerably from diseases associated with mining pollutants because of the bad and unsafe working conditions. Additionally, the mine workers were urged to keep secret any occupational incidents (Wells, 2011). It can be assumed that it is not just these miners in Zambia who are working under unsafe and unhealthy conditions.

Best practices

Implemented examples

Increasing data transparency

Regrettably, corruption within the mining and mineral sector is still a significant issue. This is particularly the case where mining activities have expanded in the lightly-regulated and remote regions of low- and middle-income countries, like Southeast Asia, South America, and Africa (Marshall, 2001; McEwen, 2011; Ernst & Young, 2012). The Extractive Industries Transparency Initiative (EITI) was established to increase transparency of the global revenue from extractives, such as petroleum and mining products, among all participating companies, governments, and civil societies. The EITI is a global coalition of governments, companies, and civil societies that is acting as a global standard for improving the openness and accountable management of revenues from natural resources. To discourage corruption, the EITI standards require the full disclosure of taxes and other payments made by oil, gas, mineral, and mining companies to governments. These payments are publicly available in an annual report (Extractive Industries Transparency Initiative, 2015).

Joining EITI can be beneficial for all participants of the multi-stakeholder group. For instance, by implementing the EITI standards, governments demonstrate commitment to reform and to dealing with corruption. This can lead to improved tax collection. The companies benefit from an enhanced and more stable investment climate because all companies are required to disclose the same information. This enables an improved engagement with citizens and society. Citizens and civil society benefit by receiving reliable information and the established multi-stakeholder platform improves the interactions between the different stakeholders (Extractive Industries Transparency Initiative, 2015).

In the extractive sector, enhanced transparency concerning revenues and improved transparency in the material flow of mining products are required. This will help provide more detailed economic information about exports and imports, which, in turn, leads to a better understanding of global supply chains in minerals, metalloid, and metals. Beside its economic relevance, this information can be used to estimate the amounts produced and refined on regional and international scales. For instance, the USGS is providing international and comprehensive data about the production, import, and export of minerals, but its data concerning the trade of minerals (exports and imports) is more referenced to the situation in the USA (United States Geological Survey, 2013). With the information of the EITI and the USGS, it may be possible to assess regions with a high potential for corruption and where mining can pose risks to environmental and human health.

Sustainable mining

Huge quantities of water are required during ore processing. The water is used for dust suppression, transporting slurry, and the needs of employees. Hence responsible approaches to water management and the implementation of water recycling systems are mandatory. By so doing, valuable water resources can be retained, the release of mining pollutants into surface water and groundwater can be reduced, and competitiveness between the mining industry and other interested groups, such as fisheries, farmers, and local municipalities, can be diminished. Conscientious use of water resources by mining industries is an important criterion for ensuring continued sustainability of mining operations. This is especially the case in water-stressed regions – to the extent that one can talk about sustainability and mining operations in the same breath. Accordingly, the ICMM is focusing on improving the industry's water management performance (International Council on Mining & Metals, 2012).

There are several case studies addressing improvement of water management mentioned in the ICMM report 'Water management in mining: a selection of case studies' (International Council on Mining & Metals, 2012). For example, in the coal mining region near the city of Emalahleni, northeast South Africa, where water resources are rare, the Emalahleni Water Reclamation Plant (EWRP) was commissioned in 2007. With the help of the EWRP, it is possible to treat water from mining operations and to pump and treat water from orphan mines. Following this treatment, an additional supply of water can be delivered from the plant to the local municipality's drinking water system. This reduces social water stress and retains drinking water resources. In addition, by pumping water out of abandoned mines, the formation of AMD and the additional dissolving of hazardous metals, metalloids, and salts can be prevented (International Council on Mining & Metals, 2012).

Remediation techniques

Taking the necessary precautions and avoiding causing environmental pollution from the outset is cheaper and more sustainable than environmental remediation. Nonetheless, more time and money should be invested to find feasible and low cost remediation techniques that can be implemented, particularly in already contaminated regions in low- and middle-income countries. Currently, there are several methods for remediating sites contaminated with inorganic pollutants (e.g. hazardous metals and metalloids). These include:

- The isolation method, which uses physical barriers made of steel, cement, and bentonite, and ground walls to immobilize pollutants

- The solidification/stabilization method, which injects agents to encapsulate contaminants in a solid matrix, or reduces the mobility of the contaminant by forming chemical bonds

- The size selection method, which separates larger cleaner particles from smaller more polluted ones

- Electrokinetic processes, which, by using low-intensity electric currents, precipitate ions and small charged particles that are then transported by water

- Bioleaching, which uses bacteria under aerobic conditions to leach out metals and metalloids (an effect comparable to the one forming AMD)

- Phytoremediation and constructed wetlands, which uses non-edible and disease-resistant plants, or plants which can provide renewable energy, that are able to take up and incorporate heavy metals and remove them from soils and contaminated water systems

- Soil washing and in-situ flushing, which is achieved by adding water, organic or inorganic acids, sodium hydroxide, water soluble solvents, and complexing agents in various combinations.

Most of these techniques are feasible and implemented only in industrial countries because in low- and middle-income countries, there are insufficient resources. Such techniques are often too cost intensive and there is less responsibility to remediate polluted and abandoned mining and ore processing sites. These examples of remediation techniques are described in more detail in Mulligan et al. (2001). The main challenge for remediation is that there is no cost-efficient remediation technique available to remove the different types of metals and metalloids in one go. This is because their different physicochemical properties and their different distribution patterns in the environment depend on the pH, soil composition, and their different bioavailability. Furthermore, there is no general method that can be used to remediate polluted sites completely. Moreover, before remediation of polluted sites can be undertaken, assessments of surface and groundwater streams and geological formations are required. Once this information is available, it is possible to find the most cost-effective, functional, and efficient methods for removing the hazardous pollutants. According to the laboratory experiments of Mkumbo (2012) in Tanzania, a combination of phytoremediation, using local plants, and solidification/stabilization techniques using buried nodules of the sorbent materials zeolite and autoclaved aerated concrete, seem to be feasible and cost-effective methods. While these can be used in low- and middle-income countries to remove heavy metals, the techniques need to be further improved (Mkumbo, 2012).

Theoretical examples

There are several initiatives that focus on improving the performances of mining companies and promoting more sustainable, environmentally-friendly, and ethically reasonable mining activities. These initiatives include the WSSD, the MMSD project, and the ICMM. Despite these initiatives, the mining sector and its accompanying ore processing and refining industries are causing one of the world's worst pollution problems (Blacksmith Institute and Green Cross, 2012). More viable and feasible incentives are required to push forward the implementation of more environmentally-friendly extraction techniques. They also need to increase the level of support for those mining companies or collectives that are seeking to comply with the local legislation, regardless of whether they are operating at a small or large scale. In addition, it is necessary to provide more education for the employees involved in the mining sector. This is especially the case in low- and middle-income countries, where the workers and the environment are affected the most. Obsolete techniques need to be abolished and more sustainable and effective methods promoted. For instance, the implementation of the FAIRMINED certificate is a first step in encouraging responsible small-scale gold mining activities. Small-scale mining communities can get the FAIRMINED certificate by following the required standards. These include requirements for them to:

- Conduct responsible, formal, and legal mining operations

- Take steps to protect the environment

- Meet strict requirements for labor conditions

- Ensure transparency in the trade of FAIRMINED minerals

- Support socio-economic development though a financial premium on the FAIRMINED products.

The FAIRMINED certificate guarantees that:

- During the production of the different mining products, no child under 15 years has worked for the mining organization and no child under 18 years has worked under hazardous or dangerous conditions

- The employees have used appropriate protective gear and attended health and safety training courses

- The product is traded fairly and that a part of the revenue is used for the social development of their communities or in new, more environmentally-friendly mining practices and technologies, minimizing the use of mercury and cyanide and mitigating the negative impacts on the environment and human health (Low, 2012; Fairmined, 2015).

Programs like this contain good, basic approaches that could be expanded and replicated at the international level and for other mining commodities as well. The implementation of FAIRMINED, FAIRTRADE, and FAIRPRODUCED labeled ores and mining commodities would be helpful in encouraging more responsible mining activities (for small-scale and large-scale operations) provided the requirements of the certificates are well controlled and reliable. With the help of trustworthy and serious certificates, it would be possible for consumers to make their own decisions as to whether they prefer to buy products that are mined and produced under ethically reasonable and more environmentally-friendly conditions. Their alternative would be to buy products where it is unclear whether the miners worked under bad and dangerous conditions, child labor was accepted, small-scale communities were exploited by mercenary authorities, and the environment polluted through using obsolete techniques.

Improvement in the recycling of metals and metalloids

In future, the focus should be on improving the secondary production of metals and metalloids and finding more sound and efficient methods of secondary extraction. This is feasible worldwide (even in low- and middle-income countries) and is better than focusing on expanding primary production. Basically, recycled metals are cheaper. The smelting and refining of scrap uses less energy and is more cost effective than the extraction, smelting, and refining of metals and metalloids from ores. For example, recycling iron saves 20% of the energy used to mine and process the ore. For copper, the comparable saving is 60% and for aluminum it is 90%. In addition, in secondary production it is not necessary to destroy and deforest valuable and vulnerable natural environments. Additionally, there is no disposal or stockpiling of the e-wastes and solid wastes associated with the processing of the ores of heavy metals and metalloids. Thus, compared to primary production, secondary production is more sustainable (Visser, 2012). Although secondary production is more sustainable, at this time, the recycling of metals and metalloid is still quite challenging. And, although in principle, metals are infinitely recyclable, under present conditions, the recycling of metals and metalloids is often inefficient, and not every single metal or metalloid can be recycled efficiently. The widescale blending of different metals and metalloids to enhance their physicochemical properties and their characteristics – their resilience, thermal and electrical conductivity, hardness, and resistance to corrosion – makes the secondary production of metals and metalloids even more difficult (Reck and Graedel, 2012; Visser, 2012). The United Nations Environment Programme (UNEP) and the International Resource Panel indicate that the capability of being recycled varies among the different metals. The estimated global end-of-life recycling rates (EOL-RR) indicate that of 60 metals which are discarded, 18, such as silver, aluminum, gold, cobalt, chromium, copper, iron, manganese, niobium, nickel, lead, palladium, platinum, rhenium, rhodium, tin, titanium, and zinc, are recycled 50% of the time (Graedel et al., 2011a, b). Three metals, iridium, magnesium, and molybdenum are recycled between 25 and 50% of the time (Figure 24). However, these data show that most discarded metals are recycled less than 1% of the time. In addition, in Figure 24, the most hazardous metals and metalloids that are released into the environment through mining activities are highlighted (white boxes).

In general, with the continuously increasing production and use of metals and metalloid-containing commodities (in electronics and construction materials), the inefficient disposal, separation, collection, and storage of metals and metalloids, and their inefficient recycling make it difficult to meet the demand. Therefore, at this time, mining, even though it is less cost efficient, is still necessary in order to provide sufficient minerals, metals, and metalloids; secondary production is not efficient enough to meet resource needs (Visser, 2012). However, improvements in and expansion of the secondary production of metals and metalloids would help to achieve a more sustainable closed-loop materials system. Such a development would reduce the deforestation and destruction of valuable environments and reduce the need to dispose of toxic heavy metals and metalloids. However, it is important that only controlled and sound methods should be used for recycling. Today, evidence of the bad practices in the recycling sector that mainly occur in low- and middle-income countries is well known. In some regions, people rifle through piles of rubbish looking for recyclable heavy metals and metalloids. For example, the inappropriate recycling of lead from lead–acid car batteries using obsolete and hazardous methods poses a high risk to human and environmental health (Blacksmith Institute and Green Cross, 2011, 2013). This topic will be discussed in more detail in the following section addressing electronic industry pollutants (e-waste).

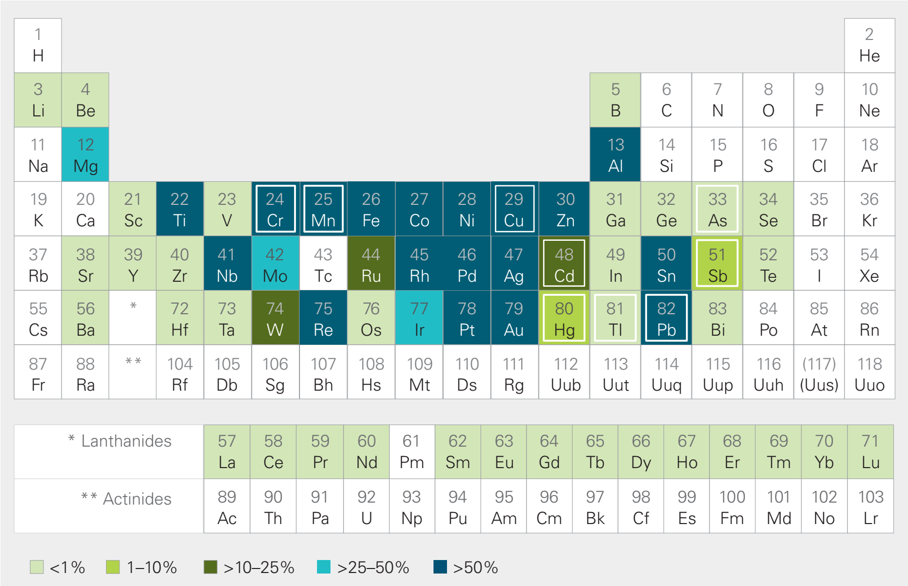


Figure 24: *Global estimates of end-of-life recycling rates for 60 metals and metalloids (Graedel et al., 2011a, b)*

Electronic Industry Pollutants (E-Waste)

Chemical characteristics and their potential risks

Introduction

In today's throw-away society, the desire, for devices with faster and newer state-of-the art technology is leading to a continuous expansion of the electronic market and to shortened innovation cycles for electrical and electronic equipment (EEE). Much of this EEE has a short lifespan and fast turnover. Frequently, obsolete or damaged EEE is not recycled or repaired, but, more likely, is simply thrown away. Thus the amount of waste electrical and electronic equipment (WEEE), such as superseded personal computers, mobile phones, entertainment equipment, and electronic consumer equipment has proliferated immensely during the last decades. The increased production and disposal of EEE represents an emerging and growing problem that can adversely affect environmental and human health. This holds especially true, since WEEE is transported from high income countries (HICs) to low- and middle-income countries (LAMICs) such as Brazil, China, India, Mexico, Nigeria, Pakistan, and Thailand (International Labour Organization, 2012; Lewis, 2011; Skinner et al., 2010; Silicon Valley Toxics Coalition, 2014). Here, the waste is discarded or processed (dismantled and recycled) under poor and inappropriate conditions, since this type of waste comprises a wide range of hazardous compounds (these are discussed in more detail in the section **E-waste pollutants of environmental concern;** Widmer et al., 2005; Wong et al., 2007c; European Parliament and Council of the European Union, 2012).

The amount of waste electrical and electronic equipment (WEEE) has proliferated immensely during the last decades.

Today, the generation of WEEE is the fastest growing waste stream worldwide (about 4% growth per year; International Labour Organization, 2012) and accounts for up to 8% of all municipal waste (Streicher-Porte et al., 2005). In general, the recent global production (data from 2006 and 2009) of WEEE is estimated to be between 20 and 50 million tonne, a large portion of which, as has already been mentioned, is sent to LAMICs (United Nations Environment Programme, 2006a; Robinson, 2009; Schluep et al., 2009). The production of WEEE in 2014/15 is predicted to be between 40 and 70 million tonne (Jain, 2008). This high variation in the volume of WEEE to be produced predicted in the literature underscores the difficulties in estimating the global generation of WEEE and the amounts of environmentally friendly or unfriendly compounds in it.

According to the Directive 2002/96/EC of the European Parliament (revised at the end of 2011) and of the Council (January 2003) on WEEE, this superseded EEE is defined as: "WEEE, which is waste, including all components, sub-assemblies and consumables, which are part of the product at the time of discarding." (European Parliament and Council of the European Union, 2012). WEEE was divided into 10 categories (Widmer et al., 2005):

- large household appliances
- small household appliances
- IT and telecommunications equipment
- consumer equipment
- lighting equipment
- electrical and electronic tools
- toys and sports equipment
- medical devices
- monitoring and control instruments
- automatic dispersers.

Although, presumably, this categorization system is becoming a broadly accepted standard, there is no international standard definition for electronic waste (e-waste) available yet. There are several forms of WEEE which may or may not be normally considered as e-waste compounds as shown in the literature (Robinson, 2009). This makes it even more difficult to assess the amounts of e-waste that are produced, or shipped, at a global scale. There are international initiatives to prevent the export of and the trade in e-waste and other hazardous products. The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal (which came into force in 1992) is a good exemplar (United Nations Environment Programme, 2014). However, there is evidence that companies from industrial countries are searching for loop holes in the regulations in order to ship e-waste to LAMICs for cheaper recycling and cheaper disposal, or to offer obsolete EEE as secondhand goods. In some cases, unusable EEE is disguised as secondhand goods and shipped to LAMICs although it is useless or never used in the receiving countries (Jain, 2008; International Labour Organization, 2012). All in all, about 181 countries are supporting the Basel Convention and of these, 53 have signed it. Other countries – Angola, Fiji, Haiti, Myanmar, Sierra Leone, Solomon Islands, South Sudan, Tajikistan, Timor-Leste, United States of America, and Vanuatu – have not even confirmed the Basel Convention, which suggests that they are probably not willing to stop their exports of hazardous e-waste to LAMICs yet. For the USA, one of the challenges might be that all federal states needs to fulfill the requirements of the Basel Convention to enable the affiliation of the USA to the Basel Convention. In addition, the implementation of the Basel Convention is mainly driven by the poorer countries affected by it and not by the HICs with strong economies. This might be another reason why the USA has not ratified the Basel Convention, yet (Martin Streicher-Porte (FHNW); personal communication). However, the International Labour Office (International Labour Organization, 2012) and Smith et al. (2006) have shown that 80% of all e-waste that is sent to LAMICs for recycling ends up in informal e-waste recycling sites. In addition to the e-waste which is shipped into LAMICs, domestically produced WEEE is increasing as well as a consequence of economic development, especially in regions such as India, China, and Africa. This further amplifies the burden of e-waste pollutants that needs to be handled by these countries (Jain, 2008).

Main Issues

The main issues associated with the displacement, disposal, and processing of e-waste in LAMICs are (International Labour Organization, 2012):

- Regulations at international, national, and local level are still lacking or they are not observed
- Often unsuitable facilities and obsolete techniques are used to process e-waste in LAMICs
- E-waste contains a wide mixture and variety of compounds making separation and treatment complex
- Employees are working under bad labor conditions
- The toxicological potential of pollutants, released through the disposal and recycling processes, is high

Existing regulations and their enforcement

Many international regulations exist. However, these are not followed or still not approved in every country. Hence, although there are several international initiatives, such as the Basel Convention or the Basel Action Network Amendment, the trade and sale of e-waste, particularly from HICs to LAMICs and informal recycling businesses, still represents a major issue. Although the enforcement of these initiatives should help to inhibit the trade in WEEE or to better understand the transboundary movements of WEEE, the WEEE trade patterns are still difficult to assess, especially in LAMICs (Widmer et al., 2005; International Labour Organization, 2012; Lu et al., 2015). For instance, India has endorsed the Basel Convention, but it has not ratified the Basel Action Network (BAN) Amendment. Until now, in India there are no specific laws or guidelines framed for the trading and recycling of e-waste (International Labour Organization, 2012). On a global scale, the controls for the shipping of e-waste containers are still not efficient enough yet to control the trade completely (International Labour Organization, 2012). At the national and local levels, there is a serious lack of governmental authorities and regulations. Where they do exist, the poor implementation of legal instruments, corruption, the absence of standards for the recycling of e-waste, and the poor participation of stakeholders in supporting/applying sustainable and more environmentally-friendly recycling methods, especially in LAMICs, further promote the informal recycling of e-waste. These deficiencies make it even easier to trade and deal in e-waste. In addition, the definition of and legislation for controlling WEEE differ considerably from country to country (International Labour Organization, 2012; Lu et al., 2015).

On a global scale, the controls for the shipping of e-waste containers are still not efficient enough yet to control the trade completely.

One of the main incentives resulting in poor compliance with international and national regulations and the informal collection, trade, and recycling of e-waste is the profitable extraction and sale of valuable compounds – platinum group elements, gold, silver, and copper (Wong et al., 2007a; Robinson, 2009).

Poor facilities and obsolete techniques

Given the large amounts of e-waste imported by LAMICs – 20 to 50 million tonne (United Nations Environment Programme, 2006a; Robinson, 2009; Schluep et al., 2009) – these countries are receiving disproportionate loads of e-waste without having the knowledge, capacity, appropriate facilities, and techniques to handle them properly (International Labour Organization, 2012).

Informal e-waste recyclers are using inappropriate, unsafe, and obsolete treatment, disposal, and e-waste recycling technologies and methods, which pose a risk to environmental and human health.

Often, the informal e-waste recyclers are using inappropriate, unsafe, and obsolete treatment, disposal, and e-waste recycling technologies and methods, which are posing a risk to environmental and human health. For instance, in LAMICs, pyro-, hydro- and bio-metallurgical processes are commonly used to recover valuable metals (Cui and Zhang, 2008). Pyro-metallurgical processing includes the incineration and smelting of e-waste containing valuable target precious metals and non-ferrous metals, such as platinum, gold, silver, and copper. More efficient processes are strongly linked with appropriate investment. Therefore, because resources are scarce, especially in LAMICs, these obsolete pyro-metallurgical methods are applied without using any emission filters or emission control systems. This leads to a release of toxic compounds, such as polycyclic aromatic hydrocarbons (PAHs), heavy metals, and halogenated hydrocarbons, into the environment mainly as aerosol particles. It is the employees of these informal businesses, the local community, and the environment in the vicinity of these e-waste recycling sites that are most affected (Tue et al., 2010; International Labour Organization, 2012). In particular, the low-temperature, open burning in the fields of halogenated flame retardants and the incomplete combustion of the plastics and organic matter contained in the burned WEEE are causing an aerial exposure to highly toxic and carcinogenic PAHs, such as benzo[a]pyrene, dioxins, and furans in particulate form (Yu et al., 2006b; Cui and Zhang, 2008). In addition, the emission of these compounds leads to the contamination of the soil and water following dry and wet disposal methods. According to the investigations of the Blacksmith Institute, the burning and melting of plastic-sheathed cables to isolate and recover the copper is one of the main activities in Ghana that is of the highest concern from a public health perspective. This is because copper acts as a catalyst for dioxin formation during incineration processes (Cui and Zhang, 2008; Sepúlveda et al., 2010; Blacksmith Institute and Green Cross, 2013). Hydro- and bio-metallurgical processes are used to dissolve and recover the target metals. For hydro-metallurgical processing, acids and chemicals, like cyanide, halide, thiourea, and thiosulphate, are used. For bio-metallurgical processing, microbes, pyritic compounds, oxygen, and water are used to accelerate the natural leaching process of metals from e-waste heaps (Leung et al., 2008). At hydro- and bio-metallurgical processing sites, the leakage of acids, solvents, and heavy metals during the recycling and the extraction processes or the inappropriate disposal and dumping of e-waste can contaminate soils and drinking water resources in the vicinity.

The diverse composition of e-waste presented in Table 7, the different materials which are blended, glued, fixed, or clamped together, and the scarcity of financial resources are making the efficient recycling of plastic and individual types of metals very difficult (Mundl, 2010). Today, sustainable and more environmentally-friendly recycling technologies, which enable a sound recycling of e-waste, are just as applicable and economic in larger middle- and higher-income countries. But they require a large capital investment, qualified and well educated employees, and high quantities of e-waste to be available. For these reasons, in lower income countries and in most of the middle-income ones, informal recycling business are more prevalent. The pyro-metallurgical, state-of-the-art recycling of e-waste comprises three steps (Empa, 2009f):

1. Removal of critical components from the e-waste in order to avoid dilution of and contamination with toxic substances during the subsequent recycling processes

2. In large-scale operations, mechanical processing is used to further concentrate the specific components to be recovered from the e-waste and to further separate hazardous materials

3. Refining of resources in the e-waste to recover the raw material with minimal environmental impact.

Mixture and variety of different compounds

Heavy metals, metalloids, halogenated hydrocarbons, and other persistent and hazardous pollutants are to be found within the e-waste. The burning of e-waste at low temperatures produces PAHs, such as dioxins and furans, or is causing the release of further halogenated flame retardants. These compounds are known to pose a high risk to environmental and human health (Robinson, 2009). In addition to these toxic compounds, e-waste consists of a broad range of other material, such as glass, ceramics, plastics and rubber, rare earths, non-ferrous metals (aluminum, copper, and lead), ferrous metals (steel and iron), and precious metals (platinum group metals, gold and silver; International Labour Organization, 2012; Lu et al., 2015). The composition of the e-waste is strongly dependent on its type; there is high variation among the 10 different categories of WEEE of Directive 2012/19/EU of the European Parliament (European Parliament and Council of the European Union, 2012). In addition, the EEE industries, especially the ones located in higher-income countries, have been put recently under increased pressure to avoid or ban the use of highly toxic compounds, such as cadmium and mercury. Such was not the case in the past. Hence, older e-waste often contains more hazardous compounds than recently produced waste (Mundl, 2010). Table 7 shows the composition of the different types of WEEE. 'Large household appliances' includes refrigerators, freezers, and washing machines; 'small household appliances' includes vacuum cleaners, clocks, fryers, and toasters; 'information and communication technologies' includes personal computers, laptops, and telephones; and 'consumer electronics' includes televisions, cameras, and audio amplifiers (Empa, 2009a).

Inadequate labor conditions

The use of obsolete and unsafe methods for e-waste collection and recycling is posing a high risk to human health. The LAMIC workers often are not aware of the toxic compounds contained in the e-waste they are collecting, dismantling, and disassembling. They are mechanically shredding electronic and electrical equipment for recycling without wearing any googles, gloves, masks, or protection clothes. In LAMICs, children and women often may be involved in collecting e-waste, such as plastic coated cables, cathode ray tubes, and printed circuit boards and in manually separating out the desired components. Sometimes, mainly because of financial constraints, they are involved in the burning activities (Prakash et al., 2010). Children and women constitute one of the most susceptible at-risk groups exposed to the heavy metals, flame retardants, and PAHs, which are contained in e-waste or which are released by open e-waste burning activities. During the smelting, leaching, and other extraction processes for the target metals, the informal workers often do not wear masks or adequate protective clothing. In addition, often there are no emission control devices or emission filters being used and hence they are exposed to toxic fumes and solvents that continuously endanger their health (Leung et al., 2008; Li et al., 2008c; Robinson, 2009; International Labour Organization, 2012).

Table 7: Material composition of the four main e-waste categories [%] (Empa, 2009a)

Material	Large household appliances	Small household appliances	ICT[A] and consumer electronics
Ferrous metal	43	29	36
Aluminum	14	9.3	5
Copper	12	17	4
Lead	1.6	0.57	0.29
Cadmium	0.0014	0.0068	0.018
Mercury	0.000038	0.000018	0.00007
Gold	0.00000067	0.00000061	0.00024
Silver	0.0000077	0.000007	0.0012
Palladium	0.0000003	0.00000024	0.00006
Indium	0	0	0.0005
Brominated plastics	0.29	0.75	18
Plastics	19	37	12
Lead glass	0	0	19
Glass	0.017	0.16	0.3
Other	10	6.9	5.7
Total	**100**	**100**	**100**

[A] information and communication technologies

Elevated levels of contaminants associated with e-waste are measured in the blood, breast milk, hair, and placentas of people involved in collecting and processing e-waste or who are living in the vicinity of e-waste storage or processing sites. In this latter instance uptake mainly happens through the inhalation of contaminated air, dust, and fumes and the drinking or eating of contaminated water and food – rice, eggs, milk, and meat (Darnerud, 2003; Zhao et al., 2006; Chan et al., 2007; Leung et al., 2008, 2010; Robinson, 2009; Tue et al., 2010). Additionally hazardous compounds are transmitted via people's hands during eating because an adequate system of running water for hand washing is lacking (International Labour Organization, 2012). The occupational and public exposure and the bioaccumulation of toxicants that are emitted and leached from e-waste, especially if they are stored and burned in the open air, can lead to acute and chronic health disorders. These disorders include skin and eye irritation, respiratory diseases (such as coughing, choking, pneumonitis and lung cancer, tuberculosis, and asthma), mental disorders, and diseases of the central nervous system (tremors, convulsions, and cancer) (Yu et al., 2006a). Moreover, increased incidences of birth defects, infant mortality, underdevelopment of the brains of children, blood diseases, anomalies of the immune system, and malfunction of the kidneys were found in regions with high informal e-waste collection, storage, and processing activities (Prakash et al., 2010).

Toxicological potential

As already mentioned, informal e-waste businesses in LAMICs are mostly associated with a considerable release of a diverse cocktail of highly toxic compounds. In general, about 1000 individual chemicals have been identified in e-waste streams. These include heavy metals and metalloids (A), PAHs (B), and halogenated hydrocarbons and flame retardants (C). These pose high risks to environmental and human health (Empa, 2009b; International Labour Organization, 2012). Currently, there are few studies and limited data on the impacts on the environment of the informal disposal and processing of e-waste. The adverse effects on human health, especially after long-term exposure, have not been investigated either. Nevertheless, it is known that many of the single compounds that are found in e-waste, on their own, act as

Currently, there are few studies and limited data on the impacts on the environment of the informal disposal and processing of e-waste.

neurotoxins, endocrine disruptors, allergens, or carcinogens. Also many of them are slowly degraded by natural processes and have a high potential for bioaccumulation (International Labour Organization, 2012). The adverse effects caused by exposure to mixtures of these hazardous compounds has not been sufficiently investigated at the present time. Since the composition of e-waste varies enormously, not every substance that is released into the environment from e-waste storage and processing can be considered in this report. The major groups and main substances of highest environmental concern that are contained in e-waste are summarized below and in Table 8, Table 9, and Table 10.

E-waste pollutants of environmental concern

A) Heavy metals and metalloids.

Antimony, arsenic, barium, beryllium, cadmium, cobalt, copper, chromium VI, indium, lead, lithium, mercury, nickel, thallium, tin, rare earth elements (yttrium, europium), and zinc sulfide are the metals and metalloids contained in e-waste that are of the highest environmental concern (Empa, 2009b; International Labour Organization, 2012; Table 8).

Use

The amounts of the individual heavy metals and metalloids that are used for the production of EEE in the electronic industry is not assessable. The amounts of the elements that are used in the semiconductor or the electronic industry have increased significantly – from the 12 elements that were used in 1980 to the 60 elements used in the 21th century (Appendix Figure 5; Theis, 2007). For instance, information about specific agents and compounds that are used in mobile phones and tablets and their specific purposes in these electronic devices are not easily accessible and are generally unknown to the public. Often, these details are secret or this information is not made available because of patent laws. In addition, complex alloys of different chemical compounds, metals, and metalloids are blended together, which makes it more difficult to get an overview of the chemicals used in EEE (Brunning, 2014). Although data about compounds used in such EEE as mobile phones and tablets are limited, some necessary elements which constitute parts of this EEE can be assumed. For instance, mobile phone and tablet screens often contain a mixture of indium and tin oxides which acts as an electrical conductor and enables users to control the devices using their hands. The glass of the screens often comprises aluminosilicates and potassium ions. In addition, several rare earth elements, such as yttrium, lantharium, terbium, praseodymium, europium, dysprosium, and gadolinium, are used to produce the screen colors. In modern mobile phones, often lithium ion batteries are used. These often contain lithium cobalt oxides or manganese and carbon. The micro-electrical parts in the mobile phone often consist of copper wires and gold, silver, and platinum group elements. The microphone and the speaker often contain nickel, praseodymium, gadolinium, neodymium, terbium, and dysprosium. Silicon is one of the main compound in chips, while other compounds, such as antimony, arsenic, and gallium, are used as well as electrical conductors. Often tin and lead solders are used, while lead-free solder contains metals such as tin, copper, and silver. The cases of the various devices are mainly made of magnesium compounds or plastics with flame retardants. For example, more than 30 elements are used in the manufacture of mobile phones and tablets. Additionally, data from Umicore Precious Metal Refining showed that more than 40 elements are used during the production of mobile phones (Schluep et al., 2009). These examples emphasize the large variety of compounds used in electrical devices. Table 8 details the major metals and metalloids that occur in EEE. It lists their intended uses, human toxicity, their maximum contaminant levels (MCLs) for drinking water, and their acute (MAC-EQS) and chronic (AA-EQS) environmental quality standard for aquatic organisms in surface water bodies.

Environmental behavior and occurrence

The release and distribution of metals and metalloids into the environment depend on several factors. The use of rudimentary e-waste recycling approaches, like incineration or the burning of e-waste in open fires, or using acids (cyanides and halides) to leach and extract the desired components in an open field without any controls and regulations, results in a serious release of hazardous metals and metalloids and other toxic substances into the environment (International Labour Organization, 2012).

In general, after low-temperature incineration processes in the absence of any filter systems, these compounds are emitted into the air mainly as fumes or as airborne particles bound to soot or other organic matter. Subsequently, metals and metalloids can precipitate via dry or wet deposition after rain events and contaminate surface water systems, natural and agricultural soils, or they can adsorb to the cuticles of plants that are in the vicinity of e-waste processing sites. In addition, metals and metalloids can directly diffuse into soils and groundwater from landfills as a result of natural processes or rudimentary recycling techniques via chemical or biological seepage and thus contaminate soils, agricultural crops, and drinking water resources. The distribution of metals and metalloids in soils and their uptake and incorporation by plants via roots is dependent on water availability, soil and plant type, pH, redox potential, organic content, and the metal species (Adriano, 2001; Steiner, 2004; Luo et al., 2011).

The different solubilities and bioavailabilities of the individual metals and metalloids are highly variable. The environmental behaviors of Cd, Cr, Cu, Pb, Hg, Tl, As, and Sb – the most serious and relevant metallic pollutants of environmental concern – are described in more detail in the section **Mining pollutants of environmental concern** (p. 70)**.**

In south China, concentrations of Cd of 17 mg/kg, of Cu of 11,140 mg/kg, of Pb of 4500 mg/kg, and of Zn of 3690 mg/kg were determined in soils of former e-waste incineration sites (mean values; Luo et al., 2011). The common background concentration of Cd was from 0.11 to 0.5 mg/kg (Fassett, 1975; Salomons and Förstner, 1984; Giuffré de López Camelo et al., 1997), that of Cu was from 50 to 55mg/kg (Taylor, 1964; Salomons and Förstner, 1984), that of Pb was from 13 to 26 mg/kg (Zimdahl et al., 1973; Salomons and Förstner, 1984; World Health Organization, 2011; Thomas Jefferson National Accelerator Facility, 2014) and that of Zn was from 52 to 79 mg/kg (Wedepohl, 1995).

Rice and vegetables, cultivated in the same region, showed elevated heavy metal concentrations which exceed the maximum level permitted in Chinese food (Leung et al., 2008). Children living in Guiyu, China, had significantly elevated blood lead levels (BLL) and blood cadmium levels. Of the children surveyed, about 71% (109 of 154) had a BLL higher than 100 µg/L (Zheng et al., 2008b). These values indicate that the release of metals and metalloids through rudimentary recycling businesses are posing a risk to environmental and human health and that they have a potential for bioaccumulation. Today, a reference BLL of 50 µg/L is used to identify children with BLLs that are much higher than most children's levels. If the BLL of a child between 1 and 5 years of age is equal to or higher than 450 µg/L, medical treatment is recommended (Centers for Disease Control and Prevention, 2014).

Toxicity

Several metals and metalloids are known or suspected to promote the formation of several forms of cancer. For instance, according to the International Agency for Research on Cancer (IARC), As, Be, Cd, and Cr(VI) are listed in group 1, carcinogenic to humans. In addition, Indium (In) and Pb are listed in group 2A, probably carcinogenic to humans. And antimony trioxides, Co, organic Hg compounds, and Ni are listed in group 2B, possibly carcinogenic to humans (IARC classifications see Table 8). As determined by the US Environmental Protection Agency, the MCL for drinking water for As is 0.001 mg/L, for Be and Cd 0.005 mg/L, for Cr(VI) 0.1 mg/L, for Pb 0.015 mg/L, and for Hg 0.002 mg/L. For In and Co there are no MCLs available yet. The MCLs of other metals and metalloids are presented in Table 8 as well. Several metals and metalloids act as neurotoxins and cause impairments of the nervous system. These include As, Cd, Hg, Li, Pb, and Tl. Other compounds, such as Co, Cr(VI), Cu, Li, and Ni, are known to act as skin and eye irritants or as allergens. The inhalation of As, Be, Cd, Co, Cr(VI), and Ni provokes the formation of pulmonary diseases affecting the respiratory system (Table 8).

The toxic effects to plants and animals of the metals Cd, Cr, Cu, Pb, Hg, and Tl and the metalloids As and Sb, are presented in Table 8. These heavy metals and metalloids are able to affect aquatic organisms in surface water bodies even at low concentrations. The lower the EQS values (in µg/L) of each individual compound, the higher is its potential to pose a hazard for aquatic organism. Li, Cd, Be, Tl, Co, and Pb have acute MAC-EQS of between 0.344 and 14 µg/L, while Be, Tl, Cd, Co, Li, and Pb have chronic AA-EQS ranging from 0.0092 to1.2 µg/L (Table 8; European Parliament and Council of the European Union, 2008, 2013; van Vlaardingen and Verbruggen, 2009; European Chemicals Agency, 2015). Additional AA-EQS and MAC-EQS values of other relevant compounds are presented in Table 8.

The metals Cd, Cr, Cu, Pb, Hg, and Tl and the metalloids As and Sb affect aquatic organisms in surface water bodies even at low concentrations.

Table 8: Metals and metalloids that occur in WEEE and their risks to humans and aquatic systems (Empa, 2009b; International Labour Organization, 2012)

Chemical	Examples of the occurrence of hazardous metals and metalloids in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [µg/L][C]
Antimony (antimony trioxide Sb_2O_3)	Sb_2O_3: flame retardant in EEE, cathode ray tubes (old televisions and monitors) and printed circuit boards	The IARC classifies Sb_2O_3 in group 2B, possibly carcinogenic to humans (International Agency for Research on Cancer, 2015). Sb and Sb compounds are considered as priority pollutants (United States Environmental Protection Agency, 2014c). Sb seems to give rise to inducing disruption or breakages of chromosomes. Sb is toxic to blood, kidneys, lungs, the nervous system, liver, and the mucous membranes after inhalation or ingestion (Cooper and Harrison, 2009; Science Lab, 2013).	0.006	7.2/NA (Marion Junghans (Ecotox Centre); personal communication)
Arsenic (As)	As is used to make transistors, while gallium arsenide is used in light emitting diodes	The IARC lists inorganic As in group I, carcinogenic to humans (International Agency for Research on Cancer, 2015). Acute uptake of As can cause a decrease in the production of red and white blood cells, cardiac arrhy thmias, blood-vessel damage resulting in bruising, and impaired nerve function (Agency for Toxic Substances and Disease Registry, 2007a).	0.01	50/NA (UK Technical Advisory Group on the Water Framework Directive, 2008)
Barium (Ba)	Getters in cathode ray tubes	No IARC classification. Short-term exposure leads to muscle weakness and affects heart, liver, and spleen. It causes brain swelling after short-term exposure (Osuagwu and Ikerionwu, 2010).	2	9.3/220 (van Vlaardingen and Verbruggen, 2009)
Beryllium (Be)	Motherboards of computers and power supply boxes which contain silicon-controlled rectifiers and x-ray lenses	The IARC lists Be and its compounds in group I, carcinogenic to humans (International Agency for Research on Cancer, 2015). It can cause lung cancer. Inhalation of fumes can cause chronic beryllium disease (beryllicosis) and skin diseases (Osuagwu and Ikerionwu, 2010).	0.004	0.0092/0.83 (van Vlaardingen and Verbruggen, 2009)
Cadmium (Cd)	Chip resistors and semiconductors, rechargeable Ni-Cd batteries, fluorescent layer (cathode ray tubes), printer inks and toners for photo-copying-machines	Cd is classified by the IARC in group I, carcinogenic to humans (International Agency for Research on Cancer, 1993). The uptake of Cd oxides by inhalation of smoke or occupational pollution causes acute respiratory distress syndrome or pulmonary edema. Long-term exposure leads to renal dysfunction, anemia, osteoporosis, and bone fractures (Friberg et al., 1985; Barbee Jr and Prince, 1999; Godt et al., 2006). In the human body, the kidney is the main target for bioaccumulation. There, chronic Cd uptake leads to tubulus cell necrosis (Orlowski and Piotrowski, 2003; Godt et al., 2006).	0.005	Class 1: 0.08/0.45 Class 2: 0.09/0.6 Class 3: 0.15/0.9 Class 4: 0.25/1.5[D] (European Parliament and Council of the European Union, 2008)
Chromium (VI) (Cr(VI))	Corrosion protection of untreated and galvanized steel plates and as an alloy or hardener for steel housings containing data tapes and floppy discs	According to the IARC, Cr(VI) is classified in group 1 carcinogenic to humans (International Agency for Research on Cancer, 2015). Occupational exposure of Cr(VI) in the long-term leads to perforation of the nasal septum, asthma, bronchial inflammations, or lung cancer, and inflammation of the larynx and liver. Skin contact elicits allergies, dermatitis, dermal necrosis, and dermal corrosion (Lee et al., 1989; Straif et al., 2009; Bedi et al., 2013).	0.1	Cr(III): 4.7/32 Cr(VI): 3.4/NA (UK Technical Advisory Group on the Water Framework Directive, 2008)
Cobalt (Co)	Rechargeable batteries and coatings for hard disk drives	The IARC classifies cobalt and its compounds in group 2B, possibly carcinogenic to humans (International Agency for Research on Cancer, 2015). It acts as a skin irritant. Uptake via inhalation or ingestion, if repeated and prolonged, may have carcinogenic effects and is toxic to the lungs (animal study), or it can affect other organs (LabChem, 2009; International Labour Organization, 2012).	-	0.089/1.6 (van Vlaardingen and Verbruggen, 2009)
Copper (Cu)	Used as a conductor in cables and wires	The IARC classifies copper 8-hydroxyquinoline, in Group 3, not classifiable as to carcinogenicity in humans. Excessive exposure to Cu results in adverse health effects including liver and kidney damage, anemia, immunotoxicity, and developmental toxicity. After ingestion of a copper sulfate solution, adverse health effects, like gastrointestinal distress, nausea, vomiting, and abdominal pain, were observed. Occupational exposure to Cu acts as an irritant of the respiratory tract (Agency for Toxic Substances and Disease Registry, 2004a).	1.3	1/NA (based on the bioavailable concentration) (UK Technical Advisory Group on the Water Framework Directive, 2012)

A: *(Empa, 2009b; International Labour Organization, 2012)*

B: *Maximum contaminant level (United States Environmental Protection Agency, 2015c)*

C: *The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.*

D: *AA-EQS and MAC-EQS of cadmium are dependent on water hardness classes. Class 1: < 40 mg $CaCO_3$/L; Class 2: 40 to 50 mg $CaCO_3$; /L; Class 3: 50 to 100 mg $CaCO_3$/L; Class 4: 100 to 200 mg $CaCO_3$. /L;*

Chemical	Examples of the occurrence of hazardous metals and metalloids in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [µg/L][C]
Indium (In)	Liquid crystal display screens, semiconductors, injection lasers, solar cells, photodiodes, and light emitting diodes (National Toxicology Program, 2001)	The IARC classifies indium and its compounds in group 2A, probably carcinogenic to humans (International Agency for Research on Cancer, 2015). The probably carcinogenic potential is deduced from animal studies. Exposure to indium compounds caused extraordinarily high incidences of malignant neoplasms of the lungs of rats and mice, increased incidences of pheochromocytomas in rats, and increased incidences of hepatocellular neoplasms in mice, even at very low test doses and short exposure periods (International Agency for Research on Cancer, 2006a).	-	26/NA (Ministry of the Environment Japan, 2014)
Lead (Pb)	Solder of printed circuit boards, glass panels and gaskets in computer monitors, cathode ray tube screens, and batteries. Lead-acid batteries used in vehicles (Blacksmith Institute and Green Cross, 2012)	The IARC classifies inorganic lead and its compounds in group 2A, probably carcinogenic to humans (International Agency for Research on Cancer, 2015). Inorganic lead, especially, causes damage to the central and peripheral nervous system, affects the blood system (increases blood pressure or anemia) and kidneys, and the brain development of children. The main target for lead toxicity is the nervous system (Agency for Toxic Substances and Disease Registry, 2007b; Osuagwu and Ikerionwu, 2010).	0.015	1.2 (based on the bioavailable concentration)/14 (European Parliament and Council of the European Union 2013)
Lithium (Li)	Lithium batteries and rechargeable batteries	No IARC classification (International Agency for Research on Cancer, 2015). Inorganic lithium compounds act as skin and eye irritants. Short-term exposure causes sneezing, coughing, and severe irritation of the respiratory system. After ingestion, mouth, trachea, and esophagus may be burned, or mental confusion, nausea, coma, and death result. Long-term exposure can affect the nervous system or it may affect the renal system (National Institute for Occupational Safety and Health, 1978). Moreover, there are assumptions that lithium exposure may affect the development of unborn children. Lithium is used therapeutically for the treatment of manic depression or bipolar disorders (Aral and Vecchio-Sadus, 2008; McKnight et al., 2012).	-	0.23/0.344 (adapted from a PNEC value) (European Chemicals Agency, 2015)
Mercury (Hg)	Relays, switches and printed circuit boards, fluorescent lamps, in some batteries, old thermometers	The IARC classifies mercury and inorganic mercury compounds in group 3, not classifiable as to its carcinogenicity to humans, and organic mercury compounds in group 2B, possibly carcinogenic to humans (International Agency for Research on Cancer, 2015). Mercury is known as a neurotoxin. Even at low doses it causes impairment of the nervous system. Typical symptoms of mercury poisoning are malfunction of peripheral visions, numbness in hands, feet, and around the mouth, extrapyramidal diseases and movement disorders, impairment in writing, of speech, hearing, and walking, mental degradation and kidney damage. Children, especially those born to mothers exposed to mercury, are highly vulnerable to mercury poisoning diseases e.g. ataxia, constriction of the visual field, congenital cerebral palsy, or mental retardation (Agency for Toxic Substances and Disease Registry, 1999).	0.002	NA/0.07 (biota standard of 20 µg/kg wet weight) (European Parliament and Council of the European Union, 2013)
Nickel (Ni)	Rechargeable batteries, electron gun in cathode ray tubes	The IARC classifies metallic nickel and nickel alloys in group 2B, possibly carcinogenic to humans and nickel compounds in group 1, carcinogenic to humans (International Agency for Research on Cancer, 2015). Nickel and its compounds are known to cause allergic reactions by promoting contact dermatitis. Chronic exposure leads to lung fibrosis and cardiovascular and kidney diseases. Nickel compounds are known for their carcinogenic activity (Denkhaus and Salnikow, 2002).	-	4/34 (based on the concentration which is bioavailable) (European Parliament and Council of the European Union, 2013)

Chemical	Examples of the occurrence of hazardous metals and metalloids in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [µg/L][C]
Thallium (Tl)	Batteries, semiconductors, in scintillation counters, laser equipment, fiber glass, and photovoltaic cells	No IARC classification although it is suspected to be more toxic than Cd, Hg, and Pb. Today, few studies about its carcinogenic potential are available (Cheam, 2001). Because of its similarity in ionic charge and its ion radius to potassium, Tl(I), especially, can be absorbed and distributed easily throughout the entire body by mimicking potassium in its movement patterns and intracellular accumulation in mammals. In the body, it accumulates easily in bones, the renal medulla, and in the nervous system (Peter and Viraraghavan, 2005). Amounts of from 0.7 to 1.1 g of soluble Tl salts are determined to be the minimum lethal dose for an adult with a body weight of 70 kg (Moeschlin, 1980). Symptoms of acute Tl poisoning are alopecia, nausea, tachycardia, diarrhea, and impairments of the lungs, heart, and gastrointestinal system. Impairments of the nervous system are more likely to result from chronic exposure to Tl. However, there is a dearth of studies about the regular chronic uptake of low doses of Tl (Saddique and Peterson, 1983; Agency for Toxic Substances and Disease Registry, 2013; Frattini, 2005; Cvjetko et al., 2010).	0.002	0.013/0.8 (van Vlaardingen and Verbruggen, 2009)
Rare earth elements (REE)	Fluorescent layer (cathode ray tube screen), screens of mobile phones, tablets, and other electronic devices, catalysts, energy-efficient light bulbs, magnets (Hirano and Suzuki, 1996; Casado, 2013)	No IARC classification (International Agency for Research on Cancer, 2015). Information about the toxicity of REE is rare, therefore more research is required. REEs seem to be very persistent in the environment (Tang and Johannesson, 2006; Brioschi et al., 2013). They have a potential for accumulation in biota and humans (Tong et al., 2004; d'Aquino et al., 2009) and there is evidence for their chronic toxicity (Hirano and Suzuki, 1996). For instance, a link was observed between occupational REE exposure and the lung disease, pneumoconiosis (Sabbioni et al., 1982) and REE exposure was related with the formation of pulmonary fibrosis (McDonald et al., 1995). In refining REEs, radioactive waste is produced which may affect human and environmental health indirectly (El-Husaini and El-Hazek, 2005).	-	For fresh surface water the maximum permissible addition of REE ranges from 1.4 µg/L for neodymium to 22 µg/L for cerium (Sneller et al., 2000)
Zinc (Zn), (sulfide, chromates)	Plating material, interior of cathode ray tube screens, mixed with REE	No IARC classification (International Agency for Research on Cancer, 2015). Excessive short-term exposure to ingesting zinc can cause stomach cramps, nausea, and vomiting. Chronic ingestion of Zn can cause anemia, damage the pancreas, and decrease levels of high-density lipoprotein cholesterol (Agency for Toxic Substances and Disease Registry, 2005).	-	10.9/NA (UK Technical Advisory Group on the Water Framework Directive, 2012)

A: (Empa, 2009b; International Labour Organization, 2012)

B: Maximum contaminant level (United States Environmental Protection Agency, 2015c)

C: The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.

B) PAHs, dioxins, and furans

Polycyclic aromatic hydrocarbons (PAHs), such as: benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, dibenzo[a,h]anthracene, dibenzo[a,l]pyrene, indeno[1,2,3-cd]pyrene, etc., polyhalogenated dibenzodioxins (PHDDs; for instance, polychlorinated dibenzodioxins, PCDDs), and polyhalogenated dibenzofurans (PHDFs) (for instance polychlorinated dibenzofurans, PCDFs) are the most toxic and carcinogenic compounds. They are produced by the incomplete combustion of organic matter and rudimentary WEEE processing or obsolete recycling methods (Yu et al., 2006b; Chan et al., 2007; Cui and Zhang, 2008; Sepúlveda et al., 2010; Blacksmith Institute and Green Cross, 2013).

Use

PAHs, dioxins, and furans are not intentionally manufactured and they have no known commercial applications other than for research purposes (Empa, 2009b; International Agency for Research on Cancer, 2012a). These compounds are generally formed as unwanted by-products and they are subsequently released into the environment through the incomplete combustion of organic matter during residential/commercial biomass burning. This is a process that happens during cement production and other industrial combustion (production) processes, combustion of fossil fuels, and the incineration or open air burning of biomass (agricultural waste, deforestation, and wild fires), particularly if no soot particle filters are used. In 2007, it was estimated that the global annual atmospheric emission of 16 PAHs ranged from 331 to 818 Gg (as the interquartile range). In addition, it was shown that the proportion of emitted highly carcinogenic PAHs is higher in LAMICs (6.22%) than in HICs (5.73%) because of a lack of regulations and emission controls and the use of obsolete combustion methods (Shen et al., 2013).

In terms of e-waste, the unregulated burning of polyvinyl-sheathed (or other related plastic coated) EEE, or the melting of halogenated polymer casings from electronic devices or coated wires to recycle plastics or to extract valuable metals, such as copper, are the most relevant processes involved in the formation of PAHs, PHDDs, and PHDF (Christmann et al., 1989; Söderström and Marklund, 2002; Wang et al., 2002; Liu et al., 2008; International Labour Organization, 2012). It is known that metals like Cu and Fe, which are contained in e-waste, act as catalysts for the formation of PHDDs and PHDFs as shown in equations 1 to 7. In 1996, it was calculated that about 13,100 ± 2000 kg/year of dioxins and furans were produced unintentionally and deposited from the atmosphere worldwide (12,500 ± 1399 kg/year from terrestrial deposition and 610 ± 1500 kg/year from oceanic deposition; Iida et al., 1974; Hagenmaier et al., 1987; Brzuzy and Hites, 1996; Wang et al., 2002).

Through pyrolysis, PVC molecules cleave in HCl and organic molecules (aromatic rings; equation 1). These molecules could possibly react to form halogenated organic molecules (equation 2), though this reaction will not happen under normal conditions since it is thermodynamically inefficient (Gibbs free energy of formation: $\Delta G > 0 \rightarrow$ non-spontaneous, endergonic reaction). If HCl is converted to Cl_2 with a catalyst such as copper chloride, the formation of halogenated aromatic compounds (chlorobenzenes, dichloropenzenes, chlorophenols, etc.) and, therefore, the possible formation of halogenated aromatic hydrocarbons, such as dioxins and furans, is favored (equation 3 and 4; $\Delta G < 0 \rightarrow$ spontaneous, exothermic reaction; Wang et al., 2002). As already mentioned, the formation of polyhalogenated dioxins and furans is induced if plastics, such as polyvinyl chlorides or other related polymers, are burned at low temperatures, when the presence of halogenated flame retardants can further induce the formation of halogenated dibenzodioxins and dibenzofurans (Wang et al., 2002; Weber and Kuch, 2003). In contrast, in the absence of metallic catalysts, PAHs are formed predominantly during e-waste incineration processes (Gullett et al., 1990; Wang et al., 2002).

$$\text{PVC} \xrightarrow{\Delta} \text{HCl + organic molecules (usually of aromatic ring structures)} \qquad (1)$$

$$Bz(g) + 2HCl(g) \xrightarrow{\Delta} Cl_2Bz(g) + H_2(g) \qquad \Delta G = +143.51\ \text{kJ} \qquad (2)$$

$$2HCl(g) + {}^1/{}_2O_2 \xrightarrow{\Delta} Cl_2(g) + H_2O(g) \qquad \Delta G = -37.95\ \text{kJ} \qquad (3)$$

$$Bz(g) + Cl_2(g) \xrightarrow{\Delta} Cl_2Bz(g) \qquad \Delta G = -46.99\ \text{kJ} \qquad (4)$$

Reaction 3 can be catalyzed by copper chloride, as presented in equation 5 (Hagenmaier et al., 1987).

$$\begin{array}{l} CuCl_2 + {}^1/{}_2O_2 \xrightarrow{\Delta} CuO + Cl_2 \\ CuO + 2HCl \xrightarrow{\Delta} CuCl_2 + H_2O \\ \hline 2HCl + {}^1/{}_2O_2 \xrightarrow{\Delta} Cl_2 + H_2O \end{array} \qquad (5)$$

where ΔG = Gibbs free energy of formation
Bz = Benzene
Cl_2 = Chlorine
Cl_2Bz = Dichlorbenzene
$CuCl_2$ = Copper chloride
CuO = Copper oxide
H_2 = Hydrogen
HCl = Hydrogen chloride
H_2O = Water
O_2 = Oxygen
PVC = Polyvinyl chloride

Environmental behavior and occurrence

There are over 100 different PAHs, about 75 different PCDDs, and 135 PCDFs with varying physicochemical properties between their homologue groups and their congeners. Of these, 2,3,7,8 tetrachlorodibenzodioxin (TCDD 2,3,4,7,8-pentachlorodibenzofuran (PeCDF), and the PAH, benzo[a]pyrene (B[a]P) are the ones of most concern (Table 9) from the environmental and human toxicological perspectives. Although PAHs, dioxins and their congeners, and the furans differ in their physicochemical properties, they have in common that they are generally all poorly soluble in water (water solubility: 2,3,7,8-TCDD = insoluble in water; 2,3,4,7,8-PCDF = 0,00024 mg/L; Benzo[a]pyrene = 0.00162 mg/L). They show high octanol-water coefficients (Log K_{ow}: 2,3,7,8-TCDD = 6.8; 2,3,4,7,8-PCDF = 6.9; benzo[a]pyrene = 6.35). They have a high affinity to be adsorbed from organic matter and to geo- and bioaccumulate in the environment and biota (Lohmann and Jones, 1998; International Agency for Research on Cancer, 2012a) and, therefore, they are all known as ubiquitous pollutants. In comparison to the metals and metalloids, the PAHs, dioxins, and furans formed are particularly environmentally distributed just by the air as the constituents of fumes or as molecules bound to fly ash, dust, and other organic particles. They are less likely to be distributed by water, mainly because they are formed and emitted during incomplete combustion processes and because of their partly semi-volatile and hydrophobic characteristics (Christmann et al., 1989; Lohmann and Jones, 1998; Söderström and Marklund, 2002; Chan et al., 2007). One exception is that during the extraction of metals at acid leaching sites, PCDD/Fs are significantly leached out into soils and released into the environment as well (Leung et al., 2007). For PAHs, dioxins, and furans, the atmospheric residence times range from several hours to several days before they undergo photolysis, or, more likely, they are degraded by OH-radicals or move to sediments through dry or wet deposition where they accumulate in the soils and biota (Lohmann and Jones, 1998; Lohmann et al., 1999).

Although PAHs, dioxins and their congeners, and the furans differ in their physicochemical properties, they have in common that they are generally all poorly soluble in water.

As an example of the air pollution caused by these organic compounds, in ambient air in remote areas in HICs, concentrations of tetra- to octa-CDD/Fs homologues from 0.5 to 4 pg/m^3 are measured. In urban/industrial regions, concentrations of from 10 to 100 pg/m^3 were measured (Lohmann and Jones, 1998). In soils in industrial countries, such as the USA, Canada, Germany, South Korea, and Spain, PCDD/Fs concentrations of from 1.7 to 1080 pg/g dry weight have been measured (Eljarrat et al., 2001; Hilscherova et al., 2003; Zheng et al., 2008a).

Elevated concentrations of PCDD/Fs in shredded e-waste, leaves of trees and shrubs, dust from workshop floors, and in soils in the vicinity of a large e-waste recycling facility in Taizhou, eastern China, indicate that e-waste processing and recycling facilities are significant input sources of compounds such as PCDDs, PCDFs, and other dioxin-like compounds originating from incomplete combustion processes, like PAHs (Shen et al., 2008; Ma et al., 2008). There, in shredder waste, PCDD/Fs concentrations ranged from 31 to 11,400 pg/g dry weight and in tree and shrub leaves the concentrations ranged between 3460 and 9820 pg/g dry weight. Workshop-floor dust and soils contained PCDD/Fs at concentrations of from 2560 to 148,000 and 854 to 10,200 pg/g dry weight, respectively. Croplands in this region showed total PCDD/Fs concentrations up to 17 times higher than the arithmetic average, measured at reference sites. PAH levels in this region were up to 32 times higher when compared to the arithmetic average measured at control sites (Shen et al., 2008). Elevated levels of 2,3,7,8-TCDD and 1,2,3,7,8-PeCDF ranging from 1.98 to 4.95 pg/g dry weight were found in hair samples of people living in the vicinity of an e-waste processing site near Guiyu, China, proving that indeed dioxin-like compounds have a potential for bioaccumulation (Luksemburg et al., 2002). In addition, in Jiangxi province, average concentrations of PCDD/Fs ranging from 41.5 to 133.8 pg/g lipid were found in breast milk samples and from 177 to 843 pg/g lipid were quantified in blood samples (Zheng et al., 2008a). For comparison, similar average total concentrations of PCDD/Fs of 125 and 299 pg/g lipid were measured in breast milk and blood samples of pregnant women living in the vicinity of an industrialized area in Duisburg, Germany (Wittsiepe et al., 2007).

Toxicity

Besides their high potential for bioaccumulation, PAHs and PCDD/Fs are known for their toxic and carcinogenic potential. According to the IARC, PAHs such as dibenzo[a,h]anthracene and dibenzo[a,l]pyrene or benzo[b]fluoranthene and benzo[k]fluoranthene are classified as 2A, probably carcinogenic to humans or 2B, possibly carcinogenic to humans. The most hazardous PAH, benzo[a]pyrene, and the furan and dioxin 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) and 2,3,7,8 tetrachlorodibenzodioxin (TCDD) are classified according to the IARC in group 1, carcinogenic to humans as well (International Agency for Research on Cancer, 2015). The low MCLs of PAHs of 0.002 mg/L and of dioxins of 0.00000003 mg/L indicate that these compounds are posing a high risk to environmental and human health, whereas for TCDD it has to be considered that it is not soluble in water (MCLs and IARC classification are presented in Table 9). At present, no MCL for PCDFs has been determined (United States Environmental Protection Agency, 2009).

PCDD/Fs are known to cause adverse effects to human and animal health. For instance, in humans, excess risks for all types of cancer are associated with exposure to TCDD and PeCDF. Moreover, after the exposure to TCDD and dioxin-like compounds, changes in hormone levels were observed in humans and in animals. These changes result in increases in endocrine, reproductive and developmental defects, affecting the welfare and development of humans and other animals. High levels of TCDD exposure cause the skin disease referred to as chloracne (Kogevinas, 2001; International Agency for Research on Cancer, 2012a; Energy Justice Network, 2012).

The formation of different types of cancer, such as skin, lung, and bladder cancer, in human and animals has often been associated with exposure to PAHs as well (Boffetta et al., 1997). According to *in-vitro* and *in-vivo* animal tests, PAHs, and especially benzo[a]pyrene, are known for eliciting carcinogenic, mutagenic and genotoxic effects (Huberman et al., 1976; Szmigielski et al., 1982; Grimmer et al., 1991; Goldstein et al., 1998; Miller and Ramos, 2001).

From the environmental toxicological point of view, the AA-EQS and the MAC-EQS of B[a]P, the most hazardous PAH, are 0.00017 and 0.27 µg/L (Table 9). These indicate that even low chronic and acute exposure to this compound poses a high risk to aquatic organisms and aquatic ecosystems. For PCDD and other dioxin-like compounds no AA-EQS and MAC-EQS were available. Nevertheless, the determined EQS of these compounds, which should not be exceeded in biota to avoid poisoning water surface organisms, is 0.0065 µg/kg TEQ (toxic equivalents according to the World Health Organization 2005 Toxic Equivalence Factors; European Parliament and Council of the European Union, 2013).

Besides their high potential for bioaccumulation PAHs, PCDD/Fs are known for their toxic and carcinogenic potential.

Table 9: PAHs and other hazardous compounds formed and released in the burning of EEE and their risks to human health and aquatic systems (Empa, 2009b; International Labour Organization, 2012)

Chemical	Formation and occurrence of hazardous PAHs and halogenated hydrocarbons in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [µg/L][C]
Polycyclic aromatic hydrocarbons (PAH) (benzo[b]fluoranthene, benzo[k] fluoranthene, benzo[a]pyrene, dibenzo[a,h]anthracene, dibenzo[a,l] pyrene, indeno[1,2,3-cd]pyrene, etc.)	By-products of incomplete combustion of organic matter and polyvinyl chloride (Wang et al., 2002).	According to the IARC, PAHs such as dibenzo[a,h]anthracene and dibenzo[a,l]pyrene or benzo[b]fluoranthene and benzo[k] fluoranthene are classified in group 2A, probably carcinogenic to humans or group 2B, possibly carcinogenic to humans. The most hazardous PAH, benzo[a]pyrene is even listed in class 1, carcinogenic to humans, posing a risk to environmental health (International Agency for Research on Cancer, 2015). The formation of different types of cancer, such as skin, lung, and bladder cancer in humans have often been associated with the exposure to PAHs (Boffetta et al., 1997). According to *in-vitro* and *in-vivo* animal tests, PAHs, especially benzo[a]pyrene, are known for their carcinogenic, mutagenic, and their genotoxic effects (Huberman et al., 1976; Szmigielski et al., 1982; Grimmer et al., 1991; Goldstein et al., 1998; Miller and Ramos, 2001).	0.0002	0.00017/0.27 for B[a]P (European Parliament and Council of the European Union, 2013)
Note: the formation of polybrominated dibenzodioxins and dibenzofurans is possible as well if brominated hydrocarbons are burned PCDD/PCDF polychlorinated dibenzodioxins and dibenzofurans	PCDD and PCDF are unwanted by-products of incineration, uncontrolled burning and certain industrial processes. The open burning of plastic (polyvinyl chloride) sheathed copper wires to recover copper is one of the main reason for the formation of PCDDs and PCDFs (Christmann et al., 1989; Söderström and Marklund, 2002; Liu et al., 2008; Robinson, 2009). There is an observed link between the formation of PCDDs and PCDFs (Söderström and Marklund, 2002; Weber and Kuch, 2003).	2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) and 2,3,7,8 tetrachlorodibenzodioxin (TCDD) are classified according to IARC in group 1, carcinogenic to humans (International Agency for Research on Cancer, 2015). These compounds are known to cause adverse effects to human and animal health. In humans, excess risks for all types of cancer are associated with exposure of TCDD and PeCDF. Moreover, after exposure to TCDD and dioxin-like compounds, changes in hormone levels were observed in humans and in animals. These increases in endocrine, reproductive, and developmental defects are of the highest concern. High levels of TCDD exposure cause the skin disease referred to as chloracne (Kogevinas, 2001; International Agency for Research on Cancer, 2012a; Energy Justice Network, 2012).	0.00000003 for dioxin	No AA-EQS/MAC-EQS available. However, EQS of maximal tolerable concentrations of dioxin-like compounds in biota of 0.0065 µg/kg TEQ (toxic equivalents according to the World Health Organization 2005 Toxic Equivalence Factors) are determined (European Parliament and Council of the European Union, 2013).

A: (Empa, 2009b; International Labour Organization, 2012)

B: Maximum contaminant level (United States Environmental Protection Agency, 2015c)

C: The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.

C) Flame retardants and other halogenated hydrocarbons.

Polyvinyl chlorides (PVCs) are one of the most widely used plastics worldwide.

Chlorofluorocarbons (CFCs), perfluoroctane sulfonates (PFOS), polychlorinated (or brominated) diphenyl ethers (PCDEs/PBDEs), polychlorinated (or brominated) biphenyls (PCBs, PBBs), polyvinyl chloride (PVC), and tetrabromobisphenol-A (TBBPA) are the most hazardous flame retardants and halogenated hydrocarbons that are contained in e-waste (Empa, 2009b; International Labour Organization, 2012).

Use

Inappropriate production, disposal, and incineration of PVCs can lead to the emission of highly carcinogenic, persistent organic pollutants (POPs), such as dioxins, furans, PAHs, and halogenated biphenyls.

Polychlorinated biphenyls (PCBs) were mainly produced and used in the period 1929-1977 as electrical insulating fluids in transformers and capacitors and as hydraulic, heat transfer, and lubricating fluids in machinery. Furthermore, in combination with other agents, they were added to plastics as plasticizers and fire retardants. They were contained also in products such as caulks, adhesives, and carbonless copy paper (Erickson and Kaley, 2011). All in all, between 1929 and 1984, between 1.3 and 1.7 million tonne of PCBs were produced (Breivik et al., 2007; Stockholm Convention, 2008). Today, equipment and machinery which contain PCBs are still in use, obsolete equipment is stockpiled, and PCB wastes are not yet managed in an environmentally sound manner. According to the Stockholm Convention it is intended to securely remove all PCB stocks by 2028 (Stockholm Convention, 2008). Moreover, there is evidence that PCBs can be produced as byproducts and afterwards released into the environment during industrial or waste combustion processes as well (Müller and Dongmann, 1998; Ishikawa et al., 2007; Li et al., 2009).

Polychlorinated diphenyl ethers (PCDEs) were used as dielectric insulating fluids or as hydraulic and heat transfer fluids, lubricants, plasticizers, and flame retardants. PCDEs were applied as fungicides, slimicides, and wood preservatives (Koistinen, 2000; Domingo, 2006).

The brominated hydrocarbons, PBB, PBDE, and tetrabromo-bisphenol A (TBBPA), are primarily used as fire retardants in plastics, as thermoplastic components, or cable insulation, and they are contained in the plastic housings of EEE, printed circuit boards, etc. (International Labour Organization, 2012). TBBPA is used as reactive flame retardant (chemically bonded into the polymeric material, not volatile) or as an additive flame retardant in plastics (volatile). Often, TBBPA additives were used as flame retardants in acrylonitrile-butadiene-styrene and phenolic resins or as an intermediate in the production of other additive flame retardants (Institute for Health and Consumer Protection - European Chemicals Bureau, 2006). Today, TBBPA additives are the most widely used in the extensively produced and not yet regulated brominated flame retardants (He et al., 2010).

Polyvinyl chlorides (PVCs) are used ubiquitously – they are one of the most widely used plastics worldwide. They are contained in all kind of packaging and sheathing material (for food, EEE, and other kind of goods), plastic bottles, credit cards, and audio records. In the construction industry, PVCs are used as imitation leather or in window frames, cables, pipes, floorings, wallpapers, and window blinds (Greenpeace, 2005). As already mentioned, the inappropriate production, disposal, and incineration of PVCs can lead to the emission of highly carcinogenic, persistent organic pollutants (POPs), such as dioxins, furans, PAHs, and halogenated biphenyls. Therefore, environmentally unsound production, disposal, and incineration can affect human and environmental health indirectly (Müller and Dongmann, 1998; Shen et al., 2008; Ma et al., 2008).

The use of chlorofluorocarbons (CFCs) decreased when it was found that the release of these resulted in depletion of the stratospheric ozone layer, which may result in an increase of biologically harmful solar ultraviolet radiation (Newman et al., 2009). It was also determined that CFCs act as potent greenhouse gases (GHGs; Hansen et al., 1989). Because of these negative effects, the use of CFCs was banned on global scale through the Montreal Protocol on substances that deplete the ozone, which was negotiated in 1987 (Newman et al., 2009; Environmental News Network, 2012). Nevertheless, before they were banned, CFCs were used as cooling agents in refrigerators, freezers, air conditioners, and in cooling units in general. They were also contained in insulation foam (Newman et al., 2009).

Perfluorooctane sulfonate (PFOS) is used in the photographic industry and in photolithography. It is contained in semiconductors, photo-resistant-, and anti-reflective coatings. Furthermore, it is a component of EEE, firefighting foam, hydraulic fluids, and textiles. Today, the production and application of PFOS is restricted according to the requirements of the Stockholm Convention and there are initiatives for a voluntary phasing out of PFOS production from several chemical production facilities (Swedish Chemicals Inspectorate and Swedish Environmental Protection Agency, 2004; United Nations Environment Programme, 2013d).

Environmental behavior and occurrence

Most of these halogenated compounds, especially PCBs, PCDEs, PBBs, PBDEs, and PFOS, are fulfilling the persistent, bioaccumulation, and toxicity (PBT) criteria of the Stockholm Convention. All of these compounds are known to have long environmental residence times and they remain unchanged in the environment for extended periods of time. They are ubiquitous pollutants found in soil, water, and, notably, the air being distributed throughout the environment by natural processes. In addition, these compounds are known for their bioaccumulative potential. Thus, they are accumulating in the fatty tissue of living organisms and humans and they are enriched throughout the food chain. Given their high toxicity, they are affecting humans and wildlife. Because of their characteristics, their production and use is restricted or even banned worldwide within the scope of the Stockholm Convention (United Nations Environment Programme, 2013d).

Nevertheless, although the Stockholm Convention has been implemented, elevated concentrations of those halogenated compounds still can be found in the environment. For instance, in the breast milk of women living in the vicinity of an e-waste recycling site in Bui Dau, Vietnam, increased concentrations of 20-250 ng/g lipid weight of PBDE and its congeners were measured, indicating their potential for bioaccumulation. In comparison, the breast milk of Swedish women showed lower mean concentrations of 4 ng PBDE/g lipid weight while the maximum concentrations were 28.2 ng PBDE/lipid weight (Lind et al., 2003). In addition, in soil and sediment samples next to an open e-waste disposal and recycling site in Guiyu Guangdong, China, elevated PBDE concentrations ranging from 0.26 to 824 ng/g dry weight were detected (Wang et al., 2005). In this region, a monthly average PBDE concentration of 16.8 ng/m^3 was measured in particles with aerodynamic diameters smaller than 2.5 µm (PM2.5). These particles were detected in the air in the vicinity of a site with high e-waste burning activities (Wong et al., 2007c). This concentration exceeds the industrial EPA air screening level of 1.4 ng/m^3 (United States Environmental Protection Agency, 2014b). As a comparison, in Europe, background levels of PBDE in soils range between 0.065 to 12 ng/g dry weight (Hassanin et al., 2004).

PCB concentrations measured in soils at the open burning sites of e-waste recycling facilities in Guiyu were up to 458 µg/kg (Wong et al., 2007c). In comparison, the maximum measured environmental concentration of PCBs in five European cities (Glasgow, Torino, Aveiro, Ljubljana, and Uppsala) was 172 µg/kg dry weight (Cachada et al., 2009).

TBBPA concentrations of 25.2 ± 2.7 ng/g were determined in soil samples from China (Yu et al., 2008). In Spanish soils from an industrial region, comparable TBBPA concentrations were measured ranging between 3.4 and 32.2 ng/g dry weight (Sánchez-Brunete et al., 2009). Elevated median TBBPA concentrations ranging between 28 to 173 ng/g lipid weight were found in the muscles of six individual bird species that had been fed with food originating from an e-waste recycling region in Qingyuan, South China (He et al., 2010). In this region, TBBPA mean concentrations of 68 ng/L were found in water, 295 ng/g dry weight in soil samples, and 8917 ng/g dry weight in plant leaf samples. These results show that TBBPA has the potential to accumulate primarily in soil plants and wildlife. Maybe it would be appropriate to add this highly bioaccumulative product to the list of the restricted or banned brominated flame retardants along with PBB and PBDE. A summary of the fields of applications of these halogenated hydrocarbons is presented in Table 10.

Toxicity

The polyhalogenated biphenyls and diphenyl ethers are known for their high toxicity and their carcinogenic potential. The IARC lists PCBs in group 1, carcinogenic to humans, and PBBs are included in group 2A, probably carcinogenic to humans. PCDE and PBDE have not been classified by the IARC but might be comparably toxic to humans due to their structural similarity to PCBs and PBBs, respectively (International Agency for Research on Cancer, 2015). Exposure to PCBs causes impairment of the immune system because of their immune-suppressive effects. After uptake of, or direct contact with PBCs, they can cause damage to the liver, the skin – in form of chloracne – and the reproductive system by affecting the thyroid gland. In addition, there is evidence that exposure to PCB promotes the formation of several types of cancer (Agency for Toxic Substances and Disease Registry, 2000; Stockholm Convention, 2008).

Exposure to PCBs causes impairment of the immune system because of their immune-suppressive effects.

Because of a lack of epidemiological studies, it is still not possible to find a significant correlation between exposure to PBB and the formation of human cancer, though results from animal tests showed effects similar to those of PCBs. Exposure to PBBs caused the formation of different types of cancers in rats and mice. In other animal tests, skin diseases, such as chloracne, impairments to the central nervous system, the liver, kidney, thyroid glands function, and the reproduction system were observed as well (Agency for Toxic Substances and Disease Registry, 2004b; National Toxicology Program, 2014c).

PVCs and other polyvinyl based compounds were, according to the IARC, listed in group 3, not classifiable as to its carcinogenicity to humans (International Agency for Research on Cancer, 2015). Nevertheless, it has to be considered that during the production, recycling, and incineration of PVCs, hazardous compounds, such as PAHs, dioxins, furans, halogenated biphenyls, and polychlorinated diphenyl ethers, can be produced and released into the environment (Gullett et al., 1990; Wang et al., 2002; 2005).

CFCs, PFOS, and TBBPA are not classified according to the IARC (International Agency for Research on Cancer, 2015). From the environmental and human health perspectives, CFCs are destroying the stratospheric ozone layer, which consequently results in an increase of biologically harmful and aggressive solar ultraviolet radiation (Newman et al., 2009). At high concentrations, CFCs can be transformed to even more toxic gases, such as chlorine and phosgene (New Hampshire Department of Environmental Services, 2010). Furthermore, CFCs are acting as potent GHGs (Hansen et al., 1989). For humans, the inhalation of large volumes of CFCs affects the nervous system with symptoms of alcohol-like intoxication, reduced coordination, light-headedness, headaches, tremors and convulsion, and even cardiac arrhythmia. Dermal contact can lead to skin damage referred to as frost bite (New Hampshire Department of Environmental Services, 2010).

PFOS meet the requirements of the PBT criteria of the Stockholm Convention. From a human health perspective, information about the health risks from exposure to PFOS is still lacking. Nevertheless, according to several epidemiological studies, exposure to PFOS was assumed to be linked with the formation of bladder cancer (Organisation for Economic Co-operation and Development, 2015). According to animals tests, it has been shown that exposure to PFOS is highly toxic and that these compounds have a high affinity for bioaccumulation. In two mammalian species, rats and monkeys, sub-chronic exposure to PFOS resulted in hepatotoxicity and mortality. In addition, the exposure of mammals to PFOS was associated with causing impairments in reproduction as well. The half-life times in rats is 100 days, in monkeys it is 200 days, and in humans it can be 1 year (Luebker et al., 2002; Seacat et al., 2002; 2003; Inoue et al., 2004; Organisation for Economic Co-operation and Development, 2015).

According to the risk assessment report of the Institute for Health and Consumer Protection's and the European Chemicals Bureau, TBBPA is not currently classified for environmental or human health effects (Institute for Health and Consumer Protection – European Chemicals Bureau, 2006). From the data available, TBBPA is not known as a skin, eye, or respiratory tract irritant. From animal tests with rats, no evidence was found that exposure to TBBPA caused adverse effects to the endocrine and the reproduction systems. Information about the carcinogenic potential of TBBPA has not been found yet (Institute for Health and Consumer Protection – European Chemicals Bureau, 2006). Nevertheless, rudimentary plastic recycling and the low-temperature burning processes for plastics containing TBBPA and other brominated or chlorinated flame retardants can lead to the formation and emission of hazardous polybrominated dibenzodioxins and polybrominated dibenzofurans or PCDDs and PCDFs, respectively (Thies et al., 1990; Empa, 2009b).

For the halogenated hydrocarbons considered in this report, an MCL standard level for PCB compounds in drinking water of 0.0005 mg/L and of 0.00000003 mg/L for dioxins were determined. For the other compounds no MCL is available yet (Table 9 and Table 10; United States Environmental Protection Agency, 2015c).

For all the previously mentioned flame retardants and halogenated hydrocarbons just as for PFOS/Fs, the chronic environmental quality standard (AA-EQS) of 0.00065 µg/L has been proposed. For PBDE, the proposed acute environmental quality standards (MAC-EQS) was 0.14 and for PFOS, 36 µg/L (European Parliament and Council of the European Union, 2013).

Table 10: Flame retardants and halogenated hydrocarbons occurring in WEEE and their risks to humans and aquatic systems (Empa, 2009b; International Labour Organization, 2012)

Chemical	Formation and occurrence of hazardous PAHs and halogenated hydrocarbons in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [μg/L][C]
chlorofluorocarbon (CFC)	Contained in old refrigerators and freezers, cooling units, and insulation foam. The use of CFC is decreasing because of global bans and restrictions (Montreal Protocol on substances that deplete the ozone which was negotiated in 1987; Newman et al., 2009; Environmental News Network, 2012).	Not classified according to the IARC (International Agency for Research on Cancer, 2015). CFC uptake – inhaling high concentrations – affects the central nervous system with symptoms of alcohol-like intoxication, reduced coordination, light-headedness, headaches, tremors, and convulsions. High concentrations can lead to cardiac arrhythmia. Skin contact with CFCs can cause frost bite. The exposure of CFCs to high temperatures can cause the formation of more toxic gases, such as chlorine and phosgene (New Hampshire Department of Environmental Services, 2010). In addition, CFCs are known to destroy the ozone layer, which results in an increase of biologically harmful solar ultraviolet radiation (Newman et al., 2009) and CFCs act as potent GHGs as well (Hansen et al., 1989).	–	–
polychlorinated biphenyls and polychlorinated diphenyl ethers (PCB/PCDE)	From 1929 to 1977, PCBs were commercially used as insulation material or as dielectric insulating fluids in older electronic products, transformers, and capacitors. They were contained in inks and plastic (International Agency for Research on Cancer, 2012a). PCDEs were used as fire retardants in plastics (thermoplastic com-ponents, cable insulation) or as dielectric insulating fluids, hydraulic and heat transfer fluids, and lubricants and plasticizers. PCDEs were contained as impurities in chlorophenol-based compounds such as fungicides, slimicides, wood preservatives, etc. (Koistinen, 2000; Domingo, 2006).	PCBs are classified in group 1, carcinogenic to humans (International Agency for Research on Cancer, 2015). PCB exposure causes damage to the immune system (immuno-suppressive effects), liver, skin (chloracne), reproductive system, gastro-intestinal and respiratory tract, and thyroid gland, and promotes the formation of cancer (Agency for Toxic Substances and Disease Registry, 2000; Stockholm Convention, 2008). PCDEs have not been classified by the IARC but might be comparably toxic to humans due to their structural similarity to PCBs (International Agency for Research on Cancer, 2015).	0.0005 (PCBs)	–
polybrominated diphenyls and polybrominated diphenyl ethers (PBB/PBDE)	PBB and PBDEs are used as fire retardants in plastics (thermoplastic components, cable insulation). They are contained in the plastic housings of EEE, printed circuit boards, etc.	According to the IARC the PBBs are classified as group 2A, probably carcinogenic to humans. Similar to the effects of PCB (see above). According to animal tests PBBs are known to cause different types of cancer in rats and mice, although because of a lack of epidemiological studies it is still not possible to find a significant correlation between the exposure to PBB and the formation of human cancer (Agency for Toxic Substances and Disease Registry, 2004b; National Toxicology Program, 2014c). During animal tests and unintentional exposure to PBBs, the formation of chloracne or other forms of skin irritation were observed. Significant evidence of damage to the central nervous system, liver, kidneys, thyroid gland function, and reproduction system is available from animal studies (Agency for Toxic Substances and Disease Registry, 2004b). PBDEs have not been classified by the IARC but might be comparably toxic to humans due to their structural similarity to PBBs (International Agency for Research on Cancer, 2015).	–	NA/0.14 for PBDE (biota EQS 0.0085 μg/kg wet weight) (European Parliament and Council of the European Union, 2013)
perfluor octane sulfonate (PFOS)	Used in the photographic industry and in photolithography. PFOS are also contained in semiconductors and photo-resistant and anti-reflective coatings. Now, PFOS production is being voluntarily phased out (Swedish Chemicals Inspectorate and Swedish Environmental Protection Agency, 2004).	No IARC classification (International Agency for Research on Cancer, 2015). According to several animal tests it has been demonstrated that PFOSs are highly toxic and that they have a high potential for bioaccumulation. The half-life times in rats, monkeys and in humans are 100 days, 200 days or 1 year respectively. In both species, rats and monkeys, sub-chronic exposure to PFOS results in hepatotoxicity and mortality. Impairments in the reproductive systems of mammals was linked to exposure to PFOS (Luebker et al., 2002; Seacat et al., 2002; 2003; Inoue et al., 2004; Organisation for Economic Co-operation and Development, 2015). From a human toxicological point of view, adequate information about the health risk from exposure to PFOS is not available. However, according to some epidemiologic studies, exposure to PFOS was linked to the formation of bladder cancer (Organisation for Economic Co-operation and Development, 2015).	–	0.00065/36 (European Parliament and Council of the European Union, 2013)

A: (Empa, 2009b; International Labour Organization, 2012)

B: Maximum contaminant level (United States Environmental Protection Agency, 2015c)

C: The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.

Chemical	Formation and occurrence of hazardous PAHs and halogenated hydrocarbons in WEEE[A]	Health concerns (humans)	MCL[B] [mg/L]	Environmental quality standard (in surface water bodies) AA-EQS/MAC-EQS [µg/L][C]
polyvinyl chloride (PVC)	PVC is used as cable insulation, computer housing or as housing material of other EEE because of its fire-retardant properties.	According to the IARC, PVCs are classified as group 3, not classifiable as to its carcinogenicity to humans (International Agency for Research on Cancer, 2015). The burning of PVCs can cause the formation of hazardous and highly carcinogenic substances, such as PAHs, PCDD and PCDFs, and other dioxin-like compounds (Gullett et al., 1990; Wang et al., 2002; 2005).	–	–
tetrabromobisphenol A (TBBPA)	TBBPAs are used as flame retardants in plastics (thermoplastic components, cable insulation). For example, TBBPA is most widely used in printed wiring boards and casings of electronic devices. It is used as a reactive flame retardant in epoxy and polycarbonate resins, or as an additive flame retardant in acrylonitrile-butadiene-styrene (ABS) resins and phenolic resins. TBBPAs are used as intermediates to produce other flame retardants as well. (Institute for Health and Consumer Protection - European Chemicals Bureau, 2006).	No IARC classification (International Agency for Research on Cancer, 2015). TBBPA is not currently classified for environmental or human health effects (Institute for Health and Consumer Protection - European Chemicals Bureau, 2006). TBBPA is not known as a skin, eye, or respiratory tract irritant and according to animal tests with rats, no evidences were found that exposure to TBBPA caused adverse effects to the endocrine and the reproductive systems. Information about the carcinogenic potential of TBBPA has not been found yet (Institute for Health and Consumer Protection - European Chemicals Bureau, 2006). Nevertheless, rudimentary plastic recycling and low-temperature burning processes of plastics containing TBBPA and other brominated flame retardants leads to the formation and emission of hazardous polybrominated-dibenzodioxins and polybrominated-dibenzofurans (Thies et al., 1990; Empa, 2009b).	–	–

A: (Empa, 2009b; International Labour Organization, 2012)

B: Maximum contaminant level (United States Environmental Protection Agency, 2015c)

C: The acute and the chronic environmental quality standards (EU-standard), AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) represent chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.

Input pathways of e-waste pollutants

Generally, for e-waste pollutants there are two possible main input pathways by which they can enter the environment. If e-waste is disposed of inappropriately, solvable toxicants, such as several heavy metals (for instance Pb and Sb) can be leached from e-waste landfills especially after stronger rain events. They then remain in the soil or they can be further transported via surface runoff into rivers or they can drain into groundwater aquifers (Robinson, 2009). However, the main entry of e-waste pollutants happens through inappropriate recycling and e-waste processing practices. For example, open burning or incineration of e-waste can lead to the formation and emission of highly toxic compounds into the atmosphere. These can be distributed by air and become sediments in soils and surface waters via dry or wet deposition. This seems to be especially the case in LAMICs where, often, exhaust fumes are not controlled or filtered and regulations are lacking (Stewart and Lemieux, 2003; Leung et al., 2008; International Labour Organization, 2012). Additionally, precious and other valuable metals are leached from e-waste using strong acids. These highly toxic agents can leak from their containers and pollute water systems and soils (Robinson, 2009).

Production and pollution trends of hazardous compounds associated with e-waste

Data availability

Data about e-waste production and particularly data about the transboundary movements of WEEE is difficult to assess. Mainly this is because of the illegal or hidden export of e-waste from OECD countries to non-OECD countries to save on the expenses of e-waste disposal, recycling, and labor costs. For instance, there is evidence from the US EPA that sending WEEE for disposal and/or recycling in Asia would cost one-tenth of the expense to process the materials in the USA (International Labour Organization, 2012). With the currently available data on the production of EEE, the modelling of WEEE generation and its transboundary movements are not possible. This is especially so since such data is more likely to be available in higher-income countries than it is in LAMICs and data about the average lifespan and innovation cycles of individual items of EEE varies from region to region. (In higher-income countries the innovation cycles for and the lifespans of EEE are shorter than those in LAMICs. In these countries, older equipment is used for longer periods of time; Robinson, 2009).

In general, it can be assumed that information about the output figures for EEE and the generation of WEEE alone are not satisfactory to assess the extent of the environmental burden caused by the inappropriate disposal of EEE. It is necessary to get more details about the trade patterns of obsolete EEE because these are largely still not transparent and comprehensible.

Future trends and hot spots

Although the amount of available data about e-waste is rare, several research groups and NGOs are trying to shed light on the output figures for EEE or to get information about the amounts of WEEE generated. These researchers are trying to determine their mass fluxes and gain information about the futures of obsolete and inoperable EEE from a global perspective. They are also trying to assess the negative impacts on environmental and human health caused by the inappropriate disposals and recycling of WEEE (Widmer et al., 2005; United Nations Environment Programme, 2006a; Robinson, 2009; Empa, 2009e; Skinner et al., 2010; Mundl, 2010; International Labour Organization, 2012; Silicon Valley Toxics Coalition, 2014; United Nations Environment Programme, 2014).

Where the illegal export of WEEE is concerned, known and suspected routes of e-waste dumping are presented in Figure 25 and Figure 26 (Lewis, 2010, 2011; International Labour Organization, 2012; Silicon Valley Toxics Coalition, 2014). Australia, Japan, Korea, North America, and Western Europe are suspected of being the main exporter of e-waste to LAMICs.

Known targets for illegal e-waste disposal seem to be Brazil, China, Ghana, India, Nigeria, Mexico, Pakistan, Singapore, and Thailand. Other suspected destinations for obsolete and inoperable EEE are Argentinia, Benin, Chile, Egypt, Eastern Europe, Haiti, Indonesia, Ivory Coast, Kenya, Malaysia, Phillippines, Russia, Senegal, Tanzania, Ukraine, United Arab Emirates, Venezuela, and Vietnam. Unfortunately at present, there is no system for tracking legal or illegal exports of WEEE. Therefore, no direct quantitative data on the exported volumes of e-waste could be found and not every destination for exported and dumped e-waste could be located (Lewis, 2011). Nevetheless, there is evidence that China is one of the main destinations for e-waste. Experts suspect that upto 70% of exported WEEE is probably sent to China – primarily to southeast China near Bejing, the Yangtze River Delta, and the Pearl River Delta (Tong and Wang, 2004; Bodeen, 2007).

It can be assumed that there is a positive correlation between the demand and availability of PCs and other potential e-waste items and the gross domestic product of a country. Therefore, at this time, the regions with the highest GDPs, such as Western Europe, the United States and Australasia, are the most likely e-waste producers. During the next 10 years, regions with high economic growth, such as China, Eastern Europe, and Latin America will catch up with or even exceed the e-waste generation of the former (Robinson, 2009). Thus, besides the loads of e-waste that are illegally exported to LAMICs for disposal or recycling, the additional domestic generation of e-waste will further increase the environmental burden caused by

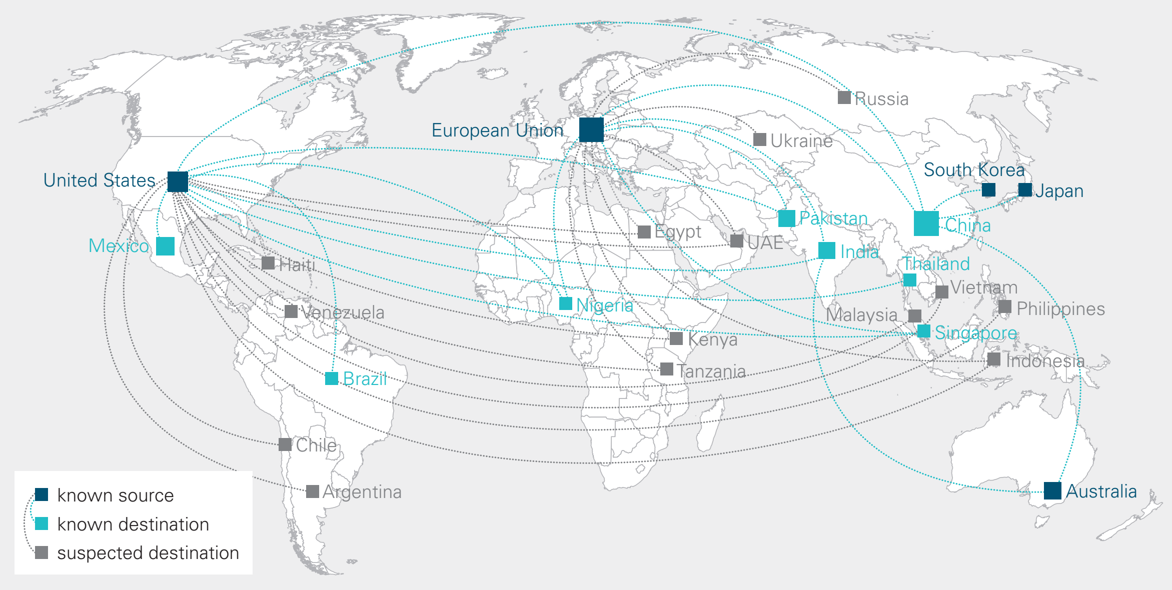


Figure 25: *Known sources of e-waste and its known and suspected shipping routes (International Labour Organization, 2012; Lewis, 2011; Silicon Valley Toxics Coalition, 2014).*

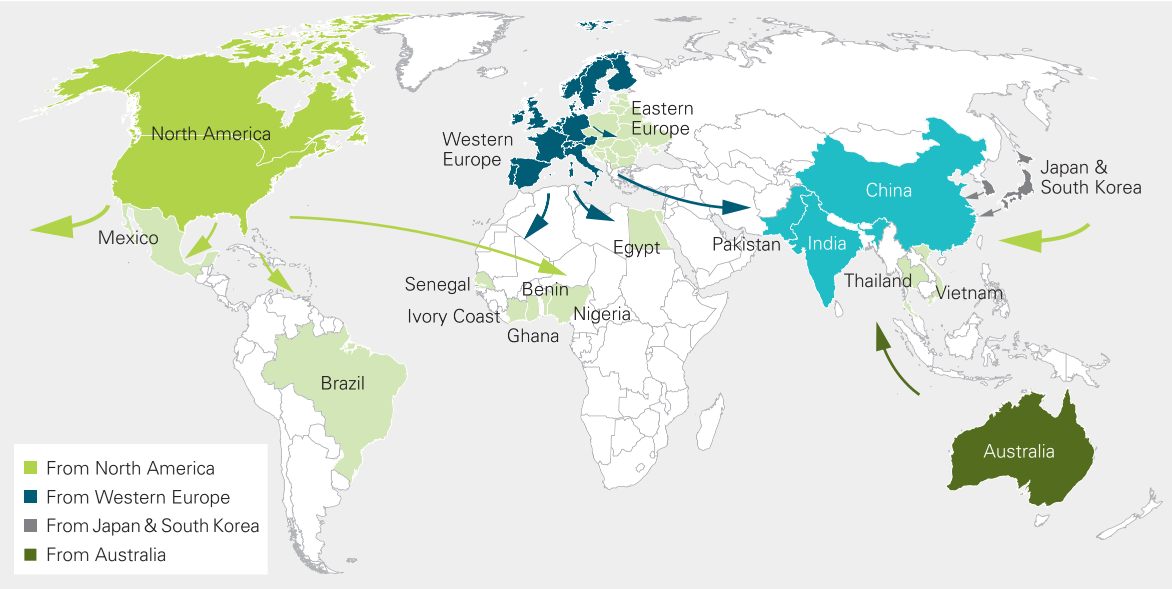


***Figure 26**: Export of e-waste from HICs to LAMICs (Lewis, 2010; International Labour Organization, 2012)*

e-waste pollutants in LAMICs experiencing an economic boom. In general, the recent global production (data from 2006 and 2009) of WEEE is suspected to range between 20 and 50 million tonne (United Nations Environment Programme, 2006a; Robinson, 2009; Schluep et al., 2009). In 2014/15 it is estimated that between 40 and 70 million tonne of WEEE might be generated (Jain, 2008).

Issues of special concern

Contaminants in the e-waste processing region of Guiyu, Guangdong Province, China

During the last decades, the people in Guiyu have changed over from a traditionally rice-growing community to an e-waste recycling and processing center (Leung et al., 2006). Today, Guiyu, with its surrounding towns in Guangdong Province, probably has become one of the largest e-waste disposal and recycling sites in the world, receiving large amounts of e-waste from domestic and international sources (Wong et al., 2007a; Greenpeace, 2009). The major recycling and processing activities in this region are toner sweeping, dismantling of EEE, recovering copper from wires and EEE, chipping and melting plastic, heating printed circuit boards over honeycombed coal blocks, and to recover gold and other valuable metals by using strong acids (cyanides, sulfuric acid, and hydrochloric acid; Puckett et al., 2002; Leung et al., 2006). The redundant e-waste is often dumped and openly burned without any controls or precautions, leaving behind an environmental burden of high severity. For instance, according to the disposal and processing of e-waste, POPs (like PAHs, dioxins, and furans) and halogenated hydrocarbons (like PCDE/PBDEs, PCB, and PBB) or inorganic pollutants (like heavy metals such as Cd, Cu, Ni, Pb and Zn) can be released in the environment, affecting environmental and human health.

For example, the sediments of a duck pond in the vicinity of an e-waste dumping and open burning site showed elevated total PAH concentrations (of the 16 PAHs banned by the US EPA) of up to 514 μg/kg. In rivers in Guiyu, the concentrations of seven carcinogenic PAHs were from two to eight times higher (28-111 μg/kg) and in duck ponds from seven to nine times higher (94-122 μg/kg) than the concentrations found in the reservoir (13.2 μg/kg). In this region, soil samples from a printer roller dump site had total PAH concentrations of up to 593 μg/kg. These values are comparable with those found at another large-scale e-waste recycling site in Taizhou, China, where total PAH concentrations ranged from 488 to 764 μg/kg dry weight (Tang et al., 2010). Currently, global guidelines and limit values for PAHs have not been established. However, although these values do not exceed the soil criteria for PAH concentrations of the 'Dutch list' (Environmental Protection Department of Hong Kong, 2004) – 1000 μg/kg, which implies that the soil is contaminated – the elevated PAH concentrations in Guiyu are of high environmental concern. This is especially so since the pollution from e-waste and the informal businesses is increasing and PAHs are known to accumulate via the food chain, be persistent, and highly toxic even at low concentrations (Environmental Protection Department of Hong Kong, 2004). In addition, sediments from the Lianjiang River (Guiyu, China) show that this river is contaminated by PCB and its congeners. Total PCB concentrations of up to

743 µg/kg were measured. This exceeds the Canadian Environmental Quality Guideline of 277 µg/kg (Leung et al., 2006). A high concentration of total mono-hepta PBDEs of 1140 µg/kg was found in soil samples at an informal dumping site for burned plastic in Guiyu, while in similar samples from a printer roller dumping site in the same area, the concentration was found to be 1169 µg/kg. Serious levels of contamination with PCDD/F and PBDEs were found in surface samples from the e-waste recycling area in Taizhou, China, as well. At this site, PBDE concentrations ranged from 27.9 to 3128.4 µg/kg and PCDD/Fs concentrations from 218.3 to 3122.2 µg/kg (Tang et al., 2014). Besides the organic pollutants, e-waste processing and recycling is often associated with the release of inorganic contaminants. For instance, sediments of the Lianjiang River were considerably contaminated with Cd (mean value 4.09 ± 3.92 mg/kg), Cu (1070 ± 1210 mg/kg), Ni (181 ± 156 mg/kg), Pb (230 ± 169 mg/kg), and Zn (324 ± 143 mg/kg; Wong et al., 2007b).

Currently, there is a dearth of detailed information about the consequences of chronic e-waste pollutants to environmental health and their environmental risks, especially in LAMICs. That is the main reason why it is difficult to give information about the severity of the pollution caused by informal e-waste activities. Nevertheless, as shown before, from the several environmental samples collected from e-waste disposal and processing sites, there is evidence concerning the concentrations of highly toxic POPs or inorganics (heavy metals and metalloids). This despite the (intended or unintended) production, use, import, and export of POPs has been banned or restricted globally since the Stockholm Convention came into force in 2004. These POPs are controlled by the Stockholm Convention to reduce their entry into environmental systems and to mitigate their impacts on environmental and human health (Leung et al., 2006). For instance, POPs, such as halogenated hydrocarbons, PCBs, PCDD/Fs, and PCDE and PBDE, are associated with such adverse health effects as impairment of the reproduction systems of humans and wildlife while acting as endocrine disruptors and in the formation of several forms of cancer (Table 10). They are known to bioaccumulate throughout the food chain or to remain and accumulate in soil or sediments (Leung et al., 2006). In addition, the release of heavy metals is affecting environmental and human health, the nervous systems, the mental development, the respiratory tracts, and the digestive tracts of wildlife and people (Leung et al., 2006).

Health consequences of disposal, dismantling, and recycling activities of WEEEs

A systematic review of epidemiological studies of the health consequences of ingesting the chemicals released by e-waste disposal and/or e-waste processing activities shows that human exposure to e-waste is significantly associated with impairments in reproduction, neurodevelopment, and mental health. In addition, toxicants released during e-waste disposal and processing are known to increase the incidence of cancerous diseases by causing DNA damage, chromosomal aberrations, and changes in gene expression (Zhao et al., 2009; Grant et al., 2013).

Grant et al. (2013) studied the health consequences of WEEE recycling and processing in southeast China, mainly in Guiyu and Taizhou. By reviewing the epidemiological studies they showed the positive correlation between exposure to e-waste and the negative impacts on human health.

Their review revealed that halogenated hydrocarbons, such as PBDEs, PCDDs, PCDFs, and PCBs, which are released during e-waste processing, caused variations in thyroid-stimulating hormone levels (Ju et al., 2008; Yuan et al., 2008; Wang et al., 2010; Zhang et al., 2010; Han et al., 2011; Grant et al., 2013). In the vicinity of an e-waste dismantling site in Guiyu, China, the lung function of school children (8 to 9 years of age) was affected. They showed lower forced vital capacity (FVC = the amount of air that can be forcibly exhaled from the lungs after taking a deep breath). These impairments in lung function are linked with the exposure to and the uptake of heavy metals, such as Cr, Mn, and Ni, which are emitted by the e-waste processing sector. The uptake of heavy metals was proven by the elevated blood levels of Mn of 374.92 nmol/L and of Ni of 5.3 mg/L: control samples contained 271.18 nmol/L of Mn and 3 mg/L of Ni (Zheng et al., 2013). In these regions with their high informal e-waste processing activities, reproductive health was affected as well. For instance, the exposure to e-waste was often accompanied by considerable increases in spontaneous abortions (Wu et al., 2012b), stillbirths (Guo et al., 2012; Xu et al., 2012), premature births reduced birth weights (Guo et al., 2012; Wu et al., 2012b; Xu et al., 2012), and reduced birth length (Wu et al., 2011b, 2012b; Grant et al., 2013). Other studies showed that increased lead levels could be found in the cord blood and meconium of neonates if their parents, and especially their mothers, were involved in e-waste recycling activities or if they lived in the vicinity of e-waste processing sites before and during their pregnancy (Li et al., 2008d; Liu et al., 2011). The elevated lead concentrations and probably the addi-

Exposure to e-waste was often accompanied by considerable increases in spontaneous abortions, stillbirths, premature births, reduced birth weights, and reduced birth length.

tional exposure to other contaminants released from e-waste processing resulted in impairment of the children's mental development. From neonatal behavioral neurological examinations, the Guiyu newborns with the higher lead concentrations showed abnormalities in temperament scores and low neonatal behavioral neurological assessment scores (Li et al., 2008d; Liu et al., 2011; Grant et al., 2013). E-waste and its pollutants are known to cause genetic mutations and cytogenetic damage. For instance, mothers involved in e-waste recycling had elevated Cr levels (median 94 µg/L) in umbilical cord blood. The exposure to Cr, in combination with other pollutants from the e-waste recycling, were correlated with DNA damage (Li et al., 2008c). In Jinghai, China, workers involved in e-waste processing had increased chromosomal aberration levels 20 times higher than those who were not working in the same sector (Liu et al., 2009). More evidence that pollutants from the e-waste sector can cause damage to DNA are mentioned in the comprehensive epidemiological study of Grant et al. (2013).

In conclusion, there is a lot of evidence that pollutants from e-waste are indeed a health risk for workers involved in e-waste businesses and for their families if they are living in the vicinity of e-waste processing and dumping sites.

Lack of implementation of policies and regulations

In Delhi, the Indian capital, the informal e-waste recycling sector has a high employment potential with an increasing trend. Especially for the urban poor, informal e-waste businesses are a preferred opportunity to make a profit (Sinha-Khetriwal et al., 2005; International Labour Organization, 2012). Delhi is a favored site for informal e-waste collection and processing (Sinha-Khetriwal et al., 2005; International Labour Organization, 2012) given:

- The good infrastructure
- Its position as a nodal point in trade
- India's strong economics
- The increase in domestic e-waste production
- The additional loads of e-waste from shipments from HICs which are the major sources of e-waste.

It is estimated that in 2005 in India, between 146,180 and 360,000 tonne of WEEE was generated domestically and it is estimated that 800,000 tonne of e-waste will be produced in India by 2012 (Zoeteman et al., 2010; Wath et al., 2011). In addition, in 2005 up to 850,000 tonne of WEEE might have been imported into India for disposal and further processing (more recent data have not been found; Zoeteman et al., 2010; Breivik et al., 2014). It has to be considered that given the high complexity of the WEEE production, trade, and processing businesses, the high levels of informal and illegal e-waste transportation and disposal activities, and the increasing trend in global WEEE generation, these numbers may well be significantly underestimated.

However, with the help of stricter governmental regulations in Delhi, a crackdown on informal e-waste businesses has been initiated. There, the effort was made to reduce the number of informal e-waste businesses, to improve safety, and to mitigate the impacts on human and environmental health, which are associated with informal e-waste processing activities (Skinner et al., 2010). Nevertheless, instead of stopping the informal businesses, these were just trans-located to satellite towns, such as Saharanpur and Meerut, while the e-waste trade in the city continues (Waste Management World, 2011).

Figure 27 shows the possible formal, semi-formal, and informal paths of the e-waste trade within India. In addition, the graphic shows that while e-waste can originate from domestic e-waste production sources, such as private consumers, government institutions, industrial consumers, or manufactures, the largest amount of e-waste is imported from HICs. Furthermore, it can be seen that the different formal, semi-formal, and informal stakeholders involved in the trade and processing of e-waste are interlinked (Skinner et al., 2010). First (green path), the e-waste arising from formal sources is given to friends, donated to institutions or sold to responsible formal dismantlers/recyclers. Second (blue path), primarily for economic reasons, most semi-formal stakeholders act as a link between the formal and informal e-waste businesses by sending e-waste to informal dismantlers and recyclers. Third, the informal sector (orange path) is dismantling and processing e-waste or they are even involved in the informal extraction of valuable materials from e-waste (Jain, 2009; Skinner et al., 2010). It must be recognized that Figure 27 shows a simplified path of e-waste trades. In practice, the flow of e-waste is much more complex and more elusive, which makes it difficult to enact effective regulations and policies (Skinner et al., 2010). As described in the section **E-waste pollutants of environmental concern** (p.106), informal e-waste recycling is mostly responsible for causing severe problems to environmental and human health.

Best practices

The illegal trade on e-waste and the informal e-waste recycling businesses are significant cross-cutting issues on a global scale. Of all countries, the LAMICs are those with the highest e-waste burdens (Skinner et al., 2010; Lewis, 2010, 2011; International Labour Organization, 2012; Silicon Valley Toxics Coalition, 2014).

To mitigate the entry of highly toxic pollutants into the environment through e-waste disposal and processing initiatives, significant efforts are required to implement best practices for e-waste treatment. The introduction of sound management practices for e-waste businesses are required at local and international levels. To facilitate implementation of best practices and sound waste management, collaboration and communications between stakeholders from the electrical and electronic industry, governments, customs authorities, regulatory and environmental agencies, intergovernmental or non-governmental organizations and local authorities need to be strengthened. In addition, purchasers of EEE and civil society, in general, can support the production of greener and more sustainable EEE by purchasing electronic products with less toxic compounds or which do not contain recycled material from informal e-waste businesses. Alternatively, they can support internationally or locally certified e-waste campaigns (for instance the WorldLoop's e-Resource Certificate Programme (WorldLoop, 2013) or the Swiss e-waste program (Empa, 2009e) to promote the controlled and safe collection, processing, and recycling of e-waste (International Labour Organization, 2012). Details of already implemented and theoretical best practices for a more environmentally-friendly trade and processing of e-waste follow.

Implemented examples

Increased data transparency through the (Step) initiative

Solving the e-waste problem (Step) is an international initiative that was established in late 2004. To date, Step has over 60 members representing manufacturers, recyclers, academics, and government and non-governmental organizations committed to solving the increasing e-waste problem (Step Initiative, 2016a). The main objectives of this initiative are to (Step Initiative, 2014):

- conduct and share scientific research
- set strategies and goals to overcome the e-waste problem
- provide training on e-waste issues
- communicate and raise awareness

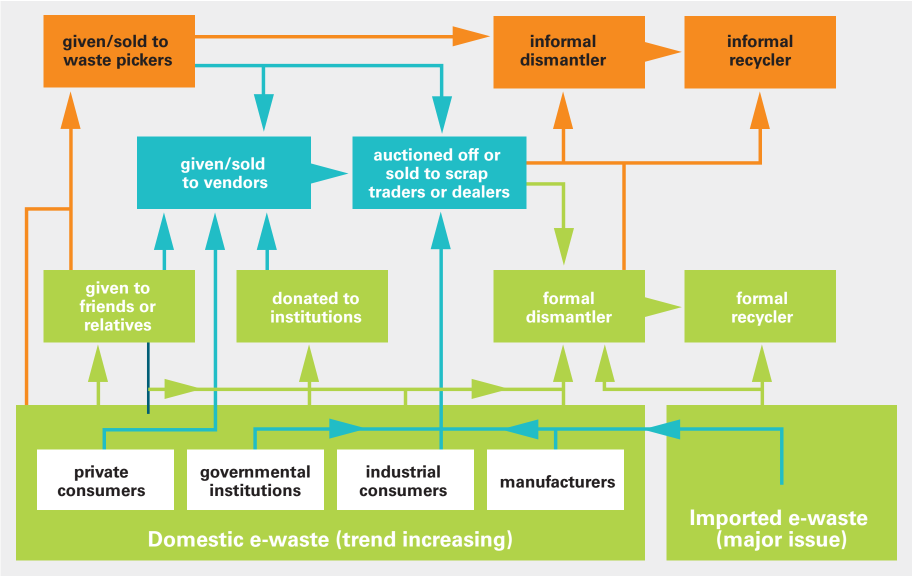


Figure 27: *The formal (green), semi-formal (blue), and informal (orange) paths of e-waste flows within India (Skinner et al., 2010)*

To fulfill their aims, the members of the Step initiative they have to comply with five principles:

1. Their work is founded on scientific assessments and integrates a comprehensive view of the social, economic, and environmental aspects of e-waste
2. They conduct research on the entire life cycle of EEE by considering their global supply, processes and material flows
3. Their research and pilot projects are feasible approaches to the problems caused by e-waste
4. They reject all illegal activities related to e-waste, including illegal exports (shipments) and reuse and recycling practices that affect environmental and human health
5. They are eager to promote safe, eco-, and energy-efficient reuse and recycling practices on a global scale in a socially responsible manner

Their five core theme areas, which are described in more detail on the homepage of the Step initiative, are (Step Initiative, 2016b):

- Policy to analyze existing approaches and e-waste policies

- Redesign of EEE to promote design for better reuse, repair, refurbishment, and recycling

- Reuse to develop replicable, sustainable, and globally consistent reuse systems for EEE

- Recycle to enhance global recycling infrastructures

- Capacity-building to increase awareness of the growing e-waste problem.

For instance, in respect of their commitments to mitigate the e-waste problem, the Step initiative is compiling a world map with data about EEE that is put on the market. It also provides information on the WEEE that is generated domestically in each country in kg/inhabitant or in total kilotonne (Figure 28), although, in general, the e-waste problem is hard to capture, mainly because of a lack of comprehensive data. These data are available to the public and they are helping to localize hot spots with e-waste problems. They are used internally and externally to find locations that generate large volumes of e-waste and where disassembling and processing programs for e-waste, or new state-of-the-art WEEE recycling facilities could be started. However, the amounts of WEEE that are exported illegally are not considered in the Step calculations, which may cause an underestimation of the amounts of e-waste accumulated and their associated environmental risks, mainly in LAMICs. During Step's editing of the data it has defined EEE and WEEE according to the EU Waste Electrical and Electronic Equip-

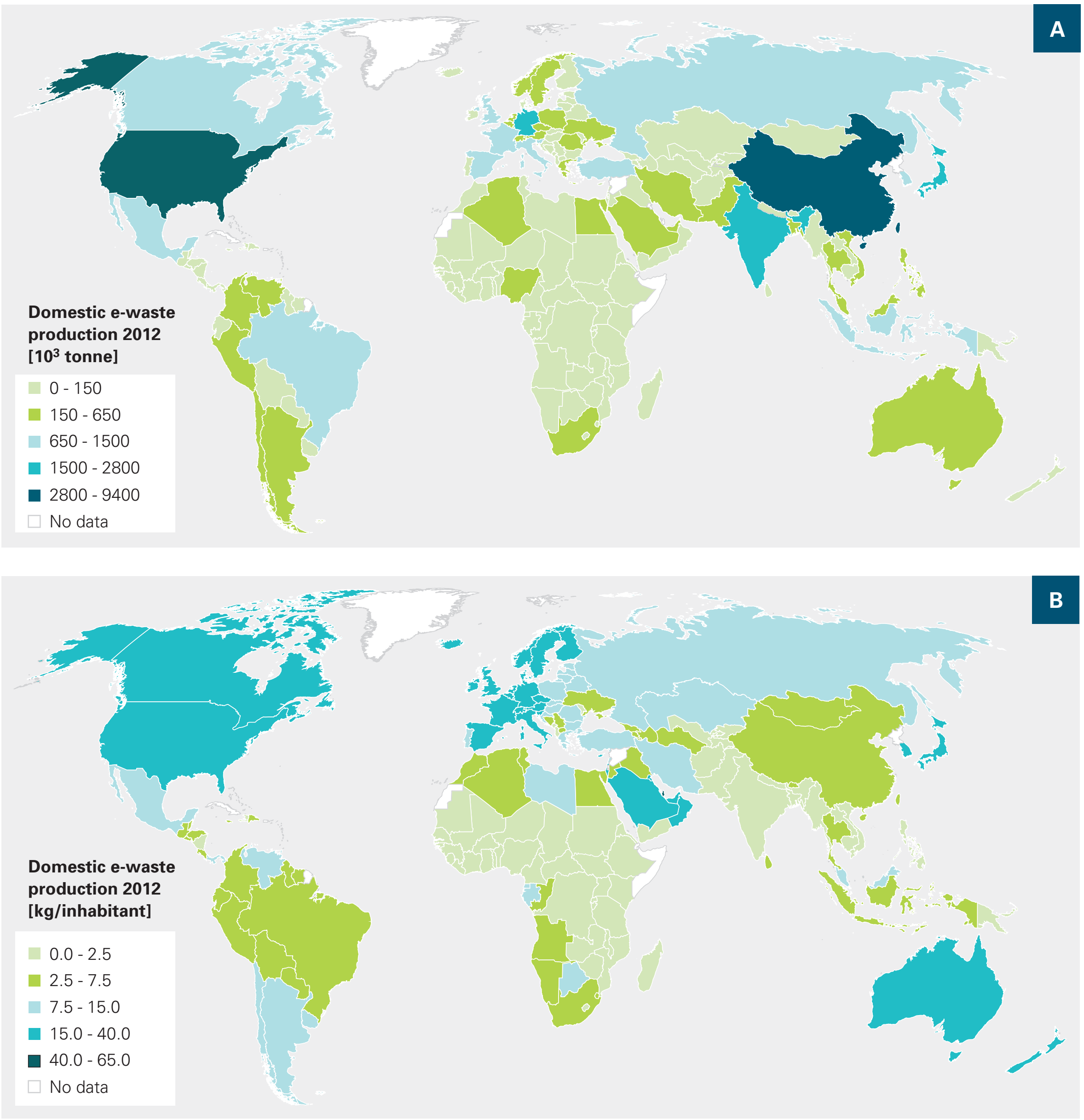


Figure 28: *World map with domestic e-waste production in 10^3 tonne (A) and in kg/inhabitant (B) for 2012 (Step Initiative, 2015).*

ment Directive categories and products. Nevertheless, although there may be some uncertainties, its world map of e-waste production is unique and is the first data base to provide such comprehensive and international data, thus increasing the transparency of e-waste data (Step Initiative, 2015).

E-waste assessment methodology and implementation of dismantling programs

Since the 1990s, Switzerland was one of the first counties in the world to introduce a national e-waste management system. The Swiss Federal Laboratories for Materials Science and Technology (Empa) has established a good reputation for assessing the serious health, socioeconomic, and environmental problems caused by inappropriate e-waste disposal and rudimentary recycling practices. It has also developed solutions to mitigate these issues by finding and implementing an effective individualized e-waste management system. Since 2003, Empa, which has acted as one of the technical control bodies of the Swiss e-waste management system, is using and adapting the knowledge gained in Switzerland to the needs of LAMICs. Empa has taken part in several e-waste projects in Africa, Asia, and Latin and South America where they are trying to improve the living conditions of local residents, by helping to better manage e-waste streams and protect resources. The projects seek to improve the economic situation in general and to reduce the health risks to humans and the environment (Empa, 2009c).

For instance, after a detailed e-waste country assessment in South Africa, an e-waste processing facility was implemented in Cape Town. From February to November 2008, this facility was able to process around 60 tonne of WEEE, generated an income about USD14,000, and provided direct employment for 19 people (Empa, 2009d). Other projects on sound e-waste management where Empa has been engaged are described on the Empa (2009c) e-waste guide web page. Their latest projects were conducted in Brazil, China, Columbia, Kenya, Morocco, Peru, Senegal, South Africa, and Uganda.

From their extensive experience, Schluep et al. (2012) explain that pure technical implementation alone is often insufficient to enable sound e-waste management. This is the case, particularly, in LAMICs where legal and institutional frameworks and infrastructure are lacking and, therefore, e-waste management requires a comprehensive and well-structured approach. In order to understand the prevalent framework of conditions, the current e-waste regulations and legislations need to be compiled and an assessment made of stakeholders, mass flow, and the environmental and socioeconomic impacts. This requires a country-specific e-waste assessment to be conducted. Along these lines, Schluep et al. (2012) have published a publicly available report, that explains their methodology of e-waste assessment. This report can be used as a reference for organizations that are interested in e-waste assessment projects enabling sound e-waste management. The report about their e-waste assessment methodology shows how to get results about the legal framework conditions, how to understand stakeholder interactions, the mass-flows of WEEE, and how to identify WEEE hotspots. This information will provide a comprehensive overview of the e-waste situation in a specific region for the relevant stakeholders. It will help to evaluate the potentials for employment or for possible improvements in the living condition of local people who are engaged in the e-waste business. The assessment of mass flow and other economic data are helpful when implementing appropriate business models for e-waste collection, processing, and recycling activities. In summary, their e-waste assessment methodology provides all the relevant information required for implementing a region-dependent e-waste management system (Schluep et al., 2012).

Besides Empa, other international organizations, such as the United Nations Industrial Development Organization (UNIDO), the United Nations Environment Programme (UNEP), the Basel Convention, the StEP Initiative, the Partnership for Action on Computing Equipment, the Swiss e-waste program, and Hewlett-Packard, are pursuing similar goals and they all apply the e-waste assessment methodologies of Empa and SOFIES SA (Schluep et al., 2012).

Improvements in WEEE collection and recycling practices

Improvements in WEEE collection and recycling practices are urgently needed. The LIFE + WEEE Label of Excellence (WEEELABEX) EU project was initiated to protect the environment by promoting sound e-waste trading and recycling practices in Europe. This project comprises the enactment of European standards with respect to WEEE collection, handling, storage, recycling, and disposal in compliance with EU health, safety, and environmental legislation. According to these standards, monitoring programs of processing companies will be started. The monitoring will be conducted by auditors, who are trained by the WEEELABEX office to ensure consistent monitoring approaches and that the same sets of standards are used for auditing. If the parties and companies involved in WEEE operations comply with the implemented standards of the WEEELABEX initiative they are awarded the project targeted conformity verification, referred to as the WEEE label of excellence (WEEELABEX, 2013). With the help of this project, consistent and new standards for WEEE collection, storage, and processing, which are already becoming international benchmarks, were successfully developed within the EU. So far, about 30 companies have been awarded the WEEELABEX conformity verification. More detailed information about this initiative are available on the webpage www.weeelabex.org/.

Development and implementation of greener technologies

The development and implementation of greener technologies leads to a reduction in the volume of WEEE produced. For instance, use of the EPEAT® global rating system, managed by the non-profit organization Green Electronics Council, Portland, Oregon, USA, helps purchasers (businesses, schools, hotels, hospitals, and governments), manufacturers, and others track down and offer environmentally preferable EEEs (Green Electronics Council, 2015). EPEAT® registered electronics meet strict environmental criteria. For instance, EPEAT® registered products use less environmentally sensitive materials in their manufacture, are designed for an increased lifecycle, consume less energy, and disposal of their WEEE products is managed soundly.

The Fairphone enterprise is another example how greener EEE can be supplied for end-users. Fairphone was started in 2010 as a project of the Waag Society, Action Aid, and Schrijf-Schrijf to increase awareness about minerals and the conflicts that are associated with the mining of these minerals in the Democratic Republic of Congo. Given the omnipresence of mobile phones, Fairphone is focusing on producing mobile phones that are designed to have a longer life and increased reparability. The source material originates from local economies and conflict-free mining sites and not from mining sites controlled by armed militias. In addition, properly recycled material is used in the production of the mobile phones. Furthermore, Fairphone guarantees that during production, the employees worked under fair and safe working conditions. Currently, they have 31 employees and they have sold about 50 thousand Fairphones (Fairphone, 2015).

Theoretical examples

Strengthening the regulatory framework and introducing attractive incentives

As described in the section **Lack of implementation of policies and regulations** (p. 122), implementing regulations alone is not sufficiently effective to improve occupational safety and to reduce the impacts on environmental and human health. The example of the informal e-waste businesses in Delhi showed that strengthening regulations and prohibitions alone are not solving the e-waste problem. In the Delhi case, the informal businesses simply shifted from the city center to remote places and the informal e-waste recyclers continued their work using harmful and rudimentary recycling methods (Sinha-Khetriwal et al., 2005; Sinha et al., 2010; International Labour Organization, 2012). As long as informal e-waste businesses provide profit-yielding employment for many people in poverty, the informal activities will continue although such businesses are dangerous and life threatening ones. This is especially so when there are no attractive incentives available that promote and support formal e-waste recycling activities. People who are involved in e-waste businesses should be informed and further educated about the perils of working with e-waste and its impact on environmental and human health. Efforts are needed to mitigate occupational accidents and health risks by raising people's awareness about their work with hazardous compounds. Incentives need to be provided that will urge them to seek safer and healthier working conditions (Wang et al., 2011).

In general in LAMICs, it is necessary to raise awareness of the environmental and human health risks in businesses where hazardous chemicals are involved, such as informal e-waste dismantling and processing activities. It is equally necessary to enable the environmentally sound management of waste and chemicals and to guarantee improvements in occupational and environmental health. In addition, guidance and training for informal e-waste business to become more formal or to cooperate and integrate into the formal sector are important (just as it is the case for informal and small scale mining businesses described in the section **Theoretical examples** (p. 100). However, this will be challenging, especially as it is mostly uneducated people with low literacy levels, living in extreme poverty who are involved in informal e-waste processing and recycling businesses (Nimpuno et al., 2011; International Labour Organization, 2012; Rockson et al., 2013). Actually, there is evidence that informal e-waste recycling activities, although using rudimentary methods, are economically advantageous businesses and even out-compete formal recycling businesses mainly because of the lower costs of complying with the legislation and the possibility to externalize environmental costs. In comparison, recyclers of the formal e-waste sector have increased operating costs since they are paying contributions for the treatment of the wastewater they produce (Skinner et al., 2010).

Introducing financial incentives, such as funding the best recycling practices or giving grants for the sound management of wastewater effluents and the disposal of WEEE, could be a very effective method to reduce the use of informal e-waste processing and recycling practices for domestic e-waste and imported e-waste from HICs (Williams et al., 2008). Another possibility would be to provide financial incentives for transferring hazardous WEEE, which cannot be easily and safely disassembled and processed by informal businesses, to formal state-of-the-art businesses or, even better, to certificated end-processors using sound and controlled processing methods for e-waste. If the capacities for sustainable and sound e-waste processing techniques are available, such an integration of formal e-waste businesses at the international or national level would help to mitigate occupational and environmental health risks (Williams et al., 2008; International Labour Organization, 2012).

Better production processes through extended producer responsibility (EPR) and the green production of EEE

Eliminating informal e-waste businesses and the illegal trade in WEEE, and establishing and launching state-of-the-art e-waste processing facilities alone are not sufficient to mitigate the environmental and human health risks from e-waste pollutants. Mitigating these risks needs additional steps taken by the EEE production industry. For instance, during production, the use of highly toxic chemicals could be reduced or limited voluntarily, by governmental restrictions, or by finding substitutes that are less hazardous and easier to extract and recycle (International Labour Organization, 2012).

One approach in this direction is the Restriction on the use of certain hazardous substances (RoHS) Directive enacted in 2002 and modified in 2011 (European Parliament and Council of the European Union, 2011). This bans or restricts hazardous material in EEE for all products brought to market in Europe. For instance, according to the RoHS Directive, the use of metals and substances such as Pb, Hg, Cd, Cr(VI), polybrominated biphenyls (PBBs), and polybrominated diphenyl ethers (PBDE) are restricted in the casing of EEE and printed circuit boards. Nevertheless, despite the introduction of the RoHS Directive, the generation and release of highly toxic and carcinogenic pollutants, such as dioxins and furans, cannot be prevented (Williams et al., 2008). Electrical and electronic products produced in LAMICs, which contain recycled material from informal e-waste businesses, or obsolete and secondhand EEE from HICs being reused in LAMICs, still may contain higher amounts of hazardous compounds, possibly because of the lack of controls and regulations in these countries (Weidenhamer and Clement, 2007; Chi et al., 2011; International Labour Organization, 2012). On a global scale, more efforts are necessary to reduce or abolish the use of highly toxic compounds like halogenated flame retardants and heavy metals such as cadmium and mercury. In future, more focus is needed to reduce the amounts of hazardous toxicants and compounds that are used in producing EEE. The production of easy-to-disassemble and recycle EEE needs to be promoted to mitigate occupational risks and to close gaps in the material flow system to avoid the release of highly toxic substances into the environment (International Labour Organization, 2012).

Furthermore, increased responsibility needs to be placed on the EEE production industry. Firstly, in the direction of sound waste management by the industry having to pay fees for the disposal and recycling of the products or wastes generated during their production. This would provide an incentive to produce EEE which contains less hazardous compounds and which is easier to recycle. Secondly, there should be increased responsibility for the EEE production sector for recycling materials in EEE at the end of the equipment's useful life. The manufacturers can reduce the amounts of virgin (primary) metals taken from the mining sector by initiating take-back and collection programs for WEEE. They can achieve this by setting up trade agreements with formal state-of-the-art facilities that implement an efficient, sustainable, and environmentally-friendly recycling of WEEE. Such waste related policies and initiatives are based on the EPR principles, which shift the responsibility from municipalities to producers by compelling producers to take financial responsibility for the disposal and recycling of their WEEE (Yu et al., 2006a). Additionally, closing gaps in the material flow cycle by improving the recycling of WEEE and by incorporating less hazardous compounds, secondary metals, or less scarce metals can lead to a mitigation of the exposure to chemical pollutants from both the e-waste processing and mining sectors.

In summary, the introduction of the RoHS Directive may help to reduce the amount of hazardous pollutants and consequently the impacts of WEEE on environmental and human health even before the WEEE is traded and disposed of inappropriately into the environment or during its recycling. Until now, this approach has been enacted only within Europe and no international directives and legislation with this focus have been developed yet. In general, the EPR approaches are supporting sound waste management of WEEE and they give incentives to reduce the amounts of WEEE produced and traded by the EEE industry. In conclusion, the regulations and approaches of the RoHS Directive and the initiatives based on the EPR principles are promoting the production of 'greener' – more sustainable and eco-friendly – EEE products. They also promote the sound disposal and management of WEEE, but further agreements and approaches at the international level are required to enforce the greener production and disposal of EEE globally.

Green production of EEE and increased data transparency

Over the last years with the continuous development of technology, the life span of EEE has been showing a generally decreasing trend. This, along with the growing population and increasing living standards has resulted in a global increase in WEEE. For instance, the life span of a PC decreased from 4.5 to 2 years during the period 1992 to 2005 (Culver, 2005; Widmer et al., 2005).

Today, in the period of excessive informal e-waste processing and recycling and the resulting occupational and environmental health risks, the production of greener and more environmentally friendly EEE is needed to mitigate the negative impacts associated especially with these e-waste businesses (International Labour Organization, 2012). There are several criteria which have to be fulfilled to design green EEE. For example, the products should be carbon neutral and the GHG production should be as low as possible. They should be easy to dismantle, easy to repair and recycle, and their durability (lifespan) should be maximized. The use of toxic compounds and primary materials (e.g. metals and plastics) should be minimized or abandoned. In addition, efforts are needed to find solutions and technologies that go beyond our current dominant technologies. Production should actively engage the aims of local communities as well as those of the stakeholders, and the reuse of EEE should be fostered. Ultimately, initiatives for taking back obsolete equipment, for sound approaches to the management of e-waste, and appropriate state-of-the-art recycling technologies should be included to close the life cycle of EEE. Such initiatives would help to prevent the negative impacts associated with disposal and recycling practices for the end-of-life products of the EEE sector – much like a cradle to the grave principle (Greenpeace, 2011).

Fortunately, because of several environmental conventions, such as the Stockholm and the Basel Conventions (United Nations Environment Programme, 2013d; 2014) and the Strategic Approach to International Chemicals Management (United Nations Environment Programme, 2006b), the production industry is being put under pressure to improve its performance and provide and promote greener and more sustainable end-products to consumers (Greenpeace, 2011). Along these lines, Greenpeace has published a 'Guide to Greener Electronics' which includes the ranking of 15 companies according to their energy efficiency, the sustainability of their operations, and their compliance with several additional criteria for the production of greener EEE. These additional criteria include whether they give information regarding:

- Their GHG production and if they have specific plans to reduce the emission of GHGs
- If they use clean energy and if their operations have a high product energy efficiency
- If they avoid hazardous substances during their production
- If they use recycled plastics
- If their products have a sustainable product life cycle (high durability, easily repaired).
- If they try to reduce energy consumption throughout the supply chain
- If they follow specific policies and practices for sustainably sourcing paper fibers and using conflict-free minerals
- If they implement effective voluntary take-back initiatives of WEEE.

Greenpeace determined that, of the companies tested, Hewlett-Packard (HP) best meets the criteria for greener electronics – the company scored 5.9 points out of 10. However, HP was awarded a very low number of points for their clean energy policy, for their product life cycle, and for the use of recycled plastic. HP is followed by Dell (5.1 points), Nokia (4.9 points), and Apple (4.6 points). These results show that although some efforts, initiatives, and improvements in production and in the provision of green technologies have been taken, further steps towards the production of sustainable and environmentally friendly EEE are required. In addition, data about energy consumption, product life cycle, and production, in general, are not transparent and difficult for the consumer to assess. Such data need to be more transparent and make it easier for the consumers to make decisions as to whether they are willing to support the development of green technologies or not.

At present, the main focus in the field of green technology is on reducing the use of hazardous compounds, not on improving the efficiency of the product life cycle or other aspects, such as ease of disassembly or facilitating the recycling of EEE. The reason why green technologies are described in this chapter with the theoretical examples of good practices is that the practices used by the main companies are still not satisfactory (Greenpeace, 2011).

One innovative idea for end-products that are easy to assemble and upgrade is the Bloom laptop which has been developed by a group of students from Stanford University and Aalto University of Finland. This laptop can be disassembled by hand easily, individual parts can be easily replaced and upgraded, and any broken elements can be exchanged easily by the consumer alone (Bhobe et al., 2010; International Labour Organization, 2012). Another idea is the vision of the mobile phone of the independent organization Phonebloks. Their idea is to design a mobile phone encouraging the development and production of EEE that produces less electronic waste, is easy to upgrade, is recyclable, and has, therefore, an increased life span (Phonebloks, 2016). Their phones will consist of individual blocks with different functions e.g. different cameras, processors, displays, and so on. The idea is that consumers can design their own phones according to their own wishes and needs. In addition, Phonebloks want to provide a technology where consumers can upgrade or repair their phone by themselves by replacing just individual parts (blocks) instead of buying a completely new phone. This reduces the amount of e-waste produced and considerably increases the life span of these phones. While these are innovative ideas and there is some interest in these products by electronic companies, these products are not likely to be adopted soon (Bhobe et al., 2010; Phonebloks, 2016).

Residual Waste from Selected Industries

Pollution risks from other industrial waste

Our report covers the following chemical pollutants/ sectors: (1) pesticides, (2) pharmaceuticals, (3) mining, and (4) e-waste. This is because our highest concern is for environmental and human health in LAMICs and because of the availability, although partially fragmentary, of comprehensive and global databases. Comprehensive databases about industrial production, exports, and imports are, however, generally not publicly available. This is mainly because of the complex production chains and the non-transparency of industrial data (Larsson and Fick, 2009). Chemical pollution from these industries is of a very varied and complex nature. Nevertheless, the scattered data about industrial activities in LAMICs that were available showed the high impacts on human health and there was evidence that industrial pollutants cause significant environmental pollution and degradation (Larsson et al., 2007; Larsson, 2010; Blacksmith Institute and Green Cross, 2012, 2013). Despite the limited availability of data, the industrial sector needs to be considered and discussed as a significant source of highly toxic pollutants and more investigations about industrial pollutants in LAMICs are required. This is especially so since:

1. The start of worldwide chemical intensification and the outsourcing of the industry from HICs to LAMICs (see section **The future of chemical pollutants in low- and middle-income countries,** p. 15; United Nations Environment Programme, 2013c; PricewaterhouseCoopers, 2008; United Nations Industrial Development Organization, 2014).

2. Infrastructure is lacking and obsolete and environmentally unfriendly methods are used for the production and processing of industrial commodities (Yusuff and Sonibare, 2004; Mohanta et al., 2010; Mehraj et al., 2013).

3. Compliance with environmental regulations, if they exist, cannot be guaranteed and there is less (or maybe even no) awareness of the adverse impacts of pollutants on environmental and human health in LAMICs (Blacksmith Institute and Green Cross, 2012, 2013; United Nations Environment Programme, 2013c).

In this section, therefore, we briefly address hazardous pollutants released from several industry segments, such as the cement, paper, textile, and rubber industries.

Textile industry

Introduction

During the manufacture (the scouring, bleaching, coloring, and finishing steps) of wearing apparel, large volumes of water (in general, 60–400 L) are needed to produce and process 1 kg of clothes. In addition, large volumes of hazardous agents are used. Both the amount of water consumed and the agents used depend on the type of fabric being processed (wool, cotton, polyester, etc.) (Yusuff and Sonibare, 2004; International Finance Corporation and World Bank Group, 2007). For instance, 1967 data from the U.S. Department of the Interior's Federal Water Pollution Control Administrations (Federal Water Pollution Control Administration, 1967) showed that washing and rinsing operations for the production of 1 kg of wool and cotton clothes required 250–580 L water, while for the production of 1 kg synthetic clothes about 25–240 L of water were needed. (Data from 1967 is used here because these older data might better represent the actual water consumption in LAMICs where older techniques are applied.) Because of the high consumption of water and chemical agents during the textile manufacturing wetting processes, wastewaters are the major source of chemical pollutants. Thus, the key environmental issues associated with the textile industry are water use, inadequate wastewater treatment, and inappropriate disposal of aqueous effluents, especially in LAMICs (Yusuff and Sonibare, 2004). For a more complete picture, it must be recognized that during the production of natural fabrics, such as cotton and wool, water is also used for growing the plants and raising the animals, which increases the water footprint of these products. Furthermore, in growing the raw materials of natural fabrics (cotton and wool from sheep or other animals) toxic pesticides might be used as well (Syrett, 2002).

Pollution potential from the textile industry

Wastewater from the textile industry often has poor quality by showing high levels (up to 2000 mg/L) of biological oxygen demand (BOD; Multilateral Investment Guarantee Agency, 2004). BOD_5 measures the amount of oxygen (mg/L) required for the microbiological decomposition of the organic material contained in the water within 5 days at a constant temperature of 20°C (United Nations, 2007). The wastewater also has an increased alkalinity, generally, a chemical oxygen demand (COD), and carries an amount of solids (measured as total suspended solids; TSS); [COD indicates the amount of oxygen (mg/L) which is needed for the oxidation of all the organic substances in the water (LAR Process Analysers AG, 2016)]. The most relevant toxic agents that might be used and released during the individual steps in textile manufacturing are listed below.

Washing and scouring operations – non-biodegradable and less degradable surfactants (alkyl phenol ethoxylates, APEs; Scott and Jones, 2000) and organic solvents (phenols; Multilateral Investment Guarantee Agency, 2004; Le Marechal et al., 2012).

Dyeing operations – benzidine-based azo-dyes (some of the azo-dyes can lead to the formation of environmentally toxic and carcinogenic amines) or sulfur dyes, and dyes which contain heavy metals (intentionally or contaminated with arsenic, cadmium, chromium, cobalt, copper, nickel, lead, and zinc), or chlorines (Multilateral Investment Guarantee Agency, 2004; Yusuff and Sonibare, 2004; International Finance Corporation and World Bank Group, 2007). Dyeing carriers can involve heavy metals or chlorines. For the dyeing of polyester and polyester-wool mixtures at lower temperatures, halogenated carriers are used to help the dyes penetrate the polyester fibers (Multilateral Investment Guarantee Agency, 2004; Syrett, 2002; Le Marechal et al., 2012).

Bleaching operations – involve the use of sulfur and chlorine-based bleaching agents (sulfur dioxide gas and sodium hyperchlorite), caustic soda (NaOH), acids, and surfactants (the use of peroxides is recommended) (Multilateral Investment Guarantee Agency, 2004; Yusuff and Sonibare, 2004; International Finance Corporation and World Bank Group, 2007; Le Marechal et al., 2012).

Cloth protection – for the protection of natural fabrics and clothes, hazardous pesticides are used sometimes (dieldrin, pentachlorophenol, and arsenic or mercury based pesticides). Synthetic clothes may contain plasticizers and brominated or fluorinated flame retardants (Multilateral Investment Guarantee Agency, 2004; Le Marechal et al., 2012).

Case study of concern of the textile industry

Rahman et al. (2008) assessed the environmental impacts of the wastewater effluents from the textile and dyeing industries on the ecosystem of Karnopara Canal at Savar, Bangladesh. By monitoring the physicochemical properties, such as pH, color, dissolved oxygen, BOD, COD, TSS, total dissolved solids, alkalinity, salinity, turbidity, electrical conductivity, iron, and ammonia, they revealed that all the water of the Karnopara Canal was outside the tolerable limits of the Department of Environment, Bangladesh standards. Thus, these highly polluted effluents had adverse impacts on the surrounding land and aquatic ecosystems and even on the local community (Rahman et al., 2008). Figure 29 is a picture of untreated effluents from the textile, the dying, and the leather industries. Data from Hämäläinen et al. (2006) showed that the estimated number of fatal occupational accidents is much higher in LAMICs than those of HICs (especially in India, China and Sub-Saharan Africa). This indicates that working conditions in LAMICs are often poor, less safe, and less controlled.

Figure 29: *Untreated wastewater from the textile, dying, and leather industries in Savar, Bangladesh (Picture: Daniel Lanteigne, 2010a).*

Leather industry

Introduction

During the production of leather, several different processes need to be carried out. Of these, the tanning process is the most important one from an environmental point of view. During the tanning processes, the skins of animals are treated to produce leather. Large amounts of different hazardous chemicals are required to make the raw animal skins more visually attractive and robust. For example, to remove and break down the hair and animal parts on the hides, sulfides are used. Chlorides are used to preserve the leather from decomposition. Often, trivalent chromium salts are used to further stabilize leather products (Blacksmith Institute and Green Cross, 2012). Similar to the textile industry, large volumes of water are needed during the leather tanning process as well. During the processing of 1 kg of raw material, 30–40 L of wastewater is produced (Ingle et al., 2011). Hence, wastewater effluents from the tanneries (especially if they are untreated) are the major exposure pathway releasing hazardous chemicals into aquatic systems (Blacksmith Institute and Green Cross, 2012). The key environmental issues associated with the leather industry are, therefore, the same as those for the textile industry – high water consumption, inadequate wastewater treatment, and inappropriate disposal of aqueous effluents. According to the database of the Blacksmith Institute, there are over 100 contaminated tannery sites (Figure 30). Of these, the greatest amount of contaminants is released from poorly run and managed small scale facilities and in legacy leather processing sites. It was calculated that more than 1.8 million persons are at risk worldwide because of the pollution of these sites (Blacksmith Institute and Green Cross, 2012).

Figure 30: *Untreated wastewater of leather tanneries in Bangladesh is released into the environment (Picture: Daniel Lanteigne, 2010b)*

Pollution potential from the leather industry

Wastewater effluents from tanneries have, similar to textile industry effluents, high levels of BOD and COD (Bosnic et al., 2000; Mohanta et al., 2010). Normally, natural and healthy water systems can handle a specific amount of effluents with a high oxygen demand, the effluents of tanneries (especially if untreated) however, often contain excessive loads of water with a high oxygen demand. This can lead to an oxygen withdrawal, adversely affecting the plants, vertebrates, and invertebrates or even causing their death (Bosnic et al., 2000; Mohanta et al., 2010). Besides these aqueous pollutants, large amounts of solid waste are produced during leather production. These solid wastes mainly contain leather particles and the residues of the dead animals, or they originate from chemical discharges and precipitated reagents used during the processing of the leather. If these solid wastes are not adequately removed from the wastewater they can precipitate as sludge and clog wastewater pipes or cover plants and sediments, thus causing the environmental degradation of aquatic systems (Bosnic et al., 2000).

From the pollutants released from the tanneries, chromium is considered to be the one of greatest concern from the environmental and human health perspectives Cr(III) (which is mainly used in the tanning process) is less toxic under certain environmental conditions. In the presence of manganese oxides or other strong oxidizers (Rai et al., 1989) this trivalent chromium can be oxidized to Cr(VI), which is classified in IARC group 1, carcinogenic to humans (International Agency for Research on Cancer, 2015). Organic solvents, sulfides, ammonia, chlorides, and additional heavy metals, such as lead and cadmium from dyes, can be found in the wastewater effluents of tanneries as well (Bosnic et al., 2000; Mohanta et al., 2010; Blacksmith Institute and Green Cross, 2012).

Case study of concern in the leather industry

Studies conducted in 2007 and 2013 by the Blacksmith Institute in the Hazaribagh district of Dhaka, Bangladesh, provide lists of the world's 30 (Hanrahan et al., 2007) and 10 (Blacksmith Institute and Green Cross, 2013) most polluted places. In the Hazaribagh region there are about 200 tanneries on about 25 ha of land, employing between

8000 and 12,000 people (Pearshouse, 2012; Blacksmith Institute and Green Cross, 2013). There, about 75 tonne of solid waste and about 22 million L of wastewater are generated per day (Azom et al., 2012). Most of the wastewater is discharged into the Buriganga River, Dhaka's water supply, without any treatment (Pearshouse, 2012; Blacksmith Institute and Green Cross, 2013). In effluents of one of those tanneries, the BOD5 was measured at 3600 mg/L and the COD at 9300 mg/L. Both far exceeded the permitted standards. Concentrations of chromium of 4043 mg/L, chloride of 45,000 mg/L, lead of 1944 mg/L, and sulfide of 145 mg/L have been measured. These are much higher than the permitted levels of 2 mg/L for chromium, 600 mg/L for chloride, 0.1 mg/L for lead, and 1 mg/L for sulfide (Rahman, 1997; Pearshouse 2012). Although these values were measured in 1997, the results from studies of the Blacksmith Institute and Green Cross (2013), Pearshouse (2012), and Azom et al. (2012) showed almost no improvement had been achieved in this region and almost no action taken in waste management (wastewater and solid waste) or for the development of sound leather production.

The pollution of the leather industry (tanneries) is not only adversely affecting the environment, but also the workers and local people of the Hazaribagh district of Dhaka, Bangladesh. There, local residents are living besides channels with untreated tannery effluent. The residents and workers from the tannery facilities suffer from rashes, itches, fever, diarrhea, and respiratory problems. The workers from the tannery facilities especially suffer from the poor occupational health and safety conditions. This is shown through the adverse health effects, such as premature aging, discolored, itchy, acid burned, and rash-covered skin, aches, dizziness and nausea, respiratory diseases, and elevated cancer rates. These arise because the tannery companies do not often provide adequate protective clothing (gloves, masks, boots, and aprons) and because of the unsafe and dirty working conditions (Pearshouse, 2012).

Paper industry

Introduction

In some regions, especially in Indonesia, the paper industry might be responsible for deforestation because of its unsustainable pulpwood harvesting practices. In addition, the pulp and paper industry is, among others, one of the world's largest consumers of energy. The industry is emitting large amounts of GHGs. Although deforestation and the high emission of GHGs have significant impacts on environmental and human health, for this report we are focusing more on the highly toxic organic and inorganic compounds that are released into the environment through paper production (Ince et al., 2011; WWF, 2015). During paper production, large volumes of water are used. For instance, even if state-of-the-art technologies are used, water consumption is about 60 L/kg of paper produced (Thompson et al., 2001; Ince et al., 2011). Data about the degree of pollution caused by the paper industry in LAMICs are much less readily available than data about textile and tannery pollutants. Nevertheless, given the large volumes of water required during paper production, the environment can be exposed to large volumes of wastewater with toxic compounds, especially if poorly-functioning, or even no wastewater treatment facilities are available. This often the case in LAMICs (Corcoran et al., 2010).

Pollution potential from the paper industry

Like most industrial effluents, the wastewater effluent of the paper industry can have elevated BOD5, COD, and TSS levels, which can adversely affect aquatic environments (Pokhrel and Viraraghavan, 2004). In addition to these elevated levels, the most relevant and hazardous agents that might be released during the several steps of paper manufacture are listed below.

Wastewaters from wood preparation processes contain suspended solids, dirt, and organic matter, and they have elevated BOD levels. The wastewater from the digester house, which is referred to as 'black liquids', contains chemicals that were used for cooking the wood as well as for extracting lignin and other hot water extracts of the wood. A comprehensive literature research by Pokhrel and Viraraghavan (2004), covering the wastewaters of the digester house, show that the highest level of BOD5 was 13,088 mg/L, that of COD was 38,588 mg/L, and that of TSS was 23,319 mg/L. In addition, higher levels of halogenated compounds (measured as adsorb-able organic halides, AOX) and volatile organic carbons (VOC), such as terpenes, alcohols, phenols, methanol, acetone, chloroform, etc., can be measured in these effluents as well (United States Environmental Protection Agency, 2002; Pokhrel and Viraraghavan, 2004). During the subsequent pulp washing, wastewater with higher BODs, CODs, and amounts of suspended solids are generated in the main (United States Environmental Protection Agency, 2002; Pokhrel and Viraraghavan, 2004). During pulp bleaching, the pollutants of highest concern are adsorbed organic compounds, inorganic chlorine compounds (ClO^{3-}), organochlorine compounds, such as dioxins, furan, and chlorophenols, and VOCs, such as acetone, methylene chloride, carbon disulfide, chloroform, chloromethane, trichloroethane, and others (United States Environmental Protection Agency, 2002; Pokhrel and Viraraghavan, 2004). The paper making process can generate wastewater with organic compounds, solvents, and heavy metals from dyes (United States Environmental Protection Agency, 2002; Pokhrel and Viraraghavan, 2004).

Case study of concern for the paper industry

Because there is a lack of data and information, no appropriate and recent case example of pollution by the paper industry in LAMICs has been found. It would be relevant to further investigate the exposure, fate, and environmental risks of pollutants released by the paper industry.

Construction industry (cement industry)

Introduction

Cement is used as an important binding agent within the construction industry. It is produced all over the world in large quantities. According to the United States Geological Survey, global production of cement was about 4 billion tonne per year in 2013 (United States Geological Survey, 2014). Cement production involves a series of different processing steps, including (Karstensen, 2006):

- Quarrying the raw materials
- Grinding the raw materials
- Fuel preparation and combustion (preparing conventional fossil fuels and alternative fuels)
- Clinker burning (involving drying, preheating, calcination, clinkering, and clinker cooling)
- Preparation of mineral additives at the cement mill
- Cement packing and dispatching.

All these steps are described in more detail in the report on Formation and Release of POPs in the Cement Industry (Karstensen, 2006). Of these processes, clinkering is the central one and, from an environmental and human health perspective, the most relevant one – not because of the cement, but because of its energy consumption. To produce clinker, the silica and calcium carbonate bearing raw materials of the cement are added to a kiln system. The clinker is formed by the drying/preheating, calcination, and sintering of the raw material at temperatures in the range of 1000 to 1500°C (Karstensen, 2006; Conesa et al., 2008; Lei et al., 2011). This process consumes large amounts of energy. A state-of-the-art furnace used for clinkering needs about 3000 MJ per tonne of produced clinker (Habert et al., 2010). To produce this energetic input, conventional fossil fuels, such as coal, lignite, petroleum coke, or oil are burned. More recently, waste material – including waste oil, used tires, paint thinners, degreasing solvents, solvents from the ink and printing industries, chemical by-products and solid waste from pharmaceutical and chemical manufacturers, municipal solid wastes, and sewage sludge – are added to the regular fuels as inexpensive substitutes for the conventional fuels to reduce costs during this energy-intensive process. The organic and inorganic air pollutants arising from this combustion process are of highest environmental concern, especially if the combustion processes in the furnace are poor (lower temperature, bad mixing, and a shortage of oxygen). The pollution is worse if the exhaust fumes of the cement production facilities are not filtered and controlled, which might be the case in LAMICs. In this case, toxic inorganic and organic pollutant can be released (Conesa et al., 2008).

Pollution potential from the cement industry

The conventional and/or substitute fuels and the raw material can contain heavy metals that can be released during the combustion processes. The higher toxic heavy metals, Hg, Tl, Pb, and Cd, are volatile or semivolatile, while As, Cr, Cu, Sb, and Zn remain in the clinker material. Inadequate combustion of organic matter and fossil fuels produces highly toxic, mutagenic, and carcinogenic products. Persistent and bioaccumulative compounds, such as dioxins, furans (PCDD/Fs), and PAHs, can be generated and released into the environment (see section **E-waste pollutants of environmental concern** (p. 106) for their impact on the environment. Other hazardous compounds, like HCl, hydrogen fluoride, oxides of nitrogen, sulfur dioxide, and VOCs, such as benzenes, toluenes, xylenes, and phenols, can be released as well (Karstensen, 2006; Conesa et al., 2008; Mehraj et al., 2013).

Case study of concern for the cement industry

A health risk assessment study focusing on the health risk to residents living in the vicinity of a cement manufacturing plant was conducted in Khrew, Jammu and Kashmir, India by Mehraj et al. (2013). In this region, cement manufactories, brick kilns, stone crushers, and automobile exhaust are the main emitters of air pollutants. There, cement production is quite high and enough of the raw materials – limestone/chalk, marl, and clay/shale – required for cement production are available to supply several factories in Khrew, Wuyan, and Khonmoh. The study revealed that in Khrew about 15,000 to 20,000 people, who live within a 2 km to 3 km radius of the cement manufacturing facilities, are directly affected by the pollutants released from cement production. In this region, cement dust, which is emitted during cement production and deposited in a thin layer, affects human and environmental health. This deposit comes about mainly because there is no efficient dust control equipment, but also because there are no adequate filter systems used during the manufacture of cement (The Vox Kashmir, 2013). Cement production can adversely affect environmental and human health through cement dust and/or chemical pollution released during the heating process. The latter pollutants are adsorbed to the dust particles. Because of its high and aggressive alkalinity, frequent inhalation of cement dust can cause respiratory diseases in the long run. This is particularly the case for workers involved directly in cement production and processing, and for residents living in the vicinity of cement production plants. Many workers in India are not wearing appropriate gloves, masks, or footwear (The Vox Kashmir, 2013; Mehraj et al., 2013). Contact with cement dust can cause serious and irreversible injuries to the eyes. Skin contact can cause damage to nerve endings, can burn the skin, or can cause irritant contact dermatitis (Hanson Heidelberg Cement Group, 2009).

When comparing the incidence of disease in Khrew with that in Burzahama, a city without any adjacent cement production facilities, there was a significant increase in the incidence of disease that can be directly associated with the continuous exposure to cement dust in Khrew (The Vox Kashmir, 2013; Mehraj et al., 2013).

Rubber industry

Introduction

Today, the production and use of rubber, naturally or synthetically produced, is indispensable in our daily lives. Given its physical properties, such as being flexible and resilient at the same time, and its waterproof and dielectric characteristics, rubber is widely used in many industrial products (conveyor belts, gasket rings, as adhesives, tires, or in fan belts, and automotive radiator hoses). It is contained in many commodities that are used in our daily lives (clothes and footwear, toys, and rubber gloves; Vishnu et al., 2011). Rubber production has increased continuously over the last decades. In 1996, about 15.5 million tonne of rubber were produced; today yearly rubber production is 27.5 million tonne. Of this, 56% is synthetic rubber and 43% originates from natural rubber material (International Rubber Study Group, 2014). In general, rubber production consumes large amounts of energy and water. Large amounts and a wide range of chemicals, and sodium sulfites and ammonia as anticoagulants, activators, dyes, acids, vulcanization agents, accelerators, and softeners are added to the raw material during the production of latex and rubber. This can lead to the release of large volumes of hazardous chemicals into the environment during the production processes (United States Environmental Protection Agency, 2002; Edirisinghe et al., 2008; Vishnu et al., 2011). Given the large volumes of water used during the cooling, cleaning, and washing processes during rubber production, large amounts of wastewater are produced. For the production of 1 kg of natural raw rubber, 40–50 L of wastewater are generated (Edirisinghe et al., 2008).

Pollutions potential from the rubber and plastic industry

If the effluents are not treated, these discharges can have high levels of BOD and COD. The effluents contain high levels of organic compounds, such as rubber particles, carbohydrates, proteins and amino acids, and uncoagulated rubber particles, and TSS. The effluents of the rubber industry are of an acidic nature. In addition, the effluents of rubber factories can contain sulfur compounds, ammonia, or acids, such as formic, acetic, or oxalic acid (United States Environmental Agency, 2005; Edirisinghe et al., 2008; Vishnu et al., 2011). The presence of high loads of organic material, hydrogen sulfides, ammonia, and amines can cause a foul-smelling odor, especially in water with high BOD and COD. The dissolved oxygen levels are low, which makes the water unsuitable for drinking for several kilometers downstream from the rubber

Figure 31: *Water pollution suspected to emanate from rubber industries near Hanwella, Sri Lanka (Picture: Revolve Water, 2014).*

production facilities (Vishnu et al., 2011). Furthermore, consistent with this deterioration in water quality, there is evidence that the continuous discharges of the wastewater effluents of the rubber industry considerably affect the biota of the water body. This is particularly so if the effluents are untreated, which might be the case in several regions in LAMICs (Arimoro, 2009).

Moreover, the inappropriate disposal of rubber material as solid waste or its incineration can cause severe environmental pollution as well. Given that rubber degrades slowly, its disposal can have serious ecological risks and adverse aesthetic effects to the terrestrial and aquatic environment. The incomplete or inadequate combustion of rubber material and solid waste can lead to the formation of highly toxic, carcinogenic, and persistent chemicals, such as PAHs and polyhalogenated hydrocarbons (dioxins and furans; United States Environmental Protection Agency, 2005; Wang and Chang-Chien, 2007).

Case study of concern for the rubber industry

In Sri Lanka, the rubber industry is considered one of the main industrial polluters. There, the effluents of rubber production plants often are discharged directly into water bodies without any treatment, resulting in environmental pollution and a deterioration in water quality (Edirisinghe et al., 2008).

In a comprehensive study by Edirisinghe et al. (2008), wastewater effluents of 62 rubber manufactories in Sri Lanka were analyzed. It showed that about 50% of the wastewaters of the Sri Lankan industries tested exceeded the general standards and tolerance limits for BOD, COD, and TSS values specified by the Sri Lankan Central Environmental Authority (CEA). For instance, an average BOD of 1063 mg/L, an average COD of 2010 mg/L, and an average TSS of 242.9 mg/L were measured. The CEA tolerance limits for wastewater effluents are 50/60 mg/L for BOD, 400 mg/L for COD, and 100 mg/L for TSS. A polluted river, which is close to the rubber industries near Hanwella, Sri Lanka is shown in Figure 31.

Market share of several industrial commodities – mapping the risks

To date, comprehensive data about industrial pollutants are neither compiled nor available. Nevertheless, with the help of data about market share it is possible to identify potential risk areas with high industrial activities. These data can give the first hints as to those regions where more risk assessment studies and further investigation would be required.

With the demographic changes and chemical intensification (see section **The future of chemical pollutants in low- and middle-income countries**, p. 15), which are more pronounced in LAMICs, general industrial production is shifting from HICs to LAMICs. The data of the International Yearbook of Industrial Statistics 2014 (United Nations Industrial Development Organization, 2014) indicated that the market share (%) of China for commodities produced by such manufacturing sectors as leather, paper, rubber, and textiles, and the share of chemical products doubled from 2005 to 2012 (not shown here). During the same period, the USA's share of these commodities decreased by one-half to three-quarters.

A more detailed look at the global market shares of commodities from the leather and footwear, paper, rubber and plastic, textile, wearing apparel, and chemical production industries (Figure 32) is informative. It can be seen that these commodities are produced in considerable quantities in LAMICs as well, while the high market shares of these different commodities for China are obvious at first sight. The increase in the market shares of these industrial commodities during 2005 and 2012, and the high levels of market share achieved for industrial commodities in China further confirm the outsourcing of industries from HICs to LAMICs. In China, particularly, the market shares of leather and footwear, textiles, and wearing

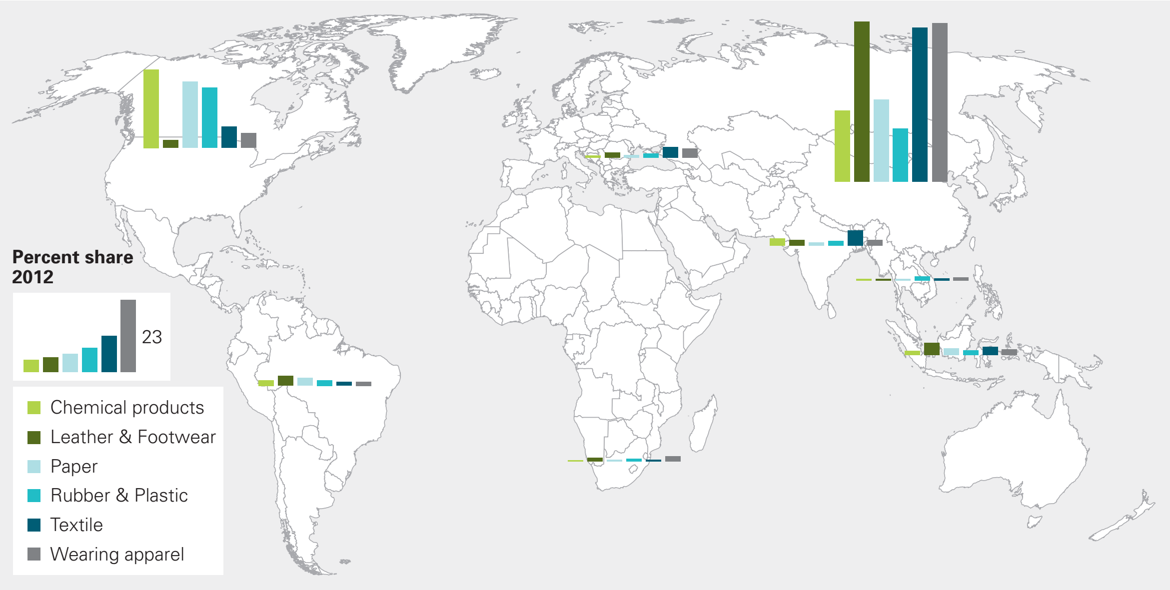


Figure 32*: Proportion (%) of the global market shares of chemical products, leather and footwear, paper, rubber and plastic, textiles, and wearing apparel in Brazil, China, India, Indonesia, South Africa, Thailand, Turkey, and the USA for 2012 (United Nations Industrial Development Organization, 2014)*

apparel far exceed those of the USA, which, with its high market shares of industrial commodities, acts as a representative of HICs. However, the market shares of chemical products, paper, and rubber and plastic commodities are comparable in both countries.

In addition, the Turkish, Indonesian, Indian, and South African market shares of wearing apparel (1.5 – 2.8%) and the Indian, Turkish, and Indonesian shares of textiles (2.5 – 4.5%) are comparable to those of the USA (4.3% for wearing apparel and 6.2% for textiles). This indicates that considerable amounts of these commodities are produced and put on the market as well. In LAMICs and China, according to the market share data presented in Figure 32, the leather and foowear production activities in Indonesia, India, and Turkey are considerable as well (1.6 – 3.5%).

Nevertheless, it must be remembered that the percentage market shares of Brazil, India, Indonesia, Thailand, Turkey, and South Africa, but not China, were based on the sum of the shares just from LAMICs in the International Yearbook of Industrial Statistics 2014 (United Nations Industrial Development Organization, 2014). Because of that, these percentage values were normalized to those of the world share, which might cause an increase in the uncertainty of the data and be incorrect if evaluated on a country scale. The market share values (%) of China had been calculated already by considering the global market share values.

Besides the market share values, data about the production of industrial raw materials could be used also to localize areas with high industrial activities. This information can then be used to identify potential risk areas where high amounts of toxic chemicals might be released into the environment. This holds true especially for regions with high industrial production rates and where unsustainable and environmentally unfriendly production practices are applied. Consequently, by considering these data, presumptive risk areas where environmental and human health might be affected could be assessed.

Figure 33 shows that the highest amounts of cement are produced in LAMICs, such as China and India (67.5 – 1880 million tonne/year). The amounts of cement produced in other LAMICs, like Turkey, Brazil, Iran, Vietnam, Egypt, Thailand, Mexico, Pakistan, Indonesia, Algeria, Malaysia, and the Philippines (in descending order), are of the same order of magnitude as those of the HICs – United States, Japan, Russia, Republic of Korea, Saudi Arabia, Italy, Germany, Spain, France, and United Arab Emirates (descending order). In 2010, production in these countries ranged between 1.5 and 67.5 million tonne/year (United States Geological Survey, 2012). Hence human and environmental health might particularly be affected in LAMICs with the highest cement production rates and where obsolete methods are used. This is particularly so if adequate devices to control the emission of industrial pollutants into the environment are lacking or if the workers and employers of the cement industry are poorly educated and not aware of the toxic chemicals and pollutants released during their work. The health of people in general is threatened if the industrial areas are densely populated, as is the case in Khrew, India (The Vox Kashmir, 2013; Mehraj et al., 2013; see the **Case study of concern for the cement industry**, p. 135).

In general, it can be assumed that the potential for excessive hazardous pollution is highest in those LAMICs that have experienced a remarkable economic boom within a short period of time, such as China (United Nations Industrial Development Organization, 2014). Often in these countries, the regulatory systems, the technical equipment, the know-how, and the financial capacity are not sufficiently well developed. They are unable to address adequately the increased industrial production and to soundly manage the handling, use, trade in, and disposal of hazardous pollutants, which are used in, or generated during, production (African Ministerial Conference on Environment and United Nations Environment Programme, 2004; United Nations Environment Programme, 2013c; European Chemical Industry Council, 2013; United Nations Industrial Development Organization, 2013).

Although there is some information about the market share and production of industrial commodities, these data are not comprehensive and are too fragmented for a proper environmental and human health risk assessment study. Therefore, to localize risk areas where human and environmental health are endangered, more comprehensive and transparent data about industrial activities (production, export, import, and water and energy consumption) and the monitoring of exhaust gases and wastewater effluents are required to predict the impacts of industrial pollutants in more detail.

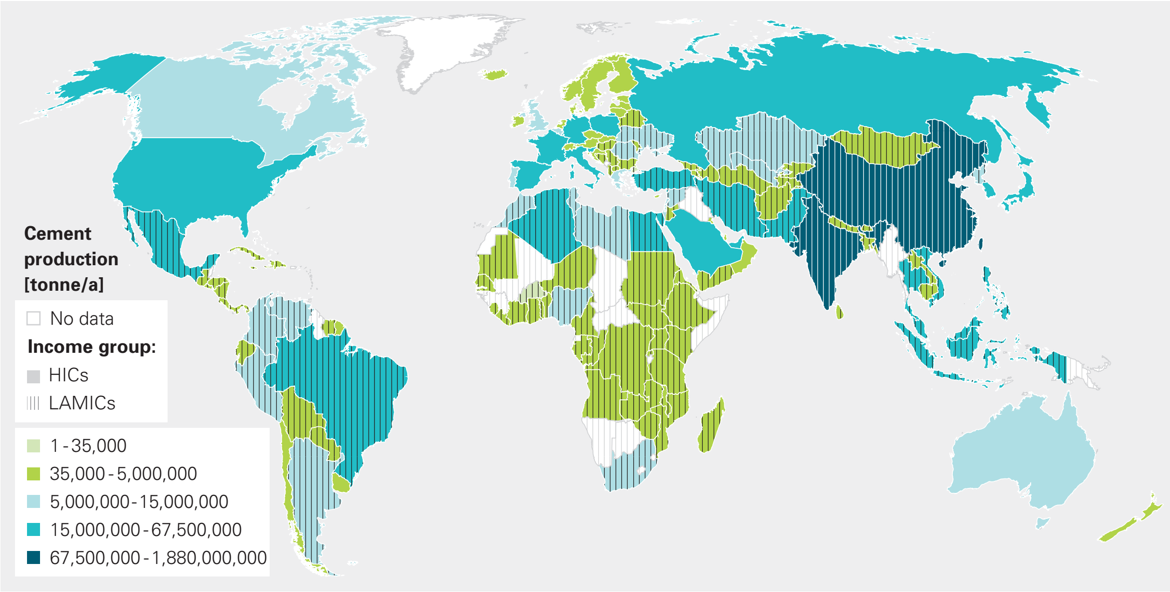


Figure 33*: 2010 cement production in different countries (United States Geological Survey, 2012)*

Knowledge Gaps and Opportunities to improve the Situation of Chemical Pollution, Exposure and Risks in LAMICS

In this report, we have described the current knowledge on chemical pollution and effects thereof on human- and environmental health in LAMICs. Despite the fact that information is rather scarce and/or fragmented, it is safe to conclude that the situation is alarming and that there is a trend that this situation is getting worse. In all the sectors evaluated, significant amounts of a large variety of chemical compounds are used, which enter the environment in often uncontrolled manner and can have negative impacts on environmental health. The negative effects of chemical pollution on human health, either caused by direct exposure, or indirectly, e.g. via the environment or food, are also significant. Because of the lack of data, the real threat for humans and the environment can only be estimated, with high probability that it could be more severe. Continuous exposures of the environment and humans to a large variety of chemical compounds, sometimes even to high concentrations, is a long term experiment with high risks. We hence believe that serious attention must be given to this risk. With the description of knowledge gaps and opportunities for action for specific fields we aim to improve the knowledge-base of chemical pollution and effects thereof in LAMICs, and help to develop mitigation options for the future.

1) Data availability and data collection

More comprehensive data, including the complete chemical life cycle, assessments of effects on environmental and human health, and comprehensive risk assessments, are needed on various scales. Data at global scale are needed to support international policy development as well as international conventions and protocols. Increasing international attention will also help national policy makers to make chemical pollution a priority topic. Country-level evidence is crucial for the development of national policies. Finally, since mitigation actions are implemented at local/catchment scale, more detailed information, with significant spatial and temporal resolution, is needed at this level. Our report shows that some data are available on the global and/or country scale, though this data is still scarce and often incomplete. Data at catchment scale are largely missing or not available at all.

As a way forward, as a first step, we suggest that existing data could/should be made publicly available. Such data includes figures of chemical production, import, export, use and chemical waste management. This sharing should also include all available data on exposure routes, concentrations and evidence of impacts on human and environmental health. Although this issue of data sharing might sound trivial, in particular in cases where data was collected with public/tax money, unresolved issues around data property and the willingness to be transparent and the subsequent ethical responsibility are major barriers. Reality shows that even existing data are seldom made publicly available, and this is not only true for LAMICs, but also holds for HICs.

Access to existing data with respective analysis would allow an identification of specific regional, or even country-wise risk hotspots. For a more detailed assessment, more data on exposure routes and exposure concentrations with higher spatio-temporal resolution, e.g. within countries, or within catchments, is needed. Finally, to complete the picture, such data would need to be complemented by surveys assessing human and environmental health as well as institutional settings, handling practices, and chemical waste management. All this contributes to the identification of the most hazardous pollutants, processes with major risks, lacking awareness, limited human capacity and knowledge, bad handling practices or even missing legislation.

2) Development of concepts and tools for monitoring and data collection

Most concepts and tools for monitoring and data collection have been developed with available expertise and resources for local settings and conditions in and for HICs. Such concepts and tools need to be adapted or newly developed for LAMICs, so that evidence on exposure routes, environmental concentrations, and effects of chemical pollutants can be collected. Adaptation of concepts and tools need to consider i) functionality under the respective climatic situation, ii) efficiency and cost-effectiveness, iii) feasibility of use by local people with limited technical skills and expertise, iv) applicability for all relevant spheres (air, soil, water and anthoposphere), v) the ability to capture both exposure and effect assessments, and vi) the ability to allow the development of locally relevant risk maps and mitigation options.

3) Development of mitigation options

Despite the fact that chemical pollution is of global importance and influenced by global trends, local mitigation measures are key to improving the situation for human and environmental health. There are no „one size fits all“ solutions. A wide portfolio of mitigation options must be developed and it must be evaluated which option fits best to the specific local situation. Ideally, finding and implementing mitigation solutions is a process taking place not in isolation but by including boundary conditions and local challenges and using a base of solid and detailed knowledge about the local situation.

4) Raise awareness in society, private sector and industry, politics and regulatory authorities as well as support the development and implementation of legislation and management tools

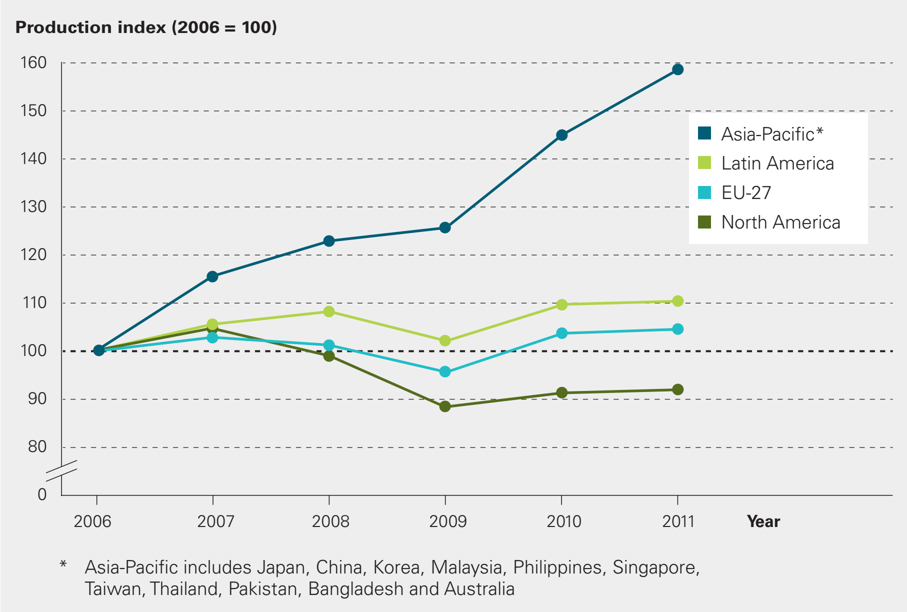
Awareness of the existing problem or the risk of the issue becoming a problem is a precondition for change. This report shows that chemical pollution is already a problem in many countries and is a problem which will increase in the years to come. The outcome of chronic chemical exposure on environmental and human health is difficult to predict and if, then only with limited reliability. Society, including policy makers, regulatory authorities, producing industries and the private sector must be better informed with clearer messages. In this regard, scientists and research play an important role as they can provide facts in an unbiased and neutral way. Furthermore, scientists can also support decision making under uncertainty.

Interdisciplinary research is a necessity for the issues of chemical pollution in LAMICs. Such research includes technical, social and natural sciences while involving a wide range of stakeholders at an early stage so that research results are taken up by policy makers and practitioners and can effectively tackle the problem of chemical pollution. Including relevant stakeholders in the research process assures that the critical questions can be voiced and tackled by researchers, the necessary and required data can be collected in a focused, practical manner, mitigation and management tools can be developed in a concerted action, and evidence can support and drive policy and legislation.

Appendix

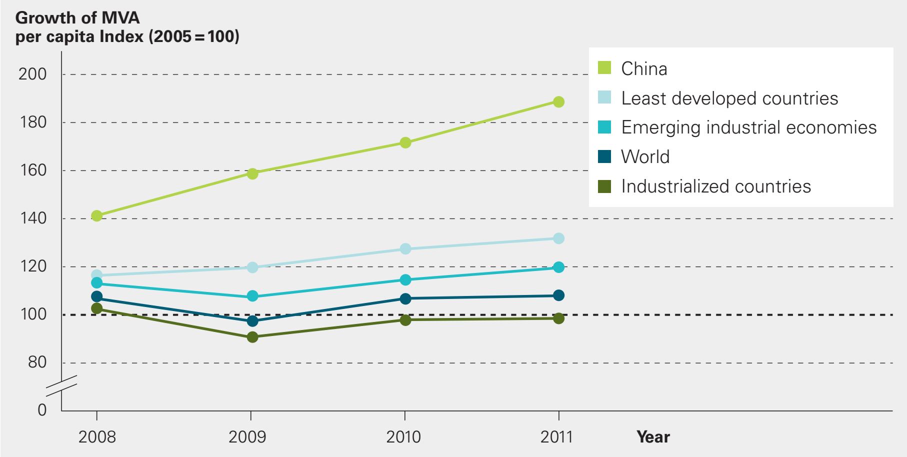
Appendix Figure 1 shows the trend in chemical production of the European Chemical Industry Council (Cefic) from 2006 to 2011 (European Chemical Industry Council, 2013). These data confirm that chemical production in almost all regions of the world has reduced. There are negative growth rates in 2008/09 that helped give rise to the economic recession in 2009. North America was the region most affected, followed by Europe and Latin America. Production in the Asia-Pacific region continued to show persistent growth over time with only a small deceleration during the recession (European Chemical Industry Council, 2013). In 2009, world chemicals production declined by 4.8% compared to 2008. This represented the largest recorded decline in world chemical production over the last 23 years. However, in 2010, global chemical production recovered in all regions, showing an increased growth rate of 10% compared to 2009. This was followed by a 4.5% increase in 2011 compared to the prior year. The growing rate of the production was headed by the Asia-Pacific region followed by production in the Latin American region. Over the last years, chemical production in Latin America and the Asia-Pacific region has far exceeded the production growth rates of Europe and the North America (European Chemical Industry Council, 2013).

World data on the growth of and distribution trends in manufacturing presented by UNIDO (United Nations Industrial Development Organization) in its International Yearbook of Industrial Statistics 2013 (United Nations Industrial Development Organization, 2013) and data presented by the Cefic (European Chemical Industry Council, 2013) are both in agreement with the data of the Global Chemicals Outlook Towards Sound Management of Chemicals from UNEP (United Nations Environment Programme, 2013c).



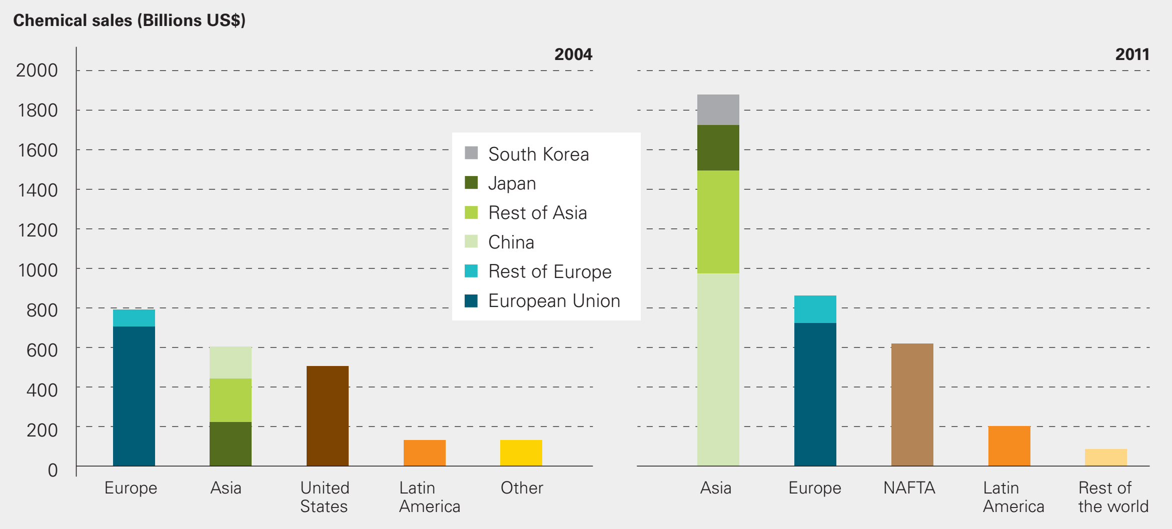
* Asia-Pacific includes Japan, China, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand, Pakistan, Bangladesh and Australia

Appendix Figure 1: *Long-term trend of chemical production. Growth rates and index numbers (2006 = 100; European Chemical Industry Council, 2013)*



Appendix Figure 2: *Major trends in the growth and distribution of manufacturing value added (MVA). Growth rates and index numbers (2005 = 100) per capita. MVA for the latest year 2011 for individual economies and for selected country groups. Data referring to country groups were based on cross-country aggregates of MVA in constant 2005 US$ (United Nations Industrial Development Organization, 2013).*

The data of the Yearbook of Industrial Statistics 2013 indicate that in addition to China, there was constant growth in industrial production and manufacturing output in the least developed countries (Appendix Figure 2). (This includes primary production of the basic chemical and secondary industrial sectors – pharmaceutical and pesticide production – and the production of electronic devices, clothes, household products, etc.) This growth in the least developed countries is shown by the growth in the manufacturing value added (MVA) in this region. In contrast, the manufacturing growth of the industrialized countries (the European Union and the United States) was strongly affected by the economic recession of 2009. By 2012, the MVA of the industrial economics had still not reached the level of the period before the financial crisis. The MVA was determined under the terms of the national accounting concept, which represents

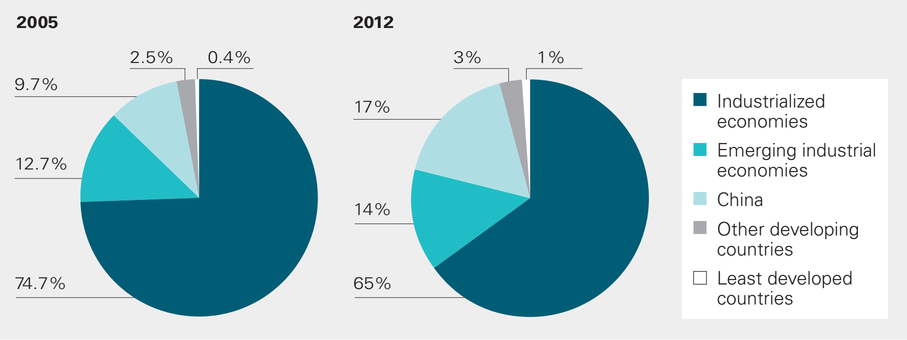


Appendix Figure 3: *World chemical production 2004 (left) and 2011 (right; African Ministerial Conference on Environment and United Nations Environment Programme, 2004; European Chemical Industry Council, 2013).*

the net contribution of the manufacturing sector to the gross domestic product (GDP; United Nations Industrial Development Organization, 2013)

The worldwide sales of chemicals for the period 2004 to 2011 in US$ billion are presented in Appendix Figure 3 (African Ministerial Conference on Environment and United Nations Environment Programme, 2004; European Chemical Industry Council, 2013). The sales figures of 2011 show that the Asian chemical production outstrips those of the other regions, posting sales of US$1890 billion in 2011. This represents 51.8% of the world's chemicals sales. In 2004, European chemical sales were constituting US$793 billion compared to Asian chemical sales of US$612 billion.

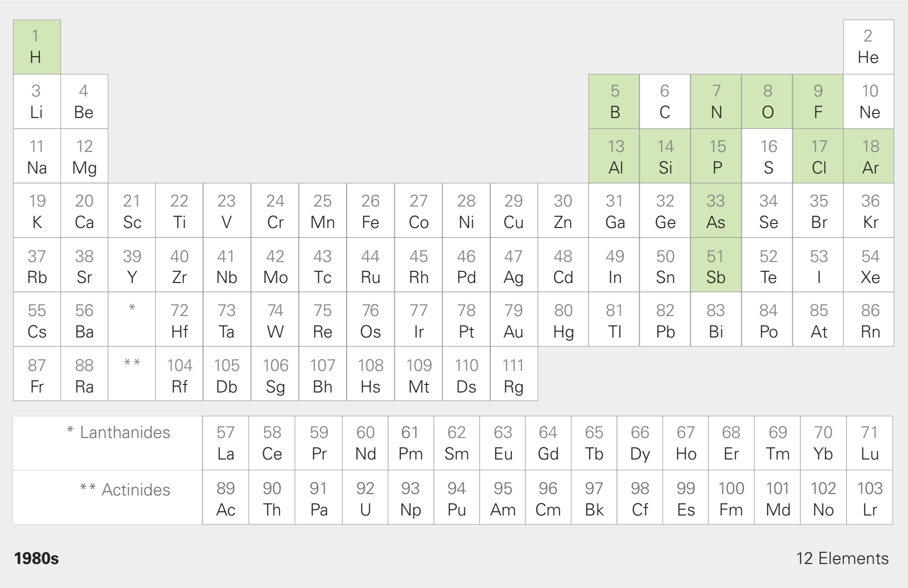
The dark blue column in Appendix Figure 3 represents the countries of the European Union; the light blue column represents the rest of Europe. The light green bar represents China; the darker green bar shows sales for rest of Asia; the olive column represents the data for Japan; and the grey bar indicates the values for South Korea. The dark brown bar represents the sales for the United States. The light brown bar combines the sales of the countries of the North American Free Trade Agreement (NAFTA: Canada, United States and Mexico). The orange bar shows the value for Latin America. The yellow bar shows the value for Canada, Mexico, Africa and Oceania together. The light orange bar illustrates the amounts of sales that are not included in the other columns. In summary, worldwide chemical sales were US$2141 billion in 2004 and US$3649 billion in 2011 (African Ministerial Conference on Environment and United Nations Environment Programme, 2004; European Chemical Industry Council, 2013)

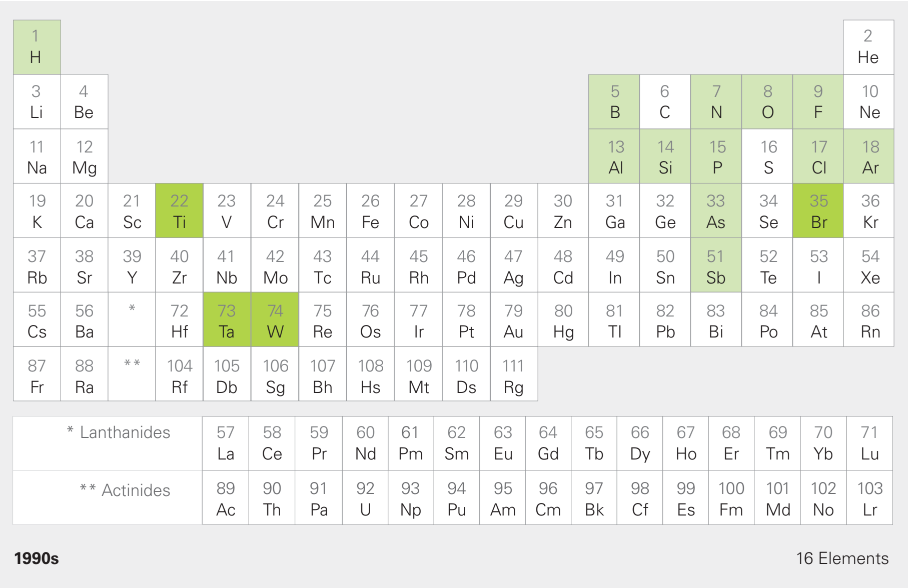


Appendix Figure 4: *Distribution of world manufacturing value added (MVA; United Nations Industrial Development Organization, 2013). [%]*

Appendix Figure 4 shows that despite the financial crisis, the industrial economies were still at the top of total manufacturing production, although the proportion of MVA had decreased by approximately 10%. However, the proportions of the MVAs of the developing countries and the emerging industrial economies, especially China, had increased (United Nations Industrial Development Organization, 2013).

These pie charts present the shares of selected groups of economic activities (e.g. basic chemical, leather, textile, and pharmaceutical production) in world MVA for different industrialized economies. China belongs to the group of emerging industrial economies. However, because of the large size of its economy, China is presented separately (United Nations Industrial Development Organization, 2013)





Appendix Figure 5: *Growing diversity in the materials used in the semiconductor industry from 1980 to 2000 (Theis, 2007).*

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