



WELCOME TO ISSUE N°2 OF THE NORMAN NETWORK NEWSLETTER

The aim of the activities of the NORMAN network is to enhance the exchange of information on emerging environmental substances, and to encourage the validation and harmonisation of common measurement methods and monitoring tools so that the requirements of risk assessors and risk managers can be better met. The NORMAN newsletter is for everyone interested in emerging substances in the environment. This newsletter keeps you up to date on scientific advances in this area and highlights the activities and events of the EU NORMAN Network.

Editorial

Information is what we need, not data

Dolf VAN WIJK, Ph.D.

Manager Environmental Sciences, Euro Chlor, Brussels, Belgium.
e-mail: dvw@cefic.be, website: www.eurochlor.org

The past few decades have seen a major increase in attempts to identify “emerging pollutants” in the environment. With rapid developments in analytical techniques this trend is likely to continue.

Our ability to find minute concentrations of substances in remote environments seems to be almost without limits. Caffeine can be detected in the middle of the North Sea. Naturally-created organobromines with structures closely similar to man-made flame retardants can be detected in 90-year-old whale blubber.

The scope for detecting minute traces of chemical compounds has become practically limitless. This poses challenges to our ability to distinguish between “background noise” and chemicals that pose potential environmental problems. The interests of all responsible stakeholders are served when samples are correctly taken and analysed, meaningfully interpreted and effectively communicated.

When new substances are identified in environmental samples this raises many questions. For example, “are

the data reliable”, “have samples been taken and stored correctly”, “how frequent and widespread are the observations”? Answers are essential to provide the right context for interpretation, and industry also has a role to play in providing answers. Simultaneously, when done properly, the resulting information provides a powerful basis to identify real “emerging pollutants” and to find cost-effective solutions.

The key question is: how to make this happen?

I am a great believer in the power of benchmarking. I am also convinced that meaningful developments strongly depend on the leadership of reliable, responsible and professional experts in the field. It is comforting to see many participating in the NORMAN project.

Undoubtedly, the trend towards detecting trace pollutants at ever lower levels will result in even more extensive volumes of data. If NORMAN can improve the process of converting data into reliable and meaningful information, this will be a major advance in early identification and resolution of potential problems.

Issue 2 – March 2007

EDITORIAL	p1
MONITORING AND BIO-MONITORING	p2
ENVIRONMENTAL AND HUMAN HEALTH RISK ASSESSMENT	p3
QUALITY ASSURANCE & QUALITY CONTROL	p7
RESEARCH PROJECTS / FINDINGS	p9
LIFE OF THE NETWORK	p14
CALENDAR OF EVENTS	p15

Partitioning behaviour of five pharmaceutical compounds to activated sludge and river sediment

Pharmaceutical compounds are a group of emerging compounds that have raised questions regarding their fate and effects in the environment. Given their intended use, their fate characteristics and, especially, their effect spectrum might differ considerably from those of "traditional" micropollutants. As stated by the authors, drugs have traditionally not been viewed as environmental pollutants. Nevertheless, their potential to cause a variety of physiological responses has raised concern for effects in the (aquatic) environment. Limited knowledge is available of the implications of exposure to complex mixtures of these compounds.

Municipal sewage treatment plants (STPs) act as point sources of pharmaceuticals to the environment. It is known that low concentrations of pharmaceutical compounds, coupled with their metabolic characteristics, lead to their incomplete removal from most STPs. Some compounds have been shown to bind to sewage sludge and may thus enter the terrestrial biosphere when biosolids are applied as fertiliser and soil conditioner. It is therefore important to understand the fate and behaviour of pharmaceuticals during waste water treatment.

In the study reviewed here, the aqueous concentration of five pharmaceuticals was determined after 0.5, 2.5, and 5 hours of exposure to

either artificial sewage sludge or river sediment. Neither substrate was previously exposed to pharmaceuticals. The compounds tested (log K_{oc} values between brackets) were: Ibuprofen (2.59), paracetamol (1.79), salbutamol (1.5), propranolol HCl (3.3), and mefenamic acid (2.66). It was found that after rapid sorption, especially to the artificial sludge, water concentrations increased again. Only a low percentage of the pharmaceuticals remained sorbed after five hours of exposure, independent of the hydrophobicity of the compound.

The results of this study indicate that processes other than hydrophobic partitioning play a dominant role in the partitioning of pharmaceuticals to solid phases. These processes might include ion exchange, surface adsorption to mineral constituents, complex formation with metal ions, and hydrogen bonding. Thus, sorption of human therapeutic agents may depend on factors such as pH and ionic strength.

The authors conclude that a major research effort should be made to assess the significance of drug residues in terms of their persistence and potential environmental impact. This could help to provide a realistic risk assessment of these compounds as well as to help understand the health and environmental consequences of not removing them from the wastewater stream and receiving environment.

SOURCE:

O.A.H. Jones, N. Voulvoulis, J.N. Lester. *Partitioning behavior of five pharmaceutical compounds to activated sludge and river sediment*. Arch. Environ. Contam. Toxicol. 50 [2006], 297-305.

REVIEWED BY:

Willie PEIJNENBURG

RIVM - The Netherlands National Institute for Public Health and the Environment
WJGM.Peijnenburg@rivm.nl

Polychlorinated biphenyls and polybrominated diphenyl ethers in indoor environment

Indoor air quality has been widely studied for approximately 30 years. Initially (in the 70s and 80s) focused on lead, asbestos and radon, in the 1990s, the scientific community began looking at indoor volatile organic compounds (VOCs). Indoor concentrations of VOCs can now be considered as relatively well known. In the past few years, research has been oriented to the study of semi-volatile organic compounds (SVOCs), heavier compounds that can be measured both in the air and in house dust. They include many types of compounds from a variety of indoor sources (insecticides, flame retardants, plasticisers...). Interest in the measurement of these compounds indoors is growing, since they are often detected in homes, they are persistent, their metabolites are measured in human blood and urine, and toxicology and epidemiology tend to prove that some of them may be toxic to the human reproduction system and human development. Although the majority of non-occupational exposure to these molecules is widely considered to occur via the diet, indoor air and house dust could also constitute

significant human exposure pathways. Thus they have to date been considered as indoor emerging substances.

Between September 2003 and November 2005, Harrad et al. measured polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in 92 micro-environments within the West Midlands conurbation, United Kingdom. The investigation covered 31 homes (both living rooms and bedrooms), 33 offices, 25 cars, and 3 public buildings (a coffee shop, a supermarket, and a post office). Passive air samplers (PUF disks) were used to provide time-integrated indoor air samples over each 28-day sampling period. Dust samples were collected in only 8 homes using the vacuum cleaner bag, which is a widely spread method for home dust sampling.

The indoor air median concentration of PBDEs was respectively 24, 71, 144, and 41 pg/m³ in homes, offices, public buildings and cars. The

lowest concentrations were measured at home and the highest in cars, in three of them in particular. Concentration in home dust was 87.1 ng/g of dust (median value). Considering time-activity patterns of 70 adults living in the West Midlands, a daily inhalation rate of 20 m³/d, and 100% absorption, daily exposure to PBDEs through inhalation was calculated. Moreover an average and a high dust ingestion scenario were considered. For median air, dust and diet concentrations, and the average dust ingestion scenario, air and dust appeared to be negligible pathways, contributing to respectively 0.9 and 0.4% of daily total exposure. However for percentile 95 air, dust and diet concentrations and the high dust ingestion scenario, dust contributed up to 37% of daily total exposure for the adult (up to 69% for the toddler). Inhalation contribution to daily total exposure remained low (5.6% for adults and 1.0 % for toddlers).

Dealing with PCBs, the indoor air median concentration was respectively 1.8, 5.9, 9.6, and 0.93 ng/m³ in homes, offices, public buildings and cars. The lowest concentrations were measured in cars and the

highest in offices. No statistically significant difference was observed from previous indoor air measurements made by the same authors between December 1996 and March 1998 in the same types of micro-environments except cars, suggesting no temporal trend. Using the same exposure scenarios and assumptions as for PBDEs, adult daily exposure to PCBs through inhalation was calculated and compared to daily dietary exposure. It appears that inhalation can have an important contribution to daily total exposure (median: 15%, up to 63% for 95th percentile).

This work is very interesting because it provides new data on PCBs and PBDEs indoor air and dust concentrations. Analytical methods are well described and the passive sampling repeatability is discussed. Dust concentrations should have been measured in a higher number of homes to obtain more consistent values, since dust appears to be a major route of exposure to PBDEs. Further research is anyway needed to develop knowledge of PBDEs and PCBs contamination of our daily environments and the associated human exposure.

SOURCE:

S. Harrad, S. Hazrati et al. *Concentrations of polychlorinated biphenyls in indoor air and polybrominated diphenyl ethers in indoor air and dust in Birmingham, United Kingdom: Implications for human exposure.* Environmental Science & Technology 40(15) [2006]: 4633-4638.

REVIEWED BY:

Corinne MANDIN

INERIS - Institut national de l'environnement industriel et des risques, Verneuil-en-Halatte
Corinne.Mandin@ineris.fr

Environmental and human health risk assessment

Linking organic pollutant (bio)availability with geosorbent properties and biomimetic methodology: A review of geosorbent characterisation and (bio)availability prediction

Most risk assessment procedures consider a fixed fraction (often 1) of the total pollution concentration as bioavailable, often resulting in an overestimation of the actual risk. By using measures to quantify the bioavailable fraction of a certain pollutant and including this information in risk assessment, one would be able to obtain a more representative picture of the actual risk posed to humans and the environment. The main problem encountered when implementing (bio)availability research on emerging compounds for risk assessment purposes is related to contradictory and incomplete literature reports.

To date, various approaches have been developed for assessing the impact of sorbents (including dissolved macromolecules) on the (bio)available fraction. Evidence to support the use of a particular method which outperformed other methods in laboratory studies in terms of its predictive capacity, is lacking. This is partly because comparison and correlation of results among biomimetic studies from different laboratories are implausible, since laboratory and field conditions, selection of compounds and field samples vary greatly.

In this contribution an overview is given of studies aimed at closing the gap between laboratory trials on availability assessment of hydrophobic organic compounds (HOCs), and the bioavailable fraction of HOC

in the field. Variation in sorbent properties, species dependent factors (such as uptake routes), and aim of the assessment (such as remediation versus assessing the likelihood of toxicity) are reviewed. It is concluded that no all-encompassing representative physical-chemical or biological test is as yet available, and the research and development of such a test is probably unfeasible, since accurate availability prediction would require acknowledgement and inclusion of diverse parameters and conditions. There is, however, justification for considering the availability of contaminants and assessing contaminated sites on a case-by-case basis.

Following an introduction on the definitions and types of availability, binding and immobilisation processes by solid phases are discussed. This discussion is extended with an overview of sorbent-related factors that affect diffusion and release of HOCs. Techniques for studying organic matter and for deriving descriptor factors that may be used to quantify binding affinities which characterise the sorbent are subsequently linked with biomimetic methods. In this part of the overview it is highlighted that the objective of the assessment is to be given a central place in selecting appropriate methods for biomimetic extraction. The merits of chemical extractants, solid-phase extraction, solid-phase micro-extraction, supercritical fluid extraction, and

solubilising agents and surfactants are highlighted in the context of predicting bioavailability of HOCs. The implications and consideration of a geosorbent molecular descriptor-biomimetic relationship for assessing availability are discussed in the synthesis part of the overview.

The main conclusion of this state-of-the-art review is self-explanatory and clearly indicates that this review paper is a "must read" for scientists

and policy-makers interested in the development and implementation of bioavailability in risk assessment: "By considering factors such as spatial and temporal differences, laboratory-generated data could be extrapolated to field conditions. Recognising the uncertainties associated with any individual methodology, it is suggested that site management decisions be based on an approach that includes multiple categories of tests to evaluate pollutant availability".

SOURCE:

G.A.C. Ehlers, A.P. Loibner. *Linking organic pollutant (bio)availability with geosorbent properties and biomimetic methodology: A review of geosorbent characterisation. and (bio)availability prediction*. Environ. Poll. 141 (2006), 494-512.

REVIEWED BY:

Willie PEIJNENBURG

RIVM - The Netherlands National Institute for Public Health and the Environment
WJGM.Peijnenburg@rivm.nl

Perfluorinated Compounds in German rivers and Drinking Water consequences for risk assessment and further research needs

In Europe, especially in Germany, perfluorinated organic compounds were one of the rising themes of environmental chemistry in 2006. Since some perfluorocarboxylates and perfluorosulphonates, mainly perfluorooctanoate (PFOA) and perfluorooctanoic sulphonate (PFOS) were detected in human blood, in drinking water and in food, and Greenpeace has launched a campaign, public interest is growing rapidly.

How it started. In summer 2006, the group of Martin Exner at Bonn University analysed several perfluorinated compounds in German rivers (Skutlarek et al. 2006). In the river Rhine they mainly found PFOA, PFOS and PFBS (perfluorobutane sulphonate). The concentrations were between 2 and 9 ng/L for PFOA, 2 and 26 ng/L for PFOS, and 6 and 46 ng/L for PFBS. Similar levels were observed in the main tributaries of the river Rhine, with the exception of the river Ruhr, where PFOA concentration was 48 ng/L. The chemists followed the river upstream and found the highest concentrations in the river Moehne and two brooks. A peak of PFOA-concentration of 33,900 ng/L was measured in the Steinbecke Brook. The source of the contamination was located in an agricultural area, where soil was washed away into both brooks. The Moehne flows through a tourist region in North Rhine-Westphalia with no fluorochemical industry. The main concern of these findings is: The river Moehne is retained by the Moehne dam, forming an important reservoir for drinking water for this region.

The source of the contamination was identified as a mixture of organic waste which was illegally distributed to farmers as fertiliser. The concentrations analysed in this mixture were higher than concentrations measured in the sewage sludge of the industrial waste water treatment plant of a main fluorochemical producer in the US.

Greenpeace campaign. In November and December 2006, Greenpeace started a campaign at the industrial park in Gendorf in Bavaria (<http://www.greenpeace.de/themen/chemie/nachrichten/>). In Gendorf, fluoropolymers are produced using ammonium perfluorooctanoate as a processing aid. After treatment, the waste water of this site is released into the river Alz. Greenpeace measured PFOS and PFOA directly at the site of release and several kilometres downstream. Although the company reduced emissions in 2006 by approximately

95 % compared to the level in 2000, the concentration of PFOA in the Alz reached a maximum of 56 µg/L. In addition, PFOA was determined in several wells of the region. In some of these wells the level of 0.1 µg PFOA /L was exceeded.

Other findings. In a research project of the German Federal Environment Agency (Umweltbundesamt - UBA), the researchers analysed several perfluorinated compounds (PFC) in the river Elbe, the German Bight, the North Sea and the Arctic (Theobald et al. 2006). This study showed that PFCs were transported via the river Elbe into the North Sea. Since no fluorochemical industry is located in this area, municipal waste water treatment plants are presumed to be an important source of the PCFs. However, further measurements are needed to confirm this hypothesis.

Regulatory activities. In 2004, the UK Environment Agency identified PFOS as a PBT-chemical (persistent, bioaccumulative, toxic). Meanwhile Sweden proposed PFOS as a candidate to be included in the Stockholm Convention on Persistent Organic Pollutants (POPs). In December 2006, the European Parliament and the Council decided to restrict marketing and use of PFOS with a few exceptions by amending Council Directive 76/769/EEC concerning restrictions on marketing and use of certain dangerous substances and preparations to include PFOS (Directive 2006/122/EC).

Some members of the parliament suggested expanding this directive to include PFOA. According to recent knowledge, PFOA is not a PBT-substance. However, the risks arising from the use of PFOA need to be assessed with high priority – a clause to re-consider the need to restrict marketing and use of PFOA following the risk assessment was included in the directive. Hence, the European Commission agreed with Germany and DuPont that a chemical safety assessment according to the rules of REACH should be performed by DuPont and the German authorities. As a starting point, the results and conclusions of a hazard assessment prepared for the OECD should be used.

Hazard Assessment PFOA. A hazard assessment for PFOA prepared by US-EPA (human health) and the German Federal Environment Agency (Umweltbundesamt, UBA, environmental part) was submitted to OECD in January 2006. Following an extensive round of commenting, the

parties are attempting to finalise and to agree the hazard assessment report between the OECD member states in April 2007.

Since PFOA is persistent in the environment due to the stability of the C-F bond, no degradation could be observed in studies on abiotic or biological degradability. The available ecotoxicological studies using APFO indicate a low acute and chronic toxicity for aquatic organisms. The effective concentrations determined are in the magnitude of 10-100 mg/L and much higher than the concentrations measured in the environment, including the findings in the river Moehne and their tributaries. In contrast to PFOS, PFOA does not show a high potential to bioconcentrate. However, there are recent Canadian publications indicating a potential for bioaccumulation in arctic mammals (e.g. Houde et al).

The main concerns for PFOA are the worldwide findings in the environment due to the high persistency and the dispersive properties, the long half-lives determined in human blood, and toxic, especially reproductive toxic effects. Hence, it was concluded in the draft hazard assessment that PFOA (and APFO) is a "candidate for further work". In detail it was proposed to estimate the exposure situation for the population and the environment and to characterise the risk arising by these exposures.

Drinking Water. Following the findings in North Rhine-Westphalia, the German Drinking Water Commission proposed the concentration of

5.0 µg/L as the trigger for immediate regulatory action. In addition, drinking water exceeding a concentration of 0.5 µg/L (sum PFOA and PFOS) should not be used to prepare baby food. A maximum concentration of 0.1 µg/L is proposed as target for lifelong uptake in drinking water for precautionary reasons (<http://www.umweltbundesamt.de/uba-info-presse/hintergrund/pft-im-trinkwasser.pdf>).

Food. High levels of PFOS found in farmed fish from Germany prompted the German Federal Institute for Risk Assessment to propose a provisional total daily intake (TDI) of 0.1 µg/kg body weight for this compound (<http://www.bfr.bund.de/cd/8144>). This value corresponds to a daily consumption of 300 g of fish burdened with 0.02 µg/g of PFOS. As a daily consumption of 300g of fish is fairly unlikely, PFOS levels of less than 0.02 µg/g of fish are considered tolerable.

Outlook. For 2007, the exposure pathways for men and the environment need to be evaluated further. Special consideration should be given to uptake from air, including possible precursors of perfluorocarboxylic acids. In addition, further measurements are needed in water, especially ground water, as a source of drinking water, and in soil. The EU project PERFORCE – introduced in Norman Newsletter issue No 1 (DeVoogt 2006) might contribute to this. In addition, the relevance of possible residues of PFCs in consumer products as another possible source of human exposure needs to be further clarified.

	PFOS [ng/L]	PFOA [ng/L]	Reference
Surface water			
North Sea, Elbe	0,03 – 7,3	0,2 – 6,8	Theobald et al. 2006
Rhein, Ruhr, Moehne	↔ 2,0 – 192	↔ 2,0 – 3.640	Skutlarek et al. 2006
Moehne	405	7.070	Skutlarek et al. 2006
Steinbecke	3.160	33.900	Skutlarek et al. 2006
Alz	1,7 – 14	5,1 – 56.100	Greenpeace 2006
North Atlantic, Arctic	0,01 – 0,05	0,04 – 0,1	Theobald et al. 2006
Drinking water			
North Rhine-Westphalia, several sources	↔ 0,2 - 22	↔ 0,2 - 519	Skutlarek et al. 2006
Bavaria, Emmerting	↔ 20	160	Greenpeace 2006

REFERENCES

- [1] De Voogt P (2006). *PERFORCE: Perfluorinated organic compounds in the European Environment*. NORMAN 1; 12-13.
- [2] Directive 2006/122/EC of the European Parliament and of the Council of 12 December 2006. OJ L 372/32, 27.12.2006.
- [3] Greenpeace Germany. <http://www.greenpeace.de/themen/chemie/nachrichten/>
- [4] Houde M, Bujas TAD, Small J, Wells RS, Fair PA, Bossart GD, Solomon KR, Muir DCG. (2006). *Biomagnification of Perfluoroalkyl compound in the Bottlenose Dolphin (Tursiops truncatus) Food Web*. Environ Sci Technol, 40, 4138-4144.
- [5] Skutlarek D, Exner M, Färber H (2006). *Perfluorinated Surfactants in Surface and Drinking Waters*. Environ Sci Pollut Res 13 (5) 299-307.
- [6] Theobald N, Hühnerfuss M, Caliebe C (2006): *Entwicklung und Validierung einer Methode zur Bestimmung von polyfluorierten organischen Substanzen im Meerwasser, Sedimenten und Biota. Untersuchungen zum Vorkommen dieser Schadstoffe in der Nord- und Ostsee*. UBA-Forschungsbericht, FKZ 202 22 213.
- [7] Trinkwasserkommission des Bundesministeriums für Gesundheit beim Umweltbundesamt (2006): *Vorläufige Bewertung von perfluorierten Verbindungen im Trinkwasser am Beispiel von Perfluorooctansäure (PFOA) und Perfluorsulfonsäure (PFOS)*. <http://www.umweltbundesamt.de/uba-info-presse/hintergrund/pft-im-trinkwasser.pdf>

REVIEWED BY:

Christoph SCHULTE
 UBA - German Federal Environment Agency, Dessau
 Christoph.Schulte@uba.de

Ecotoxicological effects of pharmaceuticals in aquatic organisms

It is now recognised that pharmaceutical compounds are widespread pollutants of the aquatic environment. Several studies have focused on their occurrence in wastewater and freshwater and on their toxicity toward aquatic non-target organisms (algae, invertebrates and fishes). The article by Fent et al. gives a historical perspective and an extensive review of available data on and knowledge of pharmaceuticals. It can be summarised under three main headings:

- occurrence in the environment ;
- modes of action in vertebrates and possible linkage with effects on aquatic organisms ;
- ecotoxicological effects.

On occurrence in the environment, Fent gives a detailed overview of concentration ranges of pharmaceuticals in wastewaters and surface waters. About 35 pharmaceuticals (covering several therapeutic classes) were detected in several countries in concentrations ranging from ng/l up to 10 µg/l in wastewaters and from the ng/l up to µg/l in surface waters. Non-steroidal anti-inflammatory compounds generally show the highest concentrations. Moreover, a few studies report the occurrence of pharmaceuticals in drinking waters, groundwaters and landfill leachates in the ng/l range.

The paper then reviews modes of action of pharmaceuticals in mammals. Pharmaceuticals, unlike other pollutants such as PAHs or pesticides, are molecules designed to exert a specific mode of action with a limited toxicity. Consequently, it makes sense to review available pharmacological and toxicological data before investigating for ecotoxicity in aquatic organisms: as extensive metabolic and toxicological studies are central to the discovery and development of drugs, this can provide valuable information to guide ecotoxicological studies. Fent's article reports that for non-mammalian animals displaying similar receptors to those in mammals, similar biological effects or adverse reactions may occur. However, Fent also notices that unexpected chronic effects may occur in lower organisms due to biological differences in pharmacodynamics and physiology: this is the case with serotonergic antidepressants (SSRIs), which can interfere with development and reproduction in invertebrates, as serotonin may have an important influence on such functions in lower invertebrates (but not in mammals).

Ecotoxicity of pharmaceuticals is then extensively reviewed and criticised. Ecotoxicological data are limited in terms of compounds tested (about 30 compounds), but also in terms of tested species, with only a few studies reporting toxicity in fish. Acute and chronic data are then evaluated. Considering acute effects on tested compounds, only fluoxetine and propranolol show toxicity values equal to or less than mg/l. Only about 20% of the tested compounds display acute toxicity values below 100 mg/l. Such results lead to the conclusion that acute risk represented by pharmaceuticals is negligible. Available acute data are of limited use for several reasons: first, such data are not representative of a specific mechanism of action for pharmaceuticals; second, data variability is high, even for same species and compounds.

Chronic ecotoxicological data are also lacking: only a few compounds have been tested for toxicity toward aquatic organisms. Antibiotic

present high toxicity toward blue-green algae but not toward green algae or other species from other trophic levels. Non-steroidal anti-inflammatory drugs exhibit limited toxicity in invertebrates, but at LOEC 1 and 5 µg/l, diclofenac induces renal lesions and alterations in the gills of rainbow trout. Data on blood lipid lowering agents are scarce and only a few values are reported, with NOEC in the range of 100 µg/l for invertebrates. SSRIs appear to be the most toxic compounds on algae and invertebrates and affect reproduction of invertebrates. The Beta-blocker propranolol is also one of the most toxic compounds, with NOEC for reproduction in aquatic invertebrates in the range of 100 ng/l.

Indeed, what holds one's attention is that chronic studies mainly focus on standardised endpoints (algal growth, cladoceran reproduction...) performed according to established guidelines. However, it is not obvious that current tests and organisms are the most suitable for investigating pharmaceuticals toxicity. Moreover, only very few studies address the question of mixtures of compounds, which is one of the main environmental issues with pharmaceuticals. Finally, the article stresses that current standardised tests are not sufficient for deriving an accurate risk assessment for pharmaceuticals. Therefore, even if (for most of the tested pharmaceuticals) effective concentrations for standardised endpoints are slightly higher than measured environmental concentrations, other investigations are required in order to provide a better assessment of the risk posed by pharmaceuticals.

As a future direction for investigating pharmaceuticals toxicity, the use of in vitro systems should be helpful for elucidating mechanisms of toxicity. A mechanism-based approach focused on target molecules should be more accurate when investigating for ecotoxicity. To conclude, the author suggests that analysis of pharmaceuticals should be directed at:

- “the search for specific and identical targets (target specificity)” ;
- “known adverse side effects in human and mammals (side effect specificity)” ;
- “general chronic effects for accounting physiological differences (species specificity)”.

Assessing for these three points may help to provide a better understanding of pharmaceuticals. To this extent, resorting to toxicological data constructed during development of the drug should be useful.

NB: The article of Fent et al. only deals with the ecotoxicological aspects of pharmaceuticals. However it should be noted that the human health-care side has to be taken into account when considering pharmaceutical compounds. If the environmental risk has to be assessed by environmentalists, implications and management of this risk have to be discussed with the various health-care players. The EMEA (European Medicine Evaluation Agency) guideline on the environmental assessment of human medicinal products states (according to Article 8(3) of Directive 2001/83/EC) that the environmental impact “should not constitute a criterion for refusal of a marketing authorisation” ; but it also states that when “the possibility of environmental risks cannot be excluded”, precautionary and safety measures should be taken in order to minimise the quantity discharged into the environment.

SOURCE:

K. Fent, A.A. Weston et al. *Ecotoxicology of human pharmaceuticals*. *Aquatic Toxicology* 76(2) [2006]: 122-159.

REVIEWED BY:

Jean-Philippe BESSE

CEMAGREF - Centre national du machinisme agricole, du génie rural, des eaux et des forêts, Lyon
besse@lyon.cemagref.fr

Determination of pharmaceuticals of various therapeutic classes in hospital effluent wastewaters

This article describes a methodology for the determination of pharmaceutical residues in hospital sewage water. Sixteen substances representing different therapeutic classes with a wide variety of chemical properties were selected as targets for the analysis. The challenge in this work was the determination of acids, bases and neutrals following a single isolation and enrichment step, using Oasis HLB adsorbent. For the determination, the authors used HPLC/ESI-MSMS, with a triple-quadrupole instrument in the MRM-mode. Two chromatographic runs were applied per sample, one in each ionisation mode, positive and negative, respectively. For all analytes, except for two in the negative ion mode (acetaminophen and ibuprofen), two ion transitions were recorded, one for detection and quantification, and one for verification. ^{13}C -phenacetin and 2-4-Dd were used as surrogate standards. Different gradients were applied for the two ion modes.

All the relevant performance criteria of the method are reported, e.g. recovery, linearity, instrumental detection limits (IDL), method detection and quantification limits (MDL and MQL). Other investigators may profit from the different experiments described in this work, e.g. the investigation of the extraction efficiency at different pH. This reviewer appreciates specifically the fact that ion suppression was demonstrated quite convincingly, as were ways to handle this problem.

The described methodology was applied to wastewater samples from the main sewer of a small hospital (75 beds). Mean concentrations ($n=6$) of twelve of the sixteen pharmaceuticals were in the range 0.02-19 $\mu\text{g}/\text{l}$, which is higher than what is usually measured in municipal waste waters. Ibuprofen was detected at the highest concentration, 150 $\mu\text{g}/\text{l}$. Thus, hospital effluents were suggested as important contributors to environmental concentrations of pharmaceutical residues.

SOURCE:

M.J. Gomez, M. Petrovic et al. *Determination of pharmaceuticals of various therapeutic classes by solid-phase extraction and liquid chromatography-tandem mass spectrometry analysis in hospital effluent wastewaters*. *Journal of Chromatography A* 1114(2) [2006]: 224-233.

REVIEWED BY:

Tomas ALSBERG

ITM - Institute of Applied Environmental Research, Stockholm University, Stockholm
tomas.alsberg@itm.su.se

Review of semi-automated determination of pesticides in water using solid phase extraction disks and gas chromatography-mass spectrometry

For this paper, Leandro applied the SPE disk technique to analysis of c. 100 pesticides in drinking water, in compliance with the EU regulatory value of 0.1 $\mu\text{g}/\text{L}$. The experimental work has been designed using C18 sorbent material and GC/MS analysis. As these are the most commonly used in routine laboratories, the described methodology can be regarded as directly usable for regulatory purposes.

This application of the SPE disk technique to pesticides analysis is of particular interest to reference laboratories, as little has been published on it so far. The major inputs, compared to cartridge-packed material, are:

- a very small particle size, providing a higher specific surface ;
- a larger cross-sectional area for a reduced height, allowing higher flow rates and larger sample volume, and eliminating the channelling effects sometimes reported with cartridges.

The studies are also of interest because of the precise evaluation of the best available extraction process using SPE disks, and of the metro-

logic evaluation of performance of the whole method. Conditioning of the SPE disk and the elution protocol were optimised. Two ways of removing the residual water in the final extract were investigated: sodium sulphate vs DryDisk. DryDisk is a PTFE membrane with pore size and thickness designed to allow solvent to pass, while the residual water is retained. Sodium sulphate was found to induce the lower losses of the spiked pesticides. Moreover, DryDisk was not efficient for the removal of water, and the authors attributed this to the high solubility of water in elution solvent mixture.

The metrologic evaluation relies on calibration curves obtained from matrix-matched standards, and on five replicates for each concentration, calibration or test sample, in the SIM GC/MS mode.

The studied pesticides (variously chlorinated, azo and phosphorus), with polarity ($\log K_{ow}$) ranging from 1.7 (metalaxyl) to 7.4 (permethrin) have satisfactorily stable recoveries (60 % to 116 %) with RDS most of the time far below 20 % @ 0.1 $\mu\text{g}/\text{L}$ in drinking water. The pesticides were all confirmed by 2 ions or more in accordance with the ISO recom-

mentations. At 0.01µg/L, 90 pesticides were confirmed. Only 10 could be screened, because of a lack of confirmation ion.

For most polar compounds, e.g. dimethoate, water solubility is too high to allow the use of C18 sorbent. Concomitantly, these pesticides give a poor response in GC/MS, and a graphitised carbon sorbent combined with LC/MS² is therefore recommended.

On the positive side, this method has a short cycle duration and a low

solvent consumption, combined with a robust, commonly available analytical protocol, compliant with the drinking water field regulation. The benefits are less clear-cut in respect of its adaptability to other types of water samples, e.g. natural and waste water, and its performance with existing or potential EQS.

Nevertheless, there is room for optimism, because the improvement brought about by the use of disks has already been proven in high-SPM-content water samples for PCDD/PCDF.

SOURCE:

C.C. Leandro, D.A. Bishop et al. *Semiautomated determination of pesticides in water using solid phase extraction disks and gas chromatography-mass spectrometry*. Journal of Agricultural and Food Chemistry 54(3) [2006]: 645-649.

REVIEWED BY:

Marie-Pierre STRUB

INERIS - Institut national de l'environnement industriel et des risques, Verneuil-en-Halatte
Marie-Pierre.Strub@ineris.fr

FURTHER READING:

- D. Barceló, S. Chiron, S. Lacorte, E. Martinez, J.S. Salau and M-C. Hennion. *Solid-phase sample preparation and stability of pesticides in water using Empore disks*. TrAC Trends in Analytical Chemistry, 13(9) [1994]: 352-361.
- M-C. Hennion. *Graphitized carbons for solid-phase extraction*. Journal of Chromatography A, 885(1-2) [2000]: 73-95.
- R. Bossi. *Analysis of polar pesticides in rainwater in Denmark by liquid chromatography-tandem mass spectrometry*. J. Chromatogr. A 957 [2002]: 27-36.
- E. Viana, M.J. Redondo, G. Font, J. Molt. *Disks versus columns in the solid-phase extraction of pesticides from water*. J. Chromatogr. A 733 [1996]: 267-274.

Extraction and clean-up strategies for the analysis of poly- and perfluoroalkyl substances in environmental matrices

The rapidly expanding field of per- and polyfluorinated alkyl substances (PFAS) research has resulted in a wide range of analytical methodologies to determine the environmental exposure to PFASs. Recently, two publications comprehensively reviewed the instrumental detection of PFAS [de Voogt et al, Villagrasa et al]. The extraction and clean-up of samples has not yet been reviewed, but is often determinant for the validity of the final result, as was apparent from the first world-wide PFASs interlaboratory study [van Leeuwen et al]. An overview of sample pretreatment, extraction and clean-up is provided below.

Due to their different polarities, the broad group of PFASs requires different extraction strategies. The ionic perfluorocarboxylic acids (PFCAs) and perfluorinated sulphonates (PFASs) require moderately polar media (Oasis WAX SPE or methanol and acetonitrile) for efficient trapping of water soluble short-chain (C₄-C₆) compounds. For longer chains, less polar or non-polar SPE phases (C₁₈ and Oasis HLB) may be applied. When an ion-pairing agent is used that decreases the polarity of the ion pair complex, a non-polar solvent (MTBE) may be used.

Non-ionic PFASs may be extracted from the matrix by non-polar media (C₁₈ SPE or hexane), but moderate polar media (Oasis HLB and Oasis

WAX SPE, a hexane-acetone mixture or acetonitrile) have also been applied for extraction of non-ionic PFASs.

Extraction of water (including wastewater). Extraction of water samples generally requires a pretreatment step in order to prevent clogging of the solid phase extraction (SPE) column. Water samples are preferentially centrifuged to separate the suspended particulate matter (SPM), because some filters have been shown to contaminate the water sample with PFASs. The choice of extraction method determines the range of compounds that can be accurately extracted from the water sample. The majority of published studies employed SPE sample enrichment, using C₁₈, Oasis-HLB and Oasis-WAX phases. Only Oasis-WAX SPE was capable of accurate extraction of short chain (C₄-C₆) PFCAs. LLE (using methyl-tert-butylether) was not capable of extracting the short chain compounds. For extension of methods to the short chain PFASs, improvements of the extraction efficiency is required. The addition of an ion pair may improve extraction efficiencies, as well as adjustment of pH or polarity modifications. The extraction of PFASs with chain lengths C₁₀ has received almost no attention. These long chain PFASs will (most likely) partition to the SPM rather than in the water phase. LLE is the method of choice for total-water extraction without preceding

separation of the liquid phase from the SPM. This method may therefore be capable of extracting long chain PFASs that are adsorbed to the SPM. The application of on-line extraction is promising for routine analysis.

Extraction of sewage sludge, sediment, soil and suspended matter. When designing extraction techniques for these matrices, electrostatic and hydrophobic interactions between PFASs and the matrix should be taken into account. Extraction techniques are all based on LSE and medium polar to polar solvents are most successful. Efficient extraction was achieved with methanol under basic conditions for C6-C14 PFCAs, whereas an acidification of the solvent reduced the yields for the short chain PFASs and PFCAs. Acetone is suitable for extraction of 8:2 fluorotelomer alcohols (FTOHs) from sediment. Finally, using an acetone-methanol mixture, pressurised liquid extraction was successfully applied for extraction of C7-C10 PFCAs from harbour sediments. More information on the binding and partitioning mechanisms for the different PFASs will aid in further development of fit-for-purpose extraction techniques for these complex matrices.

Extraction of biota. Ionic PFASs can be extracted with medium-polar to polar solvents (MTBE, methanol-water mixture or methanol). Water soluble short chain PFASs are best extracted with a polar to medium-polar solvent (mixture), whereas longer chain compounds require a less polar extraction medium. When using additional purification steps, accurate and sensitive determination of PFASs is feasible. An ion pairing agent may be used for improving extraction efficiencies. Neutral PFASs can be extracted efficiently using non- to medium-polar solvents and extraction set-ups similar to those used for classical POPs.

Extraction of air. The most commonly applied sampling technique for air samples is to concentrate a large volume of air (100-1600 m³) to a PUF/XAD column. Particulate matter is retained by glass fibre filters (GFFs). The column is extracted by medium-polar organic solvents such as methanol, petroleum ether and ethylacetate and, after concentration, the extracts are analysed by GC-MS. Care should be taken to avoid losses of the very volatile FTOHs. Very high recoveries were found for perfluorosulfonamido ethanols (FOSEs). Future work should address the losses of the highly volatile compounds as well as the high FOSE recoveries.

Clean-up strategies. Several studies have shown that matrix effects can enhance or suppress the electrospray ionisation, leading to considerable inaccuracies. Non-polar extraction solvents such as MTBE co-extract lipids from biological matrices, which may need to be removed by a suitable clean-up procedure. Current clean-up methods for biota are silica column fractionation, sulphuric acid treatment and dispersive graphitised carbon clean-up. Sediment, soils and sludge extracts have been cleaned by C18 SPE and graphitised carbon. Water can be cleaned by a simple washing step after concentration of the sample on an SPE column, although fluorinated silica is also used for clean-up of the final extract. Finally, filtration may be applied for removal of solids from the final extract. Care should be taken to avoid contamination of the extract or losses of PFASs during the clean-up procedure.

This work is based on a presentation at the Norman workshop "Chemical analysis of emerging pollutants", 27-28 November 2006, Maó, Menorca, Spain, and on a review submitted to Journal of Chromatography A.

REFERENCES:

- P. de Voogt, M. Saez. *Trac-Trends* in Analytical Chemistry 25 (2006) 326.
- M. Villagrasa, M.L. de Alda, D. Barcelo. *Analytical and Bioanalytical Chemistry* 386 (2006) 953.
- S.P.J. van Leeuwen, A. Karrman, B. Van Bavel, J. de Boer, G. Lindstrom. *Environmental Science & Technology* 40 (2006) 7854.

REVIEWED BY:

Stefan VAN LEEUWEN

IVM - Institute for Environmental Studies, Vrije Universiteit, Amsterdam
stefan.van.leeuwen@ivm.falw.vu.nl

Research projects / findings

FOOTPRINT: Functional Tools for Pesticide Risk Assessment and Management in Europe

Co-ordinator Igor DUBUS

BRGM, Orléans
<http://www.eu-footprint.org>

Pesticides are widely recognised as a major source of pollution of water resources in virtually every country where they are used and now represent a very significant threat to sustainable water quality in Europe. There is a lack of tools to support the assessment of the magnitude of the problem and the management of pesticides, and the EC

has commissioned the three-year FOOTPRINT project as part its 6th Framework Programme to support the development of EU and national policies, risk assessment and management options for pesticides. The general aim of FOOTPRINT is to develop a series of computerised tools to help assess the risk of pesticides contaminating water

resources (both surface water and groundwater) in the EU. Three separate tools will be developed, depending on the scale of operation, from the national/EU scale ('FOOT-NES') to the regional scale ('FOOT-CRS') through to the farm scale ('FOOT-FS'). All three tools will share the same underlying philosophy and background information, which means that the three tools will – for the first time – represent a truly integrated approach, from the larger scale to the smaller scale, where actions and mitigation strategies need to be implemented.



The project relies on the development of a large number of 'agro-environmental' scenarios characterising the diversity in agricultural conditions across Europe (soil, crop and climate). State-of-the-art pesticide fate models are deployed to assess the risk of a range of pesticides affecting groundwater and surface water. Interpolation routines are used to enable assessments to be performed for any pesticide, whether on the market or not, based on the development of a series of "meta-models". The approach allows robust assessments to be made for any location in Europe and allows detailed data on soils or crops to be used, where available.

The development of the three tools is optimised to meet the needs of the end-user groups at the various scales of application: EU and national policy makers, ministries and regulatory authorities at the EU/Member State level; water managers at the regional scale; and extension services and farmers at the farm scale. The first two tools are being developed as add-ons to ESRI ArcGIS while the latter one will be available as a stand-alone program and as a web portal.

The FOOT tools can be used to:

- identify zones in the landscape where contamination of water resources by pesticides is likely to occur;
- design or optimise monitoring programmes for pesticides;
- assess the risk of pesticides exceeding legal thresholds;
- evaluate the likely influence of the adoption of mitigation strategies such as changes in pesticide use or the use of buffer zones;
- support the adoption of practices more in line with the sustainable management of water quality.

The tools will be evaluated during the course of the project using a combination of field, modelling and monitoring.

For more information about FOOTPRINT, please visit the project web site at: <http://www.eu-footprint.org>. Those interested in keeping up to date with the latest project developments are invited to join the FOOTPRINT announcement list (<http://www.eu-footprint.org/keepuptodate.html>), or to contact Igor Dubus at i.dubus@brgm.fr.



Health Impacts of Long-Term Exposure to Disinfection By-Products in Drinking Water (Hiwate)

Co-ordinator Professor Mark J NIEUWENHUIJSEN

Center for Research in Environmental Epidemiology, Barcelona
<http://www.HIWATE.org>

Background

Chlorination disinfection by-products (DBPs) are formed when water is chlorinated and the organic matter in the water reacts with chlorine to form these by-products. The formation and occurrence depends on many factors, including the chlorine dose, type of treatment, pH, temperature, residence time, bromine levels (Nieuwenhuijsen et al

2000; IPCS 2000). Up to 500 different by-products have been identified (Richardson 1998). Different mixtures of by-product may exist in different locations, depending on the various factors mentioned above, making it more difficult to assess any health effects of DBPs, particularly in epidemiological studies.

The health effects of DBPs in drinking water have been a concern since DBPs were first reported in the seventies (Rook, 1974). Early studies focused on cancer outcomes, while the more recent studies have focused on reproductive outcomes (IPCS 2000). According to the recent review by IPCS (2000): “*more studies have considered bladder cancer than any other cancer.*” The authors of the most recently reported results for bladder cancer risks caution against a simple interpretation of the observed associations. The epidemiological evidence for an increased relative risk for bladder cancer is not consistent – different risks are reported for smokers and non-smokers, for men and women, and for low and high water consumption. Risk may differ among various geographic areas because the DBP mix may be different or because other water contaminants are also present. More comprehensive water quality data must be collected or simulated to improve exposure assessments for epidemiological studies.”

Reproductive health outcomes are easier to study from an exposure point of view, because of the shorter relevant exposure period. Amongst others, birth weight, prematurity, spontaneous abortion, congenital anomalies and still birth have been the focus of these studies. Various thorough reviews have been conducted and concluded that there are still many problems to overcome and that the results are inconsistent and inconclusive (Nieuwenhuijsen et al 2000, IPCS 2000).

Relatively little research has been carried out on the composition of disinfection by-products and the levels of disinfection by-products in relation to adverse birth outcomes and cancer in Europe, and therefore a large project was needed.

The HIWATE project

The overall aim is to investigate potential human health risks (e.g. cancer, premature births, small for gestational age, semen quality, still birth, congenital anomalies) associated with long-term exposure to low levels of disinfectants (such as chlorine) and disinfectant by-products (DBPs) occurring in water for human consumption and use in the food industry. The study will comprise risk/benefit analyses including quantitative assessments of risk associated with microbial contamination of drinking water versus chemical risk, and will compare alternative treatment options. The outcome will be improved risk assessment/management. The study will make use of existing studies/databases and newly collected information.

As part of the project, we will determine the disinfection by-product (DBP) composition, levels and determinants in drinking water in various regions in Europe. Representative water samples will be collected in the regions where the epidemiological studies are carried out and in other regions, to give a wider picture on their presence and levels. Samples will be analysed for trihalomethanes (THM) (including chloroform, bromodichloromethane, chlorodibromomethane and bromoform), haloacetonitriles (HANs) (including chloroacetonitrile, dichloroacetonitrile, trichloroacetonitrile, bromoacetonitrile, dibromoacetonitrile, tribromoacetonitrile, chlorobromoacetonitrile, dichlorobromoacetonitrile and dibromochloroacetonitrile), haloacetic acids (HAAs) (including chloroacetic acid, dichloroacetic acid, trichloroacetic acid, dibromoacetic acid, tribromoacetic acid, dibromochloroacetic acid, chlorobromoacetic acid, dichlorobromoacetic acid), haloacetones (HAKs) (including 1,1-dichloropropanone, 1,3-dichloropropanone, 1,1,1-trichloropropanone), MX, chlorate hydrate (CH), chloropicrin (CP), bromate, chlorite and chlorate, depending on the type of water disinfectant treatment used.

cetic acid, tribromoacetic acid, dibromochloroacetic acid, chlorobromoacetic acid, bromoacetic acid, dichlorobromoacetic acid), haloacetones (HAKs) (including 1,1-dichloropropanone, 1,3-dichloropropanone, 1,1,1-trichloropropanone), MX, chlorate hydrate (CH), chloropicrin (CP), bromate, chlorite and chlorate, depending on the type of water disinfectant treatment used.

We will assess the risk of reproductive effects in relation to disinfection practices and levels of disinfection by-products, and conduct epidemiological studies to examine the relationship between DBPs and the following outcomes:

- congenital anomalies, including neural tube, major heart, major stomach wall, and urinary tract defects, cleft palate/lip and still birth, in an intervention study and a large nation wide cross-sectional study, using registry data in the UK, where mainly chlorination is used as a disinfectant ;
- congenital anomalies, including neural tube, major heart and urinary tract defects, using registry data in Italy in regions where mainly chlorine dioxide is used as a disinfectant ;
- small for gestational age and premature birth in birth cohorts in Spain, Greece, France and Lithuania, where a range of treatments are used. We will also examine gene-environment interactions (e.g. CYP2E1, GSTT1) in these populations ;
- semen quality, using a case control design in the UK, where mainly chlorination is used for water disinfection.

We will assess the risk of cancer, particularly bladder cancer and colon cancer, in relation to disinfection by-product practices and disinfection by-products levels, including the examination of any gene-environment interactions (e.g. CYP2E1, GSTT1). The study will obtain risk estimates from existing bladder case control cancer studies in Spain, France and Finland. Epidemiological studies will be conducted, using a case control design to examine the relationship between DBPs and colon cancer in Spain and Italy.

We will conduct risk/benefit analyses including quantitative assessments of risk associated with microbial contamination of drinking water versus chemical risk, compare alternative treatment options, and produce burden of disease estimates (e.g. DALYs). And we will organise a workshop in 2009 to bring together scientists working on environmental, toxicological, epidemiological and policy aspects of chlorination DBPs, microbiologists, policy makers, and representatives from the water industry and consumer organisations in Europe to develop guidelines for policy across Europe and the future research agenda.

We encourage collaboration with groups not involved in the consortium and welcome data on disinfection by-products and their determinants in drinking water in Europe.

The work is conducted by 14 groups in 8 countries and started on November 1 2006. Further information can be obtained from the project website (www.HIWATE.org) or by contacting the project co-ordinator, Professor Mark J Nieuwenhuijsen (mnieuwenhuijsen@imim.es).

REFERENCES

- IPCS. *Disinfectants and disinfectant by-products*. Environmental Health Criteria 216, WHO, Geneva, 2000
- Nieuwenhuijsen MJ, Toledano MB, Eaton NE, Elliott P and Fawell J (2000) *Chlorination disinfection by-products in water and their association with adverse reproductive outcomes: a review*. *Occup Environ Med* 57: 73-85.
- Richardson S. *Drinking water disinfection by-products*. In: *Encyclopedia of environmental analysis and remediation*, John Wiley & Sons, Inc, ISBN 0-471-11708-0, 1998
- Rook JJ (1974). *Formation of haloforms during the chlorination of natural water*. *Water Treat Exam* 23: 234-243.

KNAPPE: Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters

Co-ordinator Benoît ROIG

Centre for Industrial Environmental Research, École des Mines d'Alès, France
<http://www.knappe-eu.org>

There is an increasing need to monitor water quality across Europe. Pharmaceutical products (PPs), as emerging contaminants, should receive particular attention. There are, currently, no regulations or norms to limit their use, nor are there any types of survey or control to prevent exposure. According to European guidelines, predicted environmental concentrations (PECs) of PPs in water must be equal to or more than 0.01 µg/L before further environmental risk assessment (ERA) is necessary [1]. Some PPs and their metabolites are not removed from water during conventional biological treatment and enter the water supply via wastewater treatment plants (WWTPs) [2]. These compounds can be biologically active even at environmental concentrations (sub-ng/L to ng/L) [3] and could therefore be harmful to aquatic species. Their persistence is of particular importance, because it increases the risk of long-term exposure which could be responsible for chronic toxicity and subtle effects in animals and plants (endocrine disruption, growth inhibition, disruption of microbial ecosystems, cytotoxicity, mutagenicity, teratogenicity...). Spatial and temporal variations of the chemicals in water also make PEC determination difficult and uncertain. In recent years, research and studies on PPs in the environment have increased; the research has, however, been fragmentary, dealing with only part of the issue (occurrence, treatment, fate, or toxicity), resulting in weak connections between the different data. To improve environmental impact assessment there is, therefore, a need to take into account the whole life-cycle of PPs.

In this context, the KNAPPE project proposes to carry out a review of the state of knowledge and put emphasis on questions deserving attention by pulling together results of previous and on-going EU projects and published data from both governmental sources and scientific literature, by involving manufacturers in supplying data on production and use of pharmaceuticals. These topics of concern include occurrence, detection, fate, behaviour, removal treatments, known environmental and health impacts of these molecules and stewardship approaches. On the basis of these data, the final objective of the project is to identify the relevant priority actions to be taken in the framework of sustainable development, more particularly in terms of lowering the presence, impacts and risk of PPs in the environment. KNAPPE will, in particular:

1. help to establish potential "traceability" of PPs in the aquatic environment and produce indicators supporting water managers, health authorities and persons involved in river basin management plans and strategies to minimise discharge of PPs in the environment ;
2. investigate the elimination efficiency of treatment processes (sewage treatment, drinking water production, specific industrial

processes). The project will suggest different strategies for PPs treatment, identifying necessary enhancements to meet future requirements (suggestions for treatment at source, or restrictions on use) and assessing cost-effective adaptations (or modification) to current treatment plants ;

3. present an overview of the eco-toxicological significance and health impacts of PPs and identify needs for developing complementary data/approaches to prioritise PPs (chemical by chemical, class by class or mode of action basis) ;
4. assess regulatory approaches at European level and existing legislation and instruments on the discharge of PPs, and carry out a gap assessment. KNAPPE will develop cornerstones for supporting the aims of WFD by highlighting opportunities arising from various instruments and measures for European preventive action ;
5. propose recommendations for environmental stewardship (pollution prevention and monitoring) integrating green technology and vigilance scheme, and develop a document aimed at all stakeholders ;
6. hold several international events (stakeholder workshops, scientific conferences) involving regulators, scientists, doctors, industry... in which discussions and exchange will take place ;
7. disseminate its recommendations and main findings throughout Europe, notably by making them available to the public on a web site and by publishing them in scientific journals, as well as by giving presentations to the scientific community and decision-makers. A CD Rom compiling all the results will be generated and distributed as widely as possible.

The KNAPPE project is a Specific Support Action (18 months' duration from 1 February 2007), funded by the European Commission. It involves 9 partners:

- Armines-Alès (FR), co-ordinator ;
- Bureau de Recherches Géologiques et Minières - BRGM (FR),
- Agricultural and Environmental Engineering Research Institute - CEMAGREF (FR) ;
- University of Portsmouth (UK) ;
- University of York (UK) ;
- Consejo Superior de Investigaciones Científicas - CSIC (ES) ;
- Federal Institute of Hydrology - BfG, Ecologic (DE) ;
- Politechnika Slaska (PL).

A range of stakeholders, including representatives of the pharmaceutical industry (EFPIA, SCI) and regulators (EPA) will be also involved in the project.

REFERENCES

- [1] EMEA (2006). The European Agency for the Evaluation of Medicinal Products (EMEA), London
- [2] Jones OAH, Voulvoulis N, Lester JN (2005). *Crit Rev Environ Sci Technol* 35: 401-427
- [3] Kummerer K (ed) (2004). *Pharmaceuticals in the environment: sources, fate, effects and risks*. Springer, Berlin, Germany

Towards Risk Based Management of European River Basins (EC FP6 CA RISKBASE)

Co-ordinator Jos BRILS
TNO, The Netherlands
<http://www.riskbase.info>



Introduction

In RISKBASE, leading European scientists and representatives of major European stakeholder groups will review and synthesise the outcome of EC RTD Framework Programme projects, and other major initiatives related to integrated risk assessment-based management of the water/sediment/soil system at the river-basin scale. The synthesis will lead to the development of integrated risk assessment-based management approaches, enabling the prevention and/or reduction of the negative impacts caused by human activities on that system.

Deliverables

1) An overarching concept, generic approach and guiding principles to integrated risk-based management of river basins, 2) Recommendations towards evolution and implementation of risk-based management in national and community policies and towards implementation in management, and 3) A proposal for the European research agenda related to risk-based management.

Working modus

Based upon ample experience in previous EC Coordination Actions (CA), Thematic Networks and/or Accompanying Measures, a simple project structure has been chosen (see Figure 1), with only a minimum number of Work Packages (WP). Each WP will be managed by one WP-leader, supported by a few other partners (contractors) in the project. The WPs will organise several workshops dedicated to specific issues related to risk-based management at the river-basin scale. Furthermore, RISKBASE will annually organise a General Assembly (GA) and will make use of EUGRIS as a web-based information exchange structure. The workshops, GA and the website will be open to all who are interested and willing to contribute to achieve the RISKBASE goals and objectives. The first GA was held in Seville on January 25 & 26th, 2007. A background document to the GA was the RISKBASE Strategy Paper, to be seen as an evolving document that is made publicly available through the RISKBASE website.

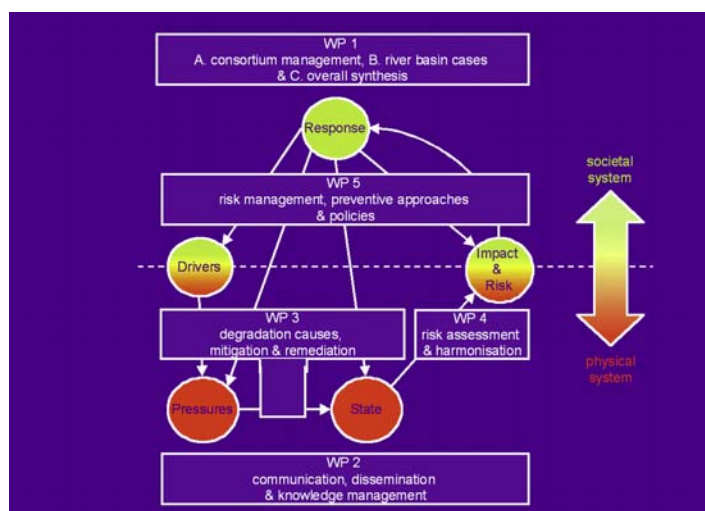


Figure 1: RISKBASE project structure.

Furthermore, during the project, each WP will select core-team members to assist the WP-leader in reviewing, synthesising and then reporting the outcome of WP-workshops. Thus an open, transparent and flexible structure has been created, ensuring the integration of

all essential knowledge, expertise and experience in order to make RISKBASE a success.

Project duration:

36 months (start: 1 September 2006; end: 31 August 2009)

Topic addressed:

RISKBASE (Contract No. 036938 GOCE) addresses Topic II.2.1 "Integrated risk-based management of the water-sediment-soil system at river-basin scale". This is a topic under the thematic sub-priority area "Global Change and Ecosystems" in the 4th FP6 call for proposals, call identifier: FP6-2005-Global-4.

RISKBASE contractors



Jos Brils

jos.brils@tno.nl
TNO, The Netherlands
Coordinator & lead WP1

Damia Barcelo

dbcqam@cid.csic.es
CSIC, Spain
Lead WP1b

Thomas Track

track@dechema.de
Dechema, Germany
Lead WP2

Winfried Blum

herma.exner@boku.ac.at
BOKU, Austria
WP1c core team

Philippe Negrel

p.negrel@brgm.fr
BRGM, France
Lead WP3

Wim Salomons

wim.salomons@home.nl
IVM, The Netherlands
WP1c core team

Werner Brack

werner.brack@ufz.de
UFZ, Germany
Lead WP4

Joop Vegter

joopvegter@mac.com
Vegter Advice, The Netherlands
WP1c core team

Dietmar Müller

dietmar.mueller@umwelt.bundesamt.at
UBA, Austria
Lead WP5

Vala Ragnarsdottir

vala.ragnarsdottir@bristol.ac.uk
University of Bristol, United Kingdom
WP1c core team

The activities of the NORMAN project started officially on 1st September 2005, with a kick-off meeting in Paris on 7-8 September 2005. The project is in its starting phase: we are laying the foundations on which to build the services that will be provided by the network. The ultimate aim is to meet users' needs in the exchange and production of good-quality and comparable data in a field where data are typically scarce and insufficient for sound decision-making. Below is a summary of the activities carried out so far and forthcoming results. More information on each of these activities is provided on the project website (www.norman-network.net).

NORMAN CONTACT POINTS

As you will see from the website, the list of NORMAN Contact Points continues to grow. Organisations and experts in various countries from Eastern Europe (Czech Republic, Hungary and Ukraine) were appointed last summer. More recently, Contact Points for Austria, Denmark, Italy, Sweden and Slovenia have been added.

Contact Points have a vital role to play in seeking out monitoring programmes, studies and research initiatives in the field of emerging pollutants in their home country, and then feeding that information into NORMAN, where it will be included in the EMPODAT database and in a dedicated 'library' on the NORMAN website for this type of report (accompanied by a short summary and contact details for further information). Contact Points add real value here, because it can be very difficult for people outside the country to access information which appears in the so-called 'grey literature'.

EXCHANGE OF INFORMATION – WORKSHOP ON “CHEMICAL ANALYSIS OF EMERGING POLLUTANTS” (MENORCA, SPAIN – 27-28 NOVEMBER 2006)

The first thematic NORMAN workshop, focusing on the analytical challenges for the measurement of emerging pollutants, was organised by CSIC - Consejo Superior de Investigaciones Científicas - of Barcelona, Spain and took place in the Institut Menorquí d'Estudis (IME) in Maó, Menorca, Spain on 27-28 November 2006. This successful event included sessions on: EU research on emerging contaminants; Polar pesticides; Pharmaceuticals; Halogenated emerging contaminants; Other emerging contaminants and Degradation & bioavailability of emerging contaminants, with a total of 20 keynote lectures and 22 posters.



NORMAN thematic workshop, Menorca, 27-28 November 2006.

The next thematic workshop will focus on “New tools for bio-monitoring of emerging pollutants”. It will be organised in Autumn 2007 by IVM Vrije Universiteit. Further information will soon be published on the website.

NORMAN DATABASES

The EMPOMAP database is now publicly available on the NORMAN website. It is soon expected to become an indispensable tool for all experts, institutes and projects involved in the collection & evaluation of data / information on emerging substances in the European Union. We also welcome participants from other countries around the world. We would like to encourage all interested parties to consider spending a little time to register and become a 'visible' member of the emerging substances community.

Are you looking for synergies in your research efforts? Are you looking for partners to discuss occurrences or toxic effects of 'your' compound and, eventually, possibilities to bid together for funding for further research? We expect the database will help to answer these and other similar questions, thereby helping to advance the work of experts in various fields of emerging substances research.

Progress is also being made with the other NORMAN databases:

- EMPODAT is expected to be launched on the web in March 2007, by which time it will be fully compatible with WISE (Water Information System for Europe). Comments from potential end-users, including industry stakeholders and experts involved in projects dealing with integrated risk assessment of environmental stressors, will be included in the final version.
- EMPOMASS is expected to be ready for public use in June 2006.

QA/QC ACTIVITIES

Methods validation protocols

The three protocols for validation of methods for monitoring and bio-monitoring of emerging pollutants (each one addressing a different stage of the validation process) are now close to finalisation, and will be published on the NORMAN website in February 2007. It has been a real challenge to formulate an overarching approach towards validation that is suitable for a wide range of biological and chemical methods; but finally a sound concept has been developed that will be applicable to most methods for monitoring or bio-monitoring of emerging pollutants (or their effects) in the environment.

The protocols should be regarded as a first proposal. They are currently being tested in three case studies conducted by the NORMAN network. Furthermore, any comments and suggestions from other experts and stakeholders will be highly appreciated. Review by and feedback from a wide range of experts is essential, as one of NORMAN's ultimate aims is to get the validation protocols implemented as part of European standards.

Case studies

The work within the three case studies is progressing. For Case 1 - Oestrogens in sewage treatment effluents – the first meeting with the laboratories was organised on 11 January in London and no result is yet available.

The first rounds of the interlaboratory studies have been completed for Case 2 and Case 3.

17 laboratories from 11 European countries participated in the first round of the ring study organised within Case 2 - Non-steroidal anti-inflammatory drugs – with 13 laboratories concluding the exercise. NSAID compounds selected in this study were: ketoprofen, naproxen, ibuprofen and diclofenac. A total number of 162 samples were distributed to the 17 laboratories. The final number of results collected was 486, of which 23 values were outliers (4,7%), and were discarded (mainly associated with the fortified MilliQ water, because of the low level of concentration, and with the wastewater sample, due to the complexity of the matrix). There was a broad level of agreement between the concentrations of fortification and the mean values recorded by the participants, but the precision of some individual participants was low throughout the exercise. That means there will need to be a protocol for sample treatment in order to minimise sources of variation in the second ring. It will need to cover sample handling, how to defer the samples and for how long, etc.

