A META- AND RISK-ANALYSIS OF GLOBAL INSECTICIDE CONTAMINATION OF AGRICULTURAL SURFACE WATERS

by

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REQUIEM

The crucified planet Earth,
should it find a voice
and a sense of irony,
might now well say
of our abuse of it,
"Forgive them, Father,
They know not what they do."

The irony would be
that we know what
we are doing.

When the last living thing
has died on account of us,
how poetical it would be
if Earth could say,
in a voice floating up
perhaps
from the floor
of the Grand Canyon,
"It is done."
People did not like it here.

-- Kurt Vonnegut, *A Man Without a Country*

Overview of Publications

This cumulative dissertation is based on the following four scientific publications:

- Stehle S, Knäbel A, Schulz R (2013) Probabilistic Risk Assessment of Insecticide Concentrations in Agricultural Surface Waters: A Critical Appraisal. *Environmental Monitoring and Assessment* 185: 6295-6310.

- Stehle S, Schulz R (2015) Agricultural Insecticides Threaten Surface Waters at the Global Scale. *Proceedings of the National Academy of Sciences of the United States of America* 112: 5750-5755.

- Stehle S, Schulz R (submitted) Pesticide Regulations in the EU – Environment Unprotected? *Environmental Science and Pollution Research* (doi:10.1007/s11356-015-5148-5).

- Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS Surface Water Models Fail to Predict Insecticide Concentrations in the Field. *Environmental Science and Technology* 46: 8397-8404.

Annotation

This cumulative dissertation is based on four scientific publications written by multiple authors. For this reason, the first person plural is used throughout this thesis.

Table of Contents

List of abbreviations

a.i.	active ingredient
App	appendix
Car	carbamate
EC_{50}	median effective concentration
EFSA	European Food Safety Authority
EQS	environmental quality standard
Est	estuarine
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FIZ	Forschungs- und Informationszentrum
FOCUS	FOrum for the Co-ordination of pesticide fate models and their USe
FW	freshwater
ha	hectare
HERQ	high environmental regulatory quality
HQ	hazard quotient
K_{OC}	soil organic carbon partition coefficient
LERQ	low environmental regulatory quality
LOD	limit of detection
LOQ	limit of quantification
MIC	measured insecticide concentration
MIC_{SW}	measured insecticide concentration in the water phase
MPC	maximum permissible concentration
N	nitrogen
Neo	neonicotinoid
OC	organochlorine
OP	organophosphate
P	phosphor
PEC	predicted environmental concentration
PRZM	pesticide root zone model
Pyr	pyrethroid
RO	research objective
RTL	regulatory threshold level
RTL_{SED}	regulatory threshold level for sediment
RTL_{SW}	regulatory threshold level for the water phase
SPEAR	species at risk
t	ton
TU	toxic unit
UP	uniform principle
US EPA	United States Environmental Protection Agency
USGS	United States Geological Survey
vTfMoA	very toxic, fast mode of action

Abstract

Global crop production increased substantially in recent decades due to agricultural intensification and expansion and today agricultural areas occupy about 38% of Earth's terrestrial surface - the largest use of land on the planet. However, current high-intensity agricultural practices fostered in the context of the Green Revolution led to serious consequences for the global environment. Pesticides, in particular, are highly biologically active substances that can threaten the ecological integrity of aquatic and terrestrial ecosystems. Although the global pesticide use increases steadily, our field-data based knowledge regarding exposure of non-target ecosystems such as surface waters is very restricted. Available studies have by now been limited to spatially restricted geographical areas or had rather specific objectives rendering the extrapolation to larger spatial scales questionable.

Consequently, this thesis evaluated based on four scientific publications the exposure, effects, and regulatory implications of particularly toxic insecticides` concentrations detected in global agricultural surface waters. FOCUS exposure modelling was used to characterise the highly specific insecticide exposure patterns and to analyse the resulting implications for both monitoring and risk assessment (publication I). Based on more than 200,000 scientific database entries, 838 peer-reviewed studies finally included, and more than 2,500 sites in 73 countries, the risks of agricultural insecticides to global surface waters were analysed by means of a comprehensive meta-analysis (publication II). This meta-analysis evaluated whether insecticide field concentrations exceed legally accepted regulatory threshold levels (RTLs) derived from official EU and US pesticide registration documents and, amongst others, how risks depend on insecticide development over time and stringency of environmental regulation. In addition, an in-depth analysis of the current EU pesticide regulations provided insights into the level of protection and field relevance of highly elaborated environmental regulatory risk assessment schemes (publications III and IV).

The results of this thesis show that insecticide surface water exposure is characterized by infrequent and highly transient concentration peaks of high ecotoxicological relevance. We thus argue in publication I that sampling based on regular intervals is inadequate for the detection of insecticide surface water concentrations and that traditional risk assessment concepts based on all insecticide concentrations including non-detects lead to severely biased results and critical underestimations of risks. Based on these considerations, publication II demonstrates that out of 11,300 measured insecticide concentrations (MICs; i.e., those actually detected and quantified), 52.4% (5,915 cases; 68.5%) exceeded the RTL for either water (RTL_{SW}) or sediments. This indicates a substantial risk for the biological integrity of global water resources as additional analyses on pesticide effects in the field clearly evidence that the regional aquatic biodiversity is reduced by approximately 30% at pesticide concentrations equalling the RTLs. In addition, publication II shows that there is a complete lack of scientific monitoring data for ~90% of global cropland and that both the actual insecticide contamination of surface waters and the resulting ecological risks are most likely even greater due to, for example, inadequate sampling methods employed in the studies and the common occurrence of pesticide mixtures. A linear model analysis identified that RTL_{SW} exceedances depend on the catchment size, sampling regime, sampling date, insecticide substance class, and stringency of countries` environmental regulations, as well as on the interactions of these factors. Importantly, the risks are significantly higher for newer-generation insecticides (i.e., pyrethroids) and are high even in countries with stringent environmental regulations. Regarding the latter, an analysis of the EU pesticide regulations revealed critical deficiencies and the lack of protectiveness and field-relevance for current presumed highly elaborated FOCUS exposure assessment (publication IV) and overall risk assessment schemes (publication III). Based on these findings, essential risk assessment amendments are proposed.

In essence, this thesis analyses the agriculture–environment linkages for pesticides at the global scale and it thereby contributes to a new research frontier in global ecotoxicology. The overall findings substantiate that agricultural insecticides are potential key drivers for the global freshwater biodiversity crisis and that the current regulatory risk assessment approaches for highly toxic anthropogenic chemicals fail to protect the global environment. This thesis provides an integrated view on the environmental side effects of global high-intensity agriculture and alerts that beside worldwide improvements to current pesticide regulations and agricultural pesticide application practices, the fundamental reformation of conventional agricultural systems is urgently needed to meet the twin challenges of providing sufficient food for a growing human population without destroying the ecological integrity of global ecosystems essential to human existence.

1 Introduction

1.1 Pesticide use in global agriculture

At present, 15.3 x 10^6 km^2 are under cultivation worldwide designating together with 34 x 10^6 km^2 of pasture and rangeland agriculture as the worlds largest terrestrial biome (Foley et al. 2011; Fig. 1). Agricultural expansion and intensification enabled world grain harvest to more than double in the past five decades (Alston et al. 2009), with the vast majority of this productivity increase resulting from Green Revolution technologies, including high-yield crop varieties, chemical fertilizers, pesticides, irrigation and mechanization (Foley et al. 2005; Matson et al. 1997). Although modern high-intensity agriculture has thus been successful in increasing the global per capita food supply, this was accompanied by a ~638% rise in nitrogenous fertilizer use, a 97% increase in irrigated cropland area, and a 854% augmentation of pesticide production between 1961 and 1999 (Green et al. 2005). Pesticides became a key element of pest management within global agriculture and today represent an annual €40 billion market worldwide (Reuters 2008). By 2050, the global pesticide production is forecasted by Tilman et al. (2001) to be 2.7 times the amount determined for 2000 (which was 2,427,173 t active ingredient [a.i.] [Kiely et al. 2004]), as a result of the increasing human population (Tilman et al. 2002), expansion of energy crop farming (Ruth 2008), resistance (Denholm et al. 2002), and predicted climate change (Kiers et al. 2008; Kattwinkel et al. 2011). In addition, a recent FAO update (FAO 2014) reports more than 800 Million people suffering malnutrition in 2014, which, amongst other measures, indicates the urgent need for a further increase in global agricultural productivity, i.e. by effective pre- and post-harvest crop loss mitigation measures. Oerke (2006) estimated that without crop protection measures, the global potential losses due to weeds, pathogens and animal pests reaches 80% for individual crops. Within this context, Schreinemachers and Tipraqsa (2012) calculated that an increase of 1.8% in pesticide use results in a 1% increase in crop output per hectare. In addition, Pimentel (2005) states that pesticide use in US agriculture returns about $4 per $1 invested for pest control; these figures clearly illustrate the benefits and economic incentives for pesticide use in global conventional farming environments. Considering a broader perspective, a recent meta-analysis based on global data (Seufert et al. 2012) reported that although the yield performance of organic farming systems is overall 25% lower compared to conventional farming systems, these yield differences are highly contextual and organic systems can under certain conditions (e.g., application of good management practices, particular crop types and agroecological conditions) rival those of conventional agriculture. However, more research is needed to fully understand the factors including the restriction of pesticide use limiting organic yields in global food production systems.

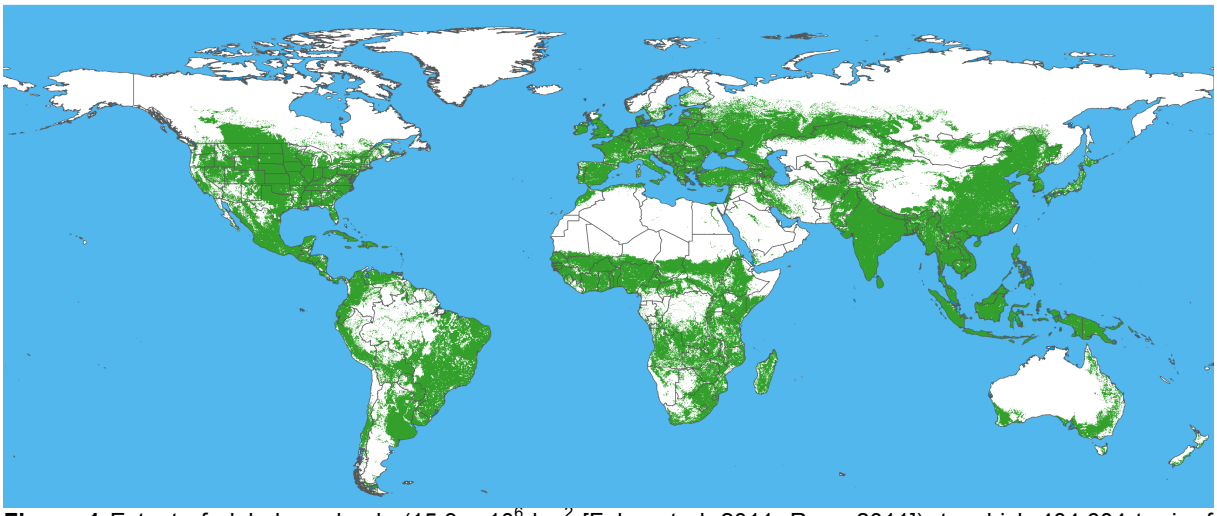

Figure 1 Extent of global croplands (15.3 x 10^6 km^2 [Foley et al. 2011; Rapp 2011]), to which 404,604 t a.i. of insecticides were applied in the year 2007 (Fishel 2013a).

Insecticides as a group of pesticides that combine extremely high ecotoxicity potentials with low application rates (Schulz 2004; Devine and Furlong 2007) account for 28% of the global crop protection market, with 404,604 t a.i. equalling a total worth of 11.2 billion US $ applied in 2007 to agricultural areas globally (Fishel 2013a). Especially large-scale monocultures typical for current high-intensity agronomic systems in many parts of the world substantially increase insect pest pressure and thus the need for insecticide use (Meehan et al. 2011). However, during the last 60 years, insect resistance management (Denholm et al. 2002), regulatory restrictions (Werner and Hitzfeld 2012), and general agrochemical market growth (Lamberth et al. 2013) led to the evolution of four major insecticide classes with different mode of actions and dates of market introduction (Table 1). Generally, the research and development of the more recent insecticide classes, such as pyrethroids and neonicotinoids, have focused on higher selectivities and greater intrinsic insecticidal activities towards targeted pests, which resulted in noticeable application rate reductions over the last decades; the use rates of modern insecticides can be as low as 10 g/ha, i.e., only 1% of that of older compound classes such as organochlorine insecticides (Devine and Furlong 2007; Lamberth et al. 2013). It is generally perceived by regulators (Fishel 2013b), industry (ECPA 2013) and the scientific community (Devine and Furlong 2007; Lamberth et al. 2013) that the development and application of newer insecticide classes such as pyrethroids and neonicotinoids, which are partly classified by the US EPA as “reduced risks” pesticides (Fishel 2013b; US EPA 2015a), led to substantial reductions of environmental impacts and concomitantly to reduced risks for non-target surface waters. However, considering that no insecticide class has been introduced to the market since 25 years (Table 1) and the increasing environmental concerns and regulatory restrictions neonicotinoids face (e.g., Hallmann et al. 2014; European Commission 2013a; Stokstad 2013; Sanchez-Bayo 2014), a comparative evaluation of the environmental risks of the other insecticide classes and specifically pyrethroids, which may gain in importance due to unmanaged risks of neonicotinoids, is crucial.

Table 1 Market introduction (Denholm et al. 2002; Elbert et al. 2008), development of insecticide market shares (Jeschke et al. 2011), and mode of action (Yu 2008) for major insecticide classes. Table taken from *Appendix II*.

Insecticide class	Introduction to the market	Insecticide market share (%) 1990 / 2008	Mode of action
Organochlorines	1940	- / -	GABA-gated chloride channel antagonists
Organophosphates/Carbamates	1950/1962	59 / 24.4	Acetylcholinesterase inhibitors
Pyrethroids	1973	18 / 15.5	Sodium channel modulators
Neonicotinoids	1991	0 / 23.7	Nicotinic acetylcholine receptor agonists

1.2 Regulatory pesticide risk assessment

1.2.1 Environmental risk assessment and management of pesticides

Pesticides as highly biologically active substance intentionally applied in large quantities to the environment pose risks to aquatic and terrestrial non-target ecosystems worldwide. In order to control these risks associated with agricultural pesticide use, elaborate regulatory and legally manifested environmental risk assessment procedures have been enforced (European Commission 2009; FIFRA 1947). The registration process, which is mandatory for a pesticide to gain authorisation, lasts several years and costs approximately US$ 25 million per compound (ECPA 2012), designating pesticides among the most intensively tested and regulated chemicals (ECPA 2003).

Within the environmental risk assessment for pesticides, an exposure estimation is combined with an effect characterisation to ensure that pesticide application does not lead to unacceptable ecological effects in the non-target environment (European Commission 2009; FIFRA 1947). Generally, the regulatory risk assessment of pesticides is based on a single substance toxicity assessment concept (i.e., mixture toxicity is not considered) and it follows a tiered approach, where higher tiers are considered to be less conservative but more complex and realistic than lower tiers (EFSA 2013). The pesticide exposure assessment requires aquatic exposure data that must be predicted using exposure models because the compounds under assessment are usually not yet on the market (EFSA 2013; US EPA 2015b). These exposure predictions are conducted using realistic worst-case assumptions regarding the determining variables, resulting in Predicted Environmental Concentrations (PEC) of pesticides in surface waters (Adriaanse et al. 1997; FOCUS 2001). Based on different steps reflecting different levels of protection and realisms, the FOrum for the Co-ordination of pesticide fate models and their USe (FOCUS) modelling approach (FOCUS 2001) is used in the European regulatory risk assessment to determine PECs that are intended to reflect pesticide surface water exposure under (realistic) worst-case conditions. FOCUS step 1 is based on very simple assumptions and accounts for extreme worst-case pesticide loadings without considering specific additional information such as crop type or climate (FOCUS 2001). In contrast, FOCUS steps 3 and 4, which are often crucial for final pesticide authorisation (Knäbel et al. 2012), are based on 10 realistic worst-case scenarios that consider site-specific environmental parameters (e.g., soil type, slopes, climatic conditions), different types of water bodies (i.e., ditch, stream, pond), as well as risk mitigation options with different levels of complexity (e.g., no-spray buffer zones) (FOCUS 2001; Knäbel et al. 2012). These higher-tier FOCUS steps use mechanistic models to consider all major nonpoint source exposure pathways (i.e.

leaching via drainage, surface runoff, and spray drift) (FOCUS 2001; Reichenberger et al. 2007; EFSA 2013) as well as fate and transport processes in the respective water bodies.

In parallel to the exposure assessment, a pesticide effect characterisation is derived from laboratory and semi-field model ecosystem experiments (micro- or mesocosms) using various aquatic organisms. In order to address uncertainties in the effect characterisation, safety factors are used, i.e., the lowest relevant observed toxicity value from a given ecotoxicological test is divided by a factor between 1 and 100 in order to derive the maximum environmental concentration level that is assumed to be ecologically acceptable (referred to here as Regulatory Threshold Level [RTL] and termed Regulatory Acceptable Concentration in the EU). Comparisons of modelled exposure data (i.e., PEC) and measured effect data including safety factors (i.e., RTL) then indicate either an acceptable environmental risk or the need for specific risk mitigation measures (e.g., no-spray field margins close to surface waters) that become part of the registration procedure as legally binding pesticide label amendments for the farmers (De Snoo 2003; Touart and Maciorowski 1997). The pesticide risk assessment procedure should ensure that pesticide field concentrations do not exceed the RTL and registration is granted only if all these requirements are met, always based on the assumption that the mitigation measures prescribed as mandatory label amendments are obeyed. In terms of pesticide legislations` overall protection goals, the EU Regulation (EC) No. 1107/2009 (European Commission 2009) claims that a high level of environmental protection is required (e.g., in article 1.1 and 4.3), which is expressed e.g., as “no unacceptable effects on the environment”, with particular regards to biodiversity, that should result from pesticide use. Concerning the US EPA pesticide regulatory risk assessment, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA 1947) states that a pesticide will only gain registration if it does not cause any “unreasonable adverse effects on the environment".

1.2.2 Regulatory threshold levels and insecticide field concentrations

In essence, RTLs denote the maximum concentration levels on whose basis individual pesticide are officially approved by regulatory authorities for usage in agriculture, after considering all aspects of exposure predictions, effect assessment, uncertainty, risk management obligations and cost-benefit evaluations. For insecticides in particular, the procedure for determining RTLs often accepts clear but transient effects on aquatic organisms, e.g., RTLs based on so-called “no observed ecologically adverse effect concentrations” derived from mesocosm studies (EFSA 2013), which, however, are assumed to be ecologically acceptable due to recovery of the affected populations within specific time frames (e.g., 8 weeks, see EFSA [2013] for details). Consequently, once an insecticide is registered and in use, real exposure levels in the field must ultimately not exceed the RTL in order to adhere to the protection goals outlined in pesticide legislations (European Commission 2009; FIFRA 1947) and to exclude ecologically unacceptable effects, biodiversity losses, and threats to aquatic ecosystems’ structures and functions (Schäfer et al. 2012; Beketov et al. 2013). The comparison of insecticide concentrations measured in agriculturally-influenced surface waters to RTLs enables therefore to (i) evaluate the actual protectiveness and effectiveness of pesticide legislations and prospective regulatory risk assessment schemes and (ii) assess the risks whether and to what extent insecticides threaten the biological integrity of aquatic ecosystems. This, however, has never been thoroughly

evaluated at the global scale so that the overall global picture of potential adverse effects of agricultural insecticide use on aquatic biocoenoses as well as the efficacy and protectiveness of pesticide risk assessment and management schemes are currently not known.

1.3 Exposure and effects of insecticides in surface waters

1.3.1 Insecticide exposure and traditional monitoring and risk assessment concepts

The application of pesticides in global high-intensity agricultural systems inevitable leads to exposure of non-target ecosystems such as surface waters. Edge-of-field losses of pesticides from agricultural fields to water bodies can exceed 10% of the amount applied (Wauchope 1978; Schulz 2004). Consequentially, numerous field studies (e.g., Schulz 2004; Morrissey et al. 2015; Schäfer et al. 2012) documented agriculturally-related pesticide contamination of aquatic ecosystems. Especially nonpoint-source pollution (i.e., exposure via spray drift, irrigation- or rainfall-induced runoff, and drainage, see Reichenberger et al. [2007] and Schulz [2004] for further information on these entry routes) is widely regarded as the major source of pesticide surface water exposure (Line et al. 1997; Loague et al. 1998; Schulz 2004). Thus, pesticides are generally characterized by a complex input dynamic, i.e., their release into surface waters is driven by meteorological conditions (e.g., wind, rain events) and seasonal application, which results in a discontinuous and complex exposure pattern (Götz et al. 2010; Rabiet et al. 2010; Edwards and Moore 2014). Herbicides and fungicides have relatively slow modes of action and thus must persist in the environment for longer time periods to act against their respective pests; these pesticides are therefore used at comparably high application rates with several consecutive applications per season. In contrast, insecticides often show fast modes of action (Yu 2008; except for neonicotinoids, see below) and thus do not need to persist in the environment to be effective against target organisms; this, in combination with their very high selectivities and intrinsic insecticidal activities (Schäfer et al. 2011b; Schulz 2004; Devine and Furlong 2007), leads to discrete insecticide applications at comparably low rates. Concerning exposure and associated risks for aquatic ecosystems, these low application rates, accompanied by short field half lives and high soil organic carbon partition coefficient (K_{OC}) values, results in highly temporally intermittent insecticide concentration patterns with infrequent and very short-term exposure events that fluctuate highly in intensity; these highly dynamic insecticide exposure characteristics have also been documented in the literature for individual insecticide compounds (e.g., Spurlock et al. 2005; Kreuger 1995; Crawford 2004; Edwards and Moore 2014). However, due to their high intrinsic acute ecotoxicity potential and their fast mode of action (Devine and Furlong 2007; Yu 2008), a single transient insecticide surface water concentration can already cause substantial adverse ecological effects (Schulz 2001; Schulz and Liess 1999; Schulz 2004; see also 1.3.3 below). While also highly toxic particularly to aquatic insects, the broad-spectrum systemic neonicotinoids differentiate from the other insecticide classes due to their different mode of action and prolonged toxicity effects (Jeschke and Nauen 2008; Tennekes and Sanchez-Bayo 2011; Sanchez-Bayo 2014), as well as their environmental persistence and high water solubilities (Morrissey et al. 2015). However, when entering surface waters, neonicotinoids also exhibit brief peak concentrations followed by rapid initial losses, but ecotoxicologically relevant concentrations can still be detected up to several months after treatment

(Morrissey et al. 2015; La et al. 2014); thus, neonicotinoids eposure profiles under specific environmental conditions (e.g., low temperature, low pH; Guzsvany et al. 2006) differ from those of other insecticide classes. However, existing neonicotinoid monitoring data are scarce (Anderson et al. 2015) and more research is needed to finally define their specific exposure characteristics in agricultural surface waters.

In general, the exposure characteristics of respective pollutants needs to be considered when the contamination of surface waters and associated risks are retrospectively evaluated using monitoring data. Traditionally operated static fixed-interval and fixed-station monitoring programs based on grab water sampling are rather unspecific (Holvoet et al. 2007; House 1994; Bundschuh et al. 2014) and tend to emphasize the importance of regularly occurring chemical stressors, such as inorganic nitrogen, many herbicides or fungicides. Particularly routine monitoring programmes of environmental agencies base their pesticide determination in rivers on a monthly or even less frequent basis (Holvoet et al. 2007; Bundschuh et al. 2014) using fixed sampling locations; thus, there is a high probability to miss and therefore substantially underrate the exposure and risk of rarely occuring, but highly toxic contaminants such as insecticides due to likely sampling at the wrong time (Xing et al. 2013). As a consequence, some authors (e.g., Liess and Schulz 2000; Schulz 2004; Xing et al. 2013) postulated that a thorough field monitoring of insecticide surface water concentrations inevitably requires an event-controlled sampling design (i.e., sampling during insecticide application to capture spray drift inputs and sampling during precipitation events to capture runoff entries). It is worth mentioning here that passive sampling has also been proposed for its potential as a reliable, robust, and cost-effective tool (see Schäfer et al. [2008] for advantages of this method in comparison to other sampling methods), which, although reflecting time-integrated average concentrations, is applicable for the quantification of episodic exposure events (Fernandez et al. 2014).

The specific exposure pattern characteristics of insecticides have also important implications for the retrospective risk assessment using monitoring data. Two main risk assessment approaches are currently used by environmental agencies and scientists to assess chemical pollution of surface waters:

(i) The deterministic approach (e.g., Iwafune et al. 2011; Jergentz et al. 2005; Karaouzas et al. 2011), which is performed by comparing a point estimate of exposure to a threshold level within a hazard quotient (HQ) approach. This risk evaluation concept is rather simplified and not conclusive as usually only the highest exposure incidence is assessed for a given contaminant, whereas the full range of insecticide concentrations remains unconsidered (Solomon et al. 2000).

(ii) The probabilistic risk assessment approach, which has been increasingly applied for the ecological risk assessment of insecticide surface water concentrations by researchers (e.g., Giddings et al. 2000; Hall 2003) and regulatory agencies (e.g., Starner et al. 2011; Spurlock 2002) over the past decade, focuses on frequencies or likelihoods of a given contaminant´s concentrations to exceed a threshold value by incorporating both variability and uncertainty into risk estimates. In detail, all available exposure data are used to derive a cumulative frequency distribution, which intentionally includes monitoring values below the limit of detection (LOD) for the estimation of threshold level exceedance frequencies (Solomon et al. 2000; Hall 2003).

However, an evaluation of the adequacy and the implications of these traditional deterministic and probabilistic risk assessment concepts for highly transient occurring pollutants such as insecticides is currently missing in the scientific literature.

1.3.2 Large-scale studies on insecticide surface water exposure: imperative for a comprehensive global assessment

Although agriculture and associated insecticide use is a global phenomena that affect surface waters worldwide (Foley et al. 2011; Ippolito et al. 2015; Fig. 1), no comprehensive global field data-based assessment of pesticide and specifically insecticide surface water exposure exists. However, few large-scale (e.g., continental) studies evaluated the insecticide exposure of aquatic ecosystems based on actual field data. For example, the US Geological Survey (USGS; findings summarized in Gilliom [2007]) summarized pesticide surface water exposure for 83 agricultural streams across the USA and reported that 57% of these exceeded a regulatory threshold or equivalent water-quality benchmark one or more times during 1992-2001. An update of these US data (Stone et al. 2014) showed 61% chronic threshold level exceedances for 36 agricultural stream sites during 2002 – 2011. Based on governmental monitoring data and standard toxicity values, a further continental scale study (Malaj et al. 2014) recently assessed the risks of organic chemicals for 4,001 sites in 91 river basins across the EU. The results showed that 14% and 42% of the monitoring sites had exceedances of acute and chronic standard toxicity values, with pesticides identified as one major contributor to chemicals risks. Besides these continental scale assessments, a review (Schulz 2004) compiled insecticide surface water concentrations published between 1982 and 2004 in the peer-reviewed literature. However, despite considering 15 countries worldwide, this study lacked a quantitative data analysis and listed only the minimum and maximum insecticide concentrations reported in each field study. A recent publication (Morrissey et al. 2015) synthesized neonicotinoid surface water concentrations from 29 studies. Although global in scale, this review solely focussed on neonicotinoids and reported aquatic exposure data for nine countries only. A further recent publication (Ippolito et al. 2015) modelled the global runoff potential for insecticide surface water exposure and compared the model results to 82 insecticide field concentrations. However, the field concentrations were derived from five countries only and no ecotoxicological evaluation (i.e., comparison of field concentrations to any sort of threshold level or toxicity value) of the insecticide exposure was performed. Finally, Knäbel et al. (2012) compared insecticide field concentrations to PECs derived from FOCUS exposure models and revealed potential deficiencies of the European regulatory exposure assessment. Again, the underlying dataset of this study was substantially restricted in geographic scope as only six countries were considered and the ecotoxicological significance of the insecticides exposure was not considered.

In summary, the few existing large-scale field studies have either examined sites in spatially restricted areas (i.e., not transcending the continental scale [Malaj et al. 2014; Gilliom 2007; Stone et al. 2014]), lacked a quantitative data analysis (Schulz 2004; Ippolito et al. 2015), did not consider RTLs (Schulz 2004; Malaj et al. 2014), performed no ecotoxicological evaluation at all (Knäbel et al. 2012; Ippolito et al. 2015), or followed other, rather specific objectives (Knäbel et al. 2012; Morrissey et al. 2015; Ippolito et al. 2015). Moreover, available large-scale studies on insecticide exposure focussed mainly

on surface waters in developed, highly regulated geographical regions (i.e., EU, USA); this raises questions on the situation in other, less developed and less regulated parts of the world, e.g., Africa, Asia, or South America, which differ substantially in terms of pesticide regulatory frameworks and rule enforcements (Ecobichon 2001; Schreinemachers and Tipraqsa 2012). Ultimately, as insecticides are applied to extensive areas worldwide (Fig. 1), the overall picture of the actual extent of insecticide surface water exposure and of the resulting potential ecological effects can only be achieved by comprehensive, global risk analyses of real-world conditions; despite more than 60 years of intense pesticide use, such analyses are, however, still not available.

1.3.3 Insecticide effects in the field

Despite their rare and short-term occurrences, insecticides` high intrinsic acute toxicities and fast modes of action (Devine and Furlong 2007; Yu 2008) lead to extremely high ecotoxicological risks for aquatic ecosystems. It has been shown, for example, that already a transient (about 1 h) insecticide contamination can have dramatic effects on the invertebrate fauna in adjacent streams even if the insecticide loss rate from the agricultural field is far less than 0.1% (Schulz and Liess 1999). The comparison with other pesticides evidences that insecticide are characterised by substantially higher toxicities (lower threshold levels), which, despite their absolute concentrations in surface waters being generally lower, lead to higher concentration to threshold level ratios, when compared to fungicides and herbicides, respectively (Stehle et al. 2011). It follows that in terms of their likely effects on important parts of aquatic communities, including macroinvertebrates (e.g., Bollmohr and Schulz, 2009), and, thus, on associated ecosystem functions (Schäfer et al. 2007; Schäfer et al. 2012;), insecticides are the major pesticide group of ecotoxicological concern (Malaj et al. 2014; Schäfer et al. 2011b). Available field studies on aquatic insecticide effects measured under normal farming practices (Table 2; see also Schulz [2004] and Schäfer et al. [2011a] for a review of insecticide effects in the field) suggest that insecticide concentrations exceeding the conservative European Uniform Principle (UP) criteria (i.e., 1/100 of the acute 48-h EC_{50} for *D. magna*) lead to severe ecological effects (e.g., changes in community structure or function, changes in invertebrate dynamics, fish kills) in the affected aquatic ecosystems. These findings are in line with results derived from a study using the SPEAR pesticide toxicity index (Liess and von der Ohe 2005), which reported long-term changes of the community composition of small agricultural streams at pesticide concentrations of 1/100 of the acute 48-h EC_{50} for *D. magna*. Moreover, a recent meta-analysis (Beketov et al. 2013) clearly evidenced based on field data for a total of 60 study sites in European and Australian agricultural streams that elevated pesticide levels severely affect regional freshwater invertebrate biodiversity already at concentrations ranging from 1/10,000 to 1/100 of the 48-h EC_{50} for *D. magna* and thus at levels considered to be protective by current EU pesticide legislations (EFSA 2013).

However, the overarching question whether insecticide exposure leads to common and widespread adverse effects in global freshwater environments cannot be answered based on the small-scale (Table 2) and regional-scale (Beketov et al. 2013; Schäfer et al. 2012) studies currently available. This lack of global information on insecticide surface water exposure (see also 1.3.2) and resulting effects hinders by now to identify and assess the overall risks of agricultural insecticide use for aquatic ecosystems and their contribution to the freshwater biodiversity losses observed globally (see 1.4

below). However, a comprehensive and systematic global assessment of insecticide surface water exposure using the elaborated RTLs, i.e., those concentrations defined to be ecologically acceptable and thus to prevent unacceptable ecological effects (see, also, 1.2.2), can provide crucial information on the actual risks of agricultural insecticide use for freshwater environments worldwide.

Table 2 Field studies reporting effects caused by insecticide exposure of small agricultural surface waters (adapted from Schulz [2004]) and related hazard quotients based on the European Uniform Principle criteria. Table taken from *Appendix I* (modified).

Insecticide	Insecticide concentration (µg/L)	UP criterion[a]	HQ[b]	Observed effect size and endpoint	Species	Source
Azinphos-methyl	0.87	0.011	**79**	46% in situ mortality	*Chironomus* spec.	Schulz et al. (2001)
Chlorpyrifos	1.3	0.001	**1300**	46% in situ mortality	*Chironomus* spec.	Moore et al. (2002)
Cypermethrin	0.03	0.003	**10**	90% abundance reduction	various invertebrate species	Shires and Bennett (1985)
Endosulfan	1.44	4.4	0.33	die-off	various fish species	Finley et al. (1999)
Fenvalerate	0.11	0.0003	**367**	55% in situ mortality	shrimp (*P. pugio*)	Baughman et al. (1989)
Parathion-ethyl	6	0.025	**240**	100% mortality	various invertebrate species	Schulz and Liess (1999)
Azinphos-methyl	0.8	0.011	**73**	86% abundance reduction	various invertebrate species	Purcell and Giberson (2007)

[a] The Uniform Principle (UP) criteria were calculated by dividing the respective median EC_{50} (*Daphnia magna*) values by a safety factor of 100 (see EFSA [2013] for details).
[b] Hazard quotients (HQs) were calculated by dividing the measured insecticide concentrations by the UP criteria. HQs > 1 are displayed in bold.

1.4 State of global surface waters

Despite their overall small spatial dimensions (i.e., less than 1% of the world`s surface [Gleick 1998]), global freshwaters accommodate a rich diversity of species and habitats. Though widely recognized as the most essential of natural resources and as provider of critical ecosystems services, global aquatic ecosystems are directly threatened by numerous human activities (e.g., Dudgeon et al. 2006; Finlayson et al. 2005). Essentially, surface waters are polluted and transformed through widespread land cover change, urbanization, industrialization, agricultural expansion and intensification, as well as engineering schemes like reservoirs or irrigation (Vörösmarty et al. 2010); in addition, global climate change further exacerbates the loss and degradation of freshwater systems. As a result, surface waters worldwide face a severe biodiversity crisis, with 50% of inland water habitats lost during the twentieth century (Finlayson et al. 2005), 10,000–20,000 freshwater species that are extinct or at risk of extinction (Strayer and Dudgeon 2010; Vörösmarty et al. 2010), and species loss rates rivalling those of terrestrial ecosystems (Finlayson et al. 2005). It is well established that habitat

loss/degradation, water pollution, and biological invasion are main (anthropogenic) drivers threatening freshwater biodiversity (Collen et al. 2014; Stendera et al. 2012). Among the suite of drivers, especially habitat loss/degradation and nutrient pollution (i.e., eutrophication) often are denoted as key stressors (Finlayson et al. 2005; Collen et al. 2014) and their global extents and resulting impacts are comparably well recognised and quantified (Nilsson et al. 2005; Dynesius and Nilsson, 1994; Smith 2003; Woodward et al. 2012). Vörösmarty et al. (2010) also identified in a global model analysis habitat loss/degradation (i.e., dam density and river fragmentation), as well as pollution as chief determinants threatening global surface waters. This study also shows that concerning the pollution category, N and P loadings pose higher threats to aquatic freshwater biodiversity than pesticides; noteworthy, Vörösmarty et al. (2010) modelled pesticide exposure and effects only in terms of the total amount that was applied at the national level and this study did not consider differences in pesticide toxicities, so that a thorough and exact quantification of pesticides contribution to biodiversity losses was not achieved. However, despite their ubiquitous and long-lasting global use, pesticides` actual effects on the aquatic biodiversity in the field have only been investigated for spatially restricted areas usually at local or regional scales (e.g., Bereswill et al. 2013; Beketov et al. 2013; Schäfer et al. 2012; see also 1.3.2 and 1.3.3). It is thus currently not known how widespread and common pesticides jeopardise the ecological integrity of freshwater systems and to what extent they contribute to biodiversity losses in surface waters globally (Rockström et al. 2009; Steffen et al. 2015; Schwarzenbach et al. 2006).

Provided the drastic biodiversity threats we currently face in freshwater systems worldwide, it is important to understand the contribution that highly toxic insecticides may have. A global analysis of insecticide field concentrations evaluated by detailed information on the aquatic biodiversity losses to be expected from these exposure levels (i.e., evaluation based on RTLs defined as concentrations which are just ecologically acceptable) can ultimately identify the contribution of insecticides to the biodiversity impairments that are observed for surface waters globally.

2 Research objectives and thesis outline

The overarching goal of the present thesis is to contribute to a new research frontier in global ecotoxicology – assessing the environmental impacts of anthropogenic chemicals through an analysis of global datasets with a view, which is, in contrast to classical environmental toxicology, focussing on actual real field situations. This fundamental intention is based on an assessment of insecticide field data and related effects on the global freshwater biodiversity by means of a meta-analysis using worldwide agriculturally-related insecticide exposure data for surface waters compared to RTLs as legally-manifested benchmarks. The overall outcome of the present thesis facilitates a new perspective on the environmental consequences of pesticide use in global agriculture and on the regulatory risk assessment of highly toxic anthropogenic chemicals.

In detail, the following four main research objectives (RO; see Fig. 2) have been addressed by the present thesis:

[1] The definition of typical insecticide exposure patterns in agricultural surface waters and analyses of the resulting implications for monitoring and retrospective risk assessment concepts (*Appendix I*).

[2] The analysis of global insecticide surface water exposure data using RTLs to assess the risks for freshwater biodiversity impairments caused by agricultural insecticide usages and the effectiveness of pesticide regulations at the global scale (*Appendix II*).

[3] The identification and statistical analysis of factors (including their interactions) that determine insecticides risks for global and European surface waters (*Appendices II and III*).

[4] The evaluation of the regulatory EU pesticide exposure and effect assessments schemes using field data, the identification of regulatory risk assessment schemes` deficiencies and the proposal of essential risk assessment amendments (*Appendices III and IV*).

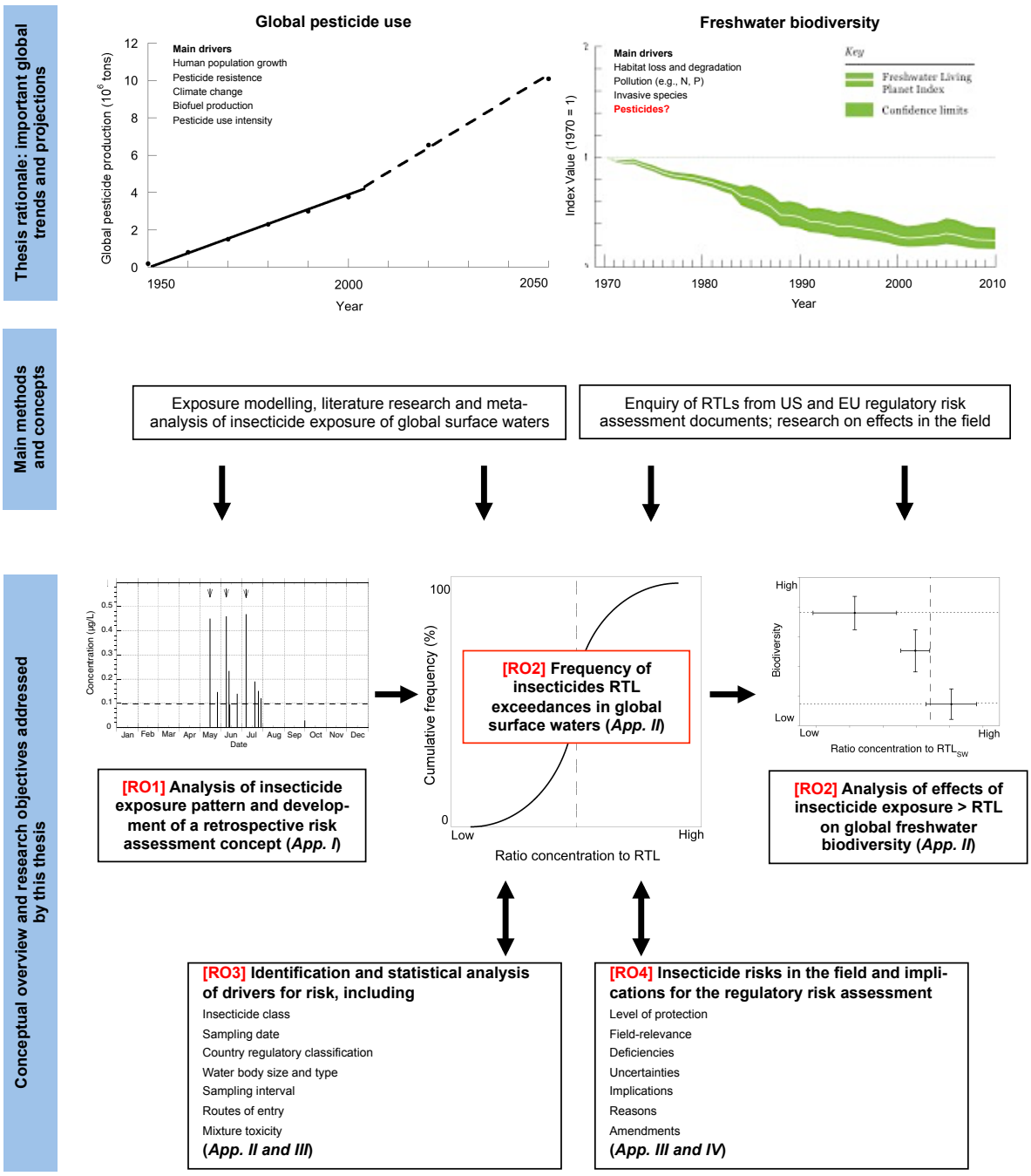

Figure 2 Overview and conceptual outline of the present thesis and summary of the four research objectives (RO) including their interrelations. References to the *Appendices* (*App.*) addressing the research objectives are also shown. The thesis rationale is based on the thematic background outlined in the introduction (see chapter 1) and concisely represented here by past trends (solid lines) and future projections (dashed lines) of global pesticide use (Tilman et al. 2001) and past trends (including confidence limits) of the global freshwater biodiversity (WWF 2014). An overview of the main methods and concepts of this thesis is provided in chapter 3 and an overall discussion of the main results and implications of this thesis is provided in chapter 4.

The four research objectives of this thesis were addressed by the following four scientific publications (see Fig. 2 and *Appendices I – IV* of this thesis).

Appendix I: *Stehle S, Knäbel A, Schulz R (2013) Probabilistic Risk Assessment of Insecticide Concentrations in Agricultural Surface Waters: A Critical Appraisal. Environmental Monitoring and Assessment 185: 6295-6310*

This publication specifies and defines typical insecticide exposure patterns in small agricultural surface waters for different crop and application scenarios and discusses the implications resulting from the highly-specific insecticide exposure characteristics for monitoring and risk assessment [RO1]. The relevance-driven risk assessment concept developed in this manuscript denotes the methodological background for the risk evaluation of insecticide surface water exposure performed in the *Appendices II – IV.*

Appendix II: *Stehle S, Schulz R (2015) Agricultural Insecticides Threaten Surface Waters at the Global Scale. Proceedings of the National Academy of Sciences of the United States of America 112: 5750-5755*

This publication addresses the fundamental question whether and to what extent insecticide surface water concentrations exceed RTLs at the global scale and thus whether insecticides threaten freshwater biodiversity and whether current pesticide regulations protect worldwide surface waters from excessive contamination [RO2]; statistical analyses identified and quantified factors explaining these risks [RO3]. In essence, this study provides for the first time evidence that the surface water contamination resulting from current global agricultural insecticide use considerable exceeds the limits set by regulatory agencies and thus constitutes a critical environmental threat. This publication thus can be perceived as ground-breaking research defining the field of global ecotoxicology using integrative assessments of real-world contamination data.

Appendix III: Stehle S, Schulz R (submitted) Pesticide Regulations in the EU – Environment Unprotected? *Environmental Science and Pollution Research* (doi:10.1007/s11356-015-5148-5)

This manuscript contextualizes insecticides` risks for European surface waters to the prospective risk assessment schemes and protection goals of current EU pesticide and surface water regulations; it analyses drivers for risks [RO3], deficiencies and uncertainties of current pesticide risk assessment concepts, discusses needs for critical revisions and recommends essential risk assessment amendments [RO4]. The in-depth analyses of the shortcomings of highly-elaborated regulatory risk assessment schemes crucial for pesticide authorisation provides an important explanatory complement to the findings of *Appendix II*.

Appendix IV: Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS Surface Water Models Fail to Predict Insecticide Concentrations in the Field. Environmental Science and Technology 46: 8397-8404

This publication evaluates the protectiveness and accuracy of the FOCUS models used for exposure predictions in the European regulatory pesticide risk assessment; it identified and quantified reasons

for the underestimation of field exposure by regulatory exposure modelling and analysed the model outcomes for different insecticide classes [RO4]. The overall results of this study thus provide potential explanations for the findings reported in the *Appendices II and III*, i.e., for incidences of insecticide RTL exceedances in the field and higher risks for newer insecticide classes.

3 Overview of methods and concepts

This chapter provides a brief overview of the main methods and concepts used to address the four ROs presented in chapter 2. Further details on the materials and methods used can be found in the *Appendices I – IV*.

3.1 Insecticide compound selection criteria

The focus of this thesis is on insecticides as they exhibit a high toxicity potential towards aquatic organisms (US EPA 2015c) important for ecosystem functions (Schäfer et al. 2012) and reasoned by the fact that they generally pose higher risks to surface waters when compared to herbicides and fungicides, respectively (Stehle et al. 2011; Werner and Hitzfeld 2012; Fig. 3). In total, more than 50 insecticide compounds covering all major insecticide classes (Yu 2008; Denholm et al. 2002; Table 1) important for global agriculture were considered for this thesis. However, field concentrations were only available for 28 insecticide compounds in the scientific literature (i.e., the scientific literature did not report exposure data for all pyrethroid and neonicotinoid compounds used in agriculture [see below]), which thus denote the population of compounds finally included in this thesis (Table 3). The basic selection criteria for the consideration of insecticide compounds were as follows (see Supporting Information of *Appendix II* for details): (i) the organochlorine insecticide endosulfan was selected because it is among the only organochlorine insecticides still in agricultural use in many countries (Lubick 2010); (ii) six organophosphate insecticides and the carbamate insecticide carbofuran were selected as representatives for these two classes based on their importance in terms of global application rates (Gianessi and Reigner 2006); (iii) all pyrethroid esters (Yu 2008) and (iv) all neonicotinoid insecticides were considered, which is justified by the fact that the use of these two insecticide classes increased steadily in recent years to fill the market gaps created by regulatory restrictions on other types of insecticides (Moran 2003; Stokstad 2013). Out of all pyrethroid and neonicotinoid compounds authorised for agricultural uses and thus potentially considered, 16 pyrethroids and four neonicotinoid insecticides could finally be included in this thesis due to the availability of field concentrations in the scientific literature (Table 3).

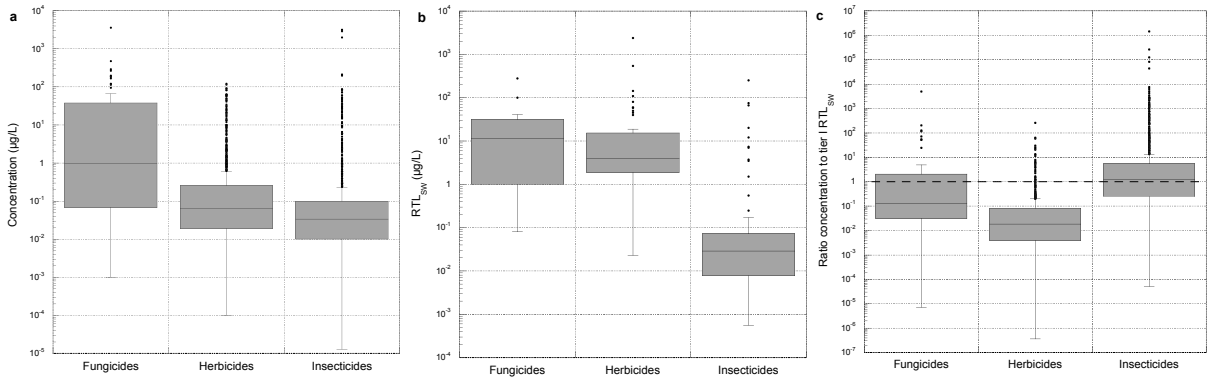

Figure 3 Boxplots of the water phase pesticide concentrations that were detected in European surface waters (a), as well as of the regulatory threshold levels (RTL_{SW}) derived from tier I of the European pesticide risk assessment (b), and related concentration to RTL_{SW} ratios (c, dashed line indicates the RTL_{SW}) for the different pesticide groups. The comparison is based on fungicide (n = 87), herbicide (n = 852), and insecticide (n = 1,408)

concentrations that were detected in 516 water-phase samples, which were analysed for the occurrence of multiple pesticide exposures. Figure taken from *Appendix III* (modified).

Table 3 Insecticides included in the present thesis, their corresponding regulatory threshold levels for water (RTL_{SW}) and sediments (RTL_{SED}) and status on approval under European pesticide Regulation (EC) No. 1107/2009 (DG SANCO 2014; cf. *Appendix III*). See *Appendix II* for further details on RTL_{SW} and RTL_{SED} derivation. n.s.: not specified due to lack of threshold level or toxicity data availability. - indicates that no freshwater (FW), estuarine water (EST), or sediment concentrations were reported for this insecticide in the literature; sediment refers to sediment and suspended particle concentrations. Insecticide classes are abbreviated as follows: organochlorine (OC), organophosphate (OP), carbamate (Carb), pyrethroid (Pyr), and neonicotinoid (Neo). Table taken from *Appendix II* (modified).

		RTL_{SW} (µg/L)			
Insecticide	**Class**	**North America FW/EST**	**Europe**	**Worldwide FW/EST**	**RTL_{SED} (µg/kg)**
Endosulfan	OC	0.05/0.02	1.3[2]	0.675/0.66	0.026
Azinphos-methyl	OP	0.08/0.105	0.32[2]	0.2/0.2125	0.89
Chlorpyrifos	OP	0.05/0.0175	0.1[1]	0.075/0.05875	1.1
Diazinon	OP	0.105/2.1	2.4[2]	1.2525/2.25	0.95
Malathion	OP	0.005/0.005	1.25[1]	0.6275/0.6275	0.9
Parathion-ethyl	OP	0.02/0.0535	0.024[2]	0.022/0.03875	0.13
Parathion-methyl	OP	0.485/0.175	0.073[2]	0.279/0.124	0.96
Carbofuran	Carb	1.115/2.3	0.0205[2]	0.56775/1.16025	0.22
Acrinathrin	Pyr	-/-	0.0087[1]	-/-	-
Bifenthrin	Pyr	0.075/0.002	0.005[1]	0.04/0.0035	4
Cyfluthrin	Pyr	0.0125/0.0012	0.0068[1]	0.00965/0.004	0.137
b-cyfluthrin	Pyr	-/-	0.00068[1]	-/-	-
Cypermethrin	Pyr	0.0018/-	0.025[1]	0.0134/-	1.8
α-cypermethrin	Pyr	0.0018/-	0.015[1]	0.0084/-	1.8
ζ-cypermethrin	Pyr	0.0018/-	-	-/-	-
Deltamethrin	Pyr	0.055/0.00085	0.0032[1]	0.0291/0.002025	1.3
Esfenvalerate	Pyr	0.025/0.025	0.01[1]	0.0175/0.0175	0.41738
Fenpropathrin	Pyr	0.265/0.0105	0.0053[2]	0.13515/0.0079	0.645
Fenvalerate	Pyr	0.016/0.004	0.0022[2]	0.0091/0.0031	0.88
λ-cyhalothrin	Pyr	0.0035/0.00205	0.0021[1]	0.0028/0.002075	10.5
Permethrin	Pyr	0.0106/0.009	0.025[2]	0.0178/0.017	0.87
Tau-fluvalinate	Pyr	0.175/-	0.022[1]	0.0985/-	n.s.
Tefluthrin	Pyr	-/-	-	-/-	47
Tralomethrin	Pyr	0.0195/-	-	-/-	-
Acetamiprid	Neo	10.5/-	0.5[1]	5.5	-
Imidacloprid	Neo	34.5/-	0.3[1]	17.4/-	-
Thiacloprid	Neo	-/-	1.57[1]	-/-	-
Thiamethoxam	Neo	-/-	2.8[1]	-/-	-

1: Approved for agricultural uses in the EU under Regulation (EC) No. 1107/2009 (DG SANCO 2014).
2: Not approved for agricultural uses in the EU under Regulation (EC) No. 1107/2009 (DG SANCO 2014).

3.2 Literature research and data selection criteria

The basis of this thesis and of the results presented in the *Appendices II - IV* is an exhaustive literature search on insecticide field concentrations (Fig. 4) using multiple search criteria and all major scientific databases (see Supporting Information of *Appendix II* for details). The literature research had no temporal restriction (i.e., time period covered: 1945 – June 2012) and comprised eight different languages. In total, more than 200,000 database entries were evaluated between June 2006 and June 2012 and additional studies were identified by footnote chasing (White 2009), i.e., consulting the reference lists of empirical and review papers. To serve as a quality-control measure for the entire literature search procedure described above, a further independent literature review was performed

externally by the scientific literature search service of the "FIZ Karlsruhe" research institution (see http://www.fiz-karlsruhe.de/search_service.html?&L=1). However, this independent literature search did not identify any additional articles that had not been identified already in our own literature search.

The studies had to meet the following selection criteria to be included in this thesis: (i) only peer-reviewed studies were considered to ensure that minimum scientific standards were met; (ii) the studies had to be written in one of the following eight languages: Chinese, English, French, German, Japanese, Russian, Spanish, or Portuguese; (iii) the insecticide concentrations reported resulted from agricultural nonpoint source pollution (excluding urban, industrial, and public health activities; pollution via point sources; aquaculture; atmospheric deposition; forest application; sheep dipping, golf course applications; accidental spills; intentional water contamination; and in-crop use); and (iv) the concentratins were detected in perennial freshwater or estuarine surface water bodies above their limit of quantification (LOQ).

In addition to information on insecticide concentrations, information on several covariates (e.g., sampling location, catchment size, sampling interval, sampling date, LOQ, etc.) were retrieved from the scientific studies.

Importantly, all results and analyses of this thesis are based on measured insecticide concentrations (MICs; i.e., those concentrations actually detected and quantified) in order to avoid a bias due to artificially high numbers of data points without quantifiable insecticide levels typical for insecticide surface water monitoring (see *Appendices I & II* for details).

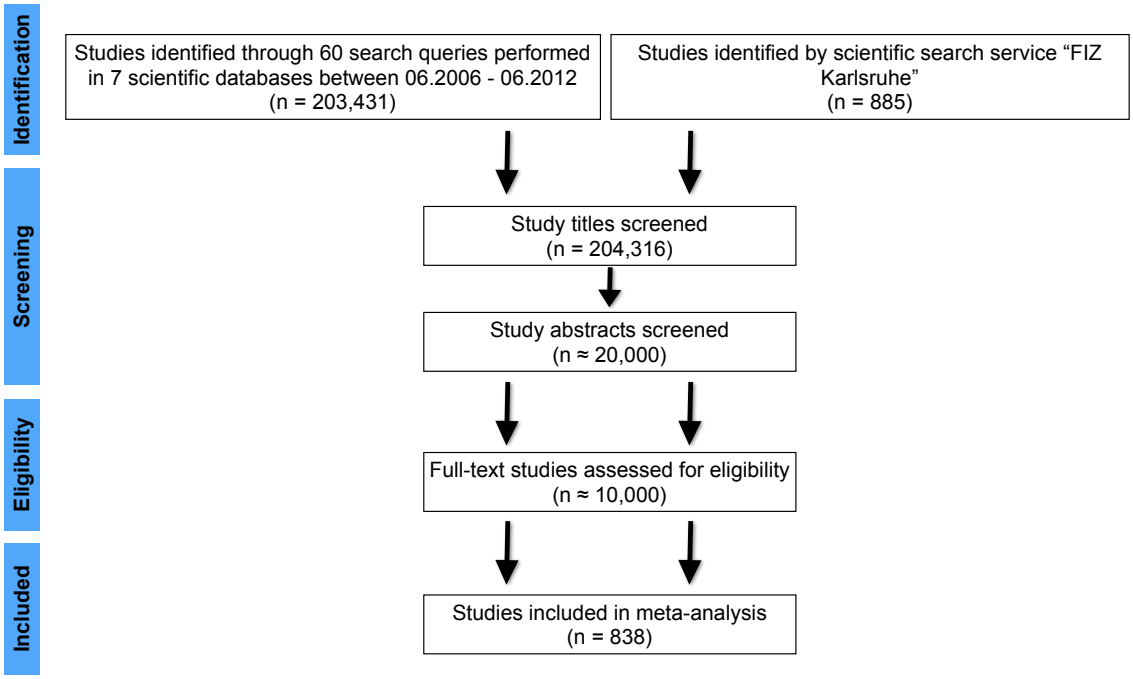

Figure 4 Overview of literature research and selection of studies for inclusion in the present thesis. See text and *Appendix II* for details.

3.3 FOCUS exposure modelling

Exposure modelling was applied threefold in this thesis: First, the FOCUS pesticide exposure models (FOCUS 2001) were used in *Appendix I* to derive generalized and realistic exposure profiles in surface waters receiving agricultural nonpoint source pollution for a typical model insecticide and real insecticide compounds and for different crop and application scenarios. Subsequent to the verification of the model results using real-world field data, exposure model outcomes were used to evaluate the adequacy of different sampling strategies and environmental risk assessment concepts for insecticide surface water exposure (*Appendix I*). Second, a comparison of insecticide field concentrations to the respective PECs derived from from the different FOCUS exposure model steps provided information on the field relevance and protectiveness of the European regulatory exposure assessment (*Appendix IV*). Third, these results of the regulatory FOCUS exposure predictions were subsequently used to identify the potential reasons for RTL exceedances of insecticides in the field (*Appendices II - IV*). In essence, the comparison of PECs to MICs extracted from scientific studies enabled to attribute PEC and RTL exceedances in the field to either model inaccuracies (i.e., failures of the regulatory risk assessment) or to farmers` non-adherence to insecticide application prescriptions.

3.4 Overview of threshold levels

A fundamental concept of this thesis is the comparison of insecticide field concentrations to RTLs defined as part of the legal pesticide authorisation procedures. In essence, we used the US and EU RTL_{SW} derived from the respective US EPA and EU pesticide registration procedures for water-phase insecticide concentrations measured in the US and the EU, as well as average values of the US and EU RTL_{SW} for insecticide concentrations detected in other parts of the world (Table 3; see *Appendix II* for details). In cases, in which a final EU RTL_{SW} was set based on higher tier effect studies (i.e., micro-/mesocosm studies), the respective tier I RTL_{SW} was also extracted from EU pesticide registration documents and used for the in-depth analysis of the EU regulatory risk assessment (see *Appendix III*). In addition to RTL_{SW}, we evaluated all water-phase insecticide concentration (MIC_{SW}) using environmental quality standards (EQS, see *Appendix II*) and specifically those defined as priority substances by the EU Water Framework Directive (European Commission 2013b; see *Appendix III*). Concerning sediment exposure, RTL_{SED} are not determined by default for most insecticide compounds within the official US or EU regulatory risk assessment procedures. In cases of missing RTL_{SED}, we applied maximum permissible concentrations (MPC [Crommentuijn et al. 2000], referred to also as RTL_{SED} in this thesis) for the evaluation of sediment insecticide contamination (see Table 3 and Supporting Information of *Appendix II* for details).

3.5 Assessment of insecticide effects on freshwater biodiversity

The evaluation of insecticide effects in the field (*Appendix II*) was based on findings from a recent meta-analysis (Beketov et al. 2013), which showed that pesticide contamination reduces regional biodiversity of stream invertebrates. This meta-analysis ruled out confounding factors and used exposure data based on methods able to reflect short-term pesticide concentrations. In essence, this

publication showed based on pesticide field concentrations for 54 compounds (29 insecticides, 20 fungicides, 5 herbicides) from a total of 60 study sites in agricultural streams in Germany, France and Australia, that with increasing pesticide exposure (expressed as three ranges of toxic units [TU] calculated using *Daphnia magna* toxicity data), the family richness of stream invertebrates significantly decreased. In order to derive information on the potential biodiversity effects of insecticide concentrations in relation to RTLs, we extracted the biodiversity and exposure data from the study of Beketov et al. (2013) and displayed their pesticide concentration data relative to the RTL_{SW} of the respective pesticides. This approach enables to link insecticide exposure levels that are expressed as concentration to RTL_{SW} ratios to resulting effects on the regional aquatic biodiversity in agricultural streams. Moreover, the application of this concept to global insecticide exposure data provides important information on the contribution of agricultural insecticides to global freshwater biodiversity declines (*Appendix II*).

3.6 Outline of main statistical analyses

We used linear model analyses for the identification and quantification of factors explaining insecticides` risks in the field on the global (*Appendix II*) and European (*Appendix III*) scale. Several field- (e.g., catchment size), substance- (e.g., insecticide class), regulatory- (e.g., stringency of regulatory quality), and methodological-related (e.g., type of sampling) variables were extracted from the studies or from various additional sources and tested for their effects on insecticide concentration to RTL ratios. Besides main effects, we also analysed relevant interactions of the variables regarding their effects on the outcome variable using tests of simple slopes between groups of categorical independent variables and a modified Johnson-Neyman technique to test for differences between regression lines at specific predicted values (Aiken and West 1991; see, also, Supporting Information *Appendix II* for details).

4 Results and discussion

This chapter briefly presents and discusses the most important results of this thesis. Please see the *Appendices I – IV* for more details on the results and related in-depth discussions.

4.1 Exposure characteristics, monitoring and risk assessment of insecticide surface water pollution [RO1]

Appendix I evidences based on exposure modelling that agricultural nonpoint source insecticide surface water pollution is highly dynamic, with even substantially contaminated streams characterized by infrequent and short-term exposure events and hourly variations in insecticide peak concentrations. This typical insecticide surface water exposure pattern is a function of distinct rainfall-, irrigation-, and application-related short-term entry events, low application rates and highly specific insecticide properties. In essence, the synthesized exposure model results proved that across diverse realistic application and crop scenarios, a maximum of six to nine highly transient (i.e., exposure duration of few hours), but at the same time highly ecotoxicologically relevant (i.e., the majority of concentrations exceeded RTL_{SW}) insecticide exposure incidences occur in agricultural surface waters (Fig. 5 a and b); they are thus typically exposed towards insecticides for less than 1% of the time per year. A comparison to real world field studies confirmed the model results as on average a maximum of five insecticide inputs, each lasting a maximum of 3 to 4 h, occur in agricultural surface waters during one insecticide application period (e.g., Liess et al. 1999; Williams et al. 1995; Jergentz et al. 2005; Schulz et al. 1998; Kreuger 1995; Spurlock et al. 2005; *Appendix I*). In summary, *Appendix I* demonstrates and quantifies based on generalized and realistic exposure simulations the specific characteristics of insecticides` "low frequency/high risk" exposure patterns in agricultural surface waters.

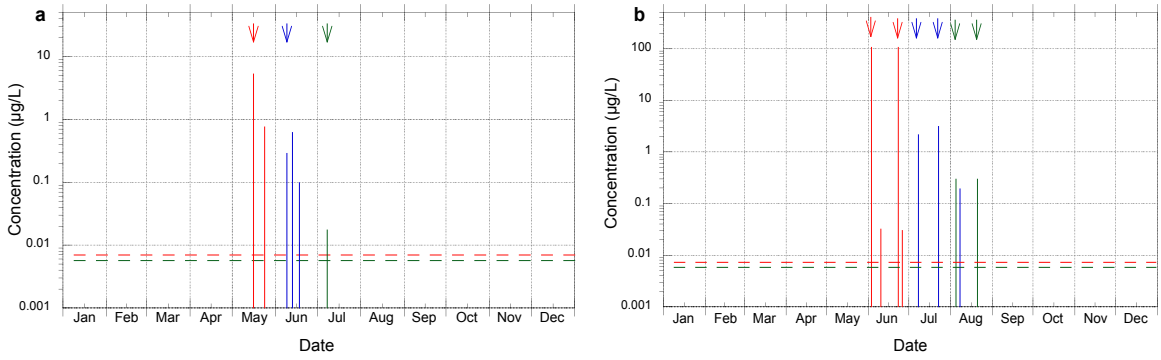

Figure 5 Realistic insecticide (red bars: malathion; blue bars: acetamiprid; green bars: deltamethrin) exposure profiles in a stream that receives agricultural nonpoint source pollution as synthesised from respective FOCUS surface water scenarios. (a) Arable crops with three insecticide applications (arrows above bars); (b) six insecticide applications to permanent crops. The dashed horizontal lines indicate the RTL_{SW}, with the red (malathion, RTL_{SW} = 0.007 µg/L) and green (deltamethrin, RTL_{SW} = 0.0056 µg/L) dashed horizontal lines indicating the RTL_{SW} for these insecticides. The RTL_{SW} for acetamiprid (498 µg/L) is not shown here. Figure taken from *Appendix I*.

This typical low frequency/high-risk exposure pattern of insecticides has important implications for surface water monitoring. We proved in *Appendix I* based on Monte Carlo simulations that event-based sampling is inevitable for the thorough detection of all of the highly dynamic and short-term

insecticide concentration peaks (Table 4); in contrast, fixed-interval sampling detected none up to a maximum of only 60% (daily sampling) of the insecticide concentrations. Moreover, an economic evaluation showed that fixed-interval sampling led to substantially higher analytical costs due to more samples taken and analysed (Table 4). In addition, with higher temporal resolutions of fixed-interval sampling strategies, the mean number of non-detects (i.e., samples without insecticide detection) increased considerably in parallel with the increasing mean number of detections; as a consequence, insecticide monitoring data sets based on fixed-interval sampling strategies are dominated by very high percentages of non-detects (99 to 100%; Table 4). These results were again proven using real-world monitoring studies (*Appendix I*) and are in line with a recent publication (Xing et al. 2013), which evidenced based on field sampling that weekly grab water sampling substantially underestimates the number of insecticide surface water concentrations present, as well as the peak concentration heights by 1 – 3 orders of magnitude. It overall follows that traditionally operated fixed-interval sampling regimes are entirely inappropriate for an accurate exposure assessment of the infrequent and highly transient insecticide concentrations, which, however, are of high ecotoxicological risks. These findings reported in *Appendix I* are therefore of importance for researchers working in the field of water pollution and governmental agencies worldwide, which by now evaluate the chemical status of surface waters based on static fixed-interval and fixed-station monitoring results.

Table 4 Effectiveness and costs associated with different sampling strategies. Values were calculated and combined by applying Monte Carlo simulations to realistic insecticide exposure patterns synthesized from FOCUS exposure model calculations (Fig. 5 a and b) for two typical agricultural streams located in arable and permanent crop agri-environments. Table taken from *Appendix I*.

Interval (No. of samples[a])	Mean[b] no. of detects (peak detection error[c] (%))	Mean[b] no. of non-detects	Percentage of non-detects	Costs per detection ($)	Total costs per year ($)
Monthly (24)	0 (100)	24	100%	n/a	7200
14-d (52)	0 (100)	52	100%	n/a	15600
Weekly (104)	1 (93.3)	103	99%	31,200	31,200
3.5-d (208)	2 (86.6)	206	99%	31,200	62,400
Daily[d] (730)	6 (60)	724	99.2%	36,500	219,000
Event[e] (40)	15 (0)	25	62.5%	1000	15,000

[a] No. of samples refers to two typical agricultural streams, where one is located in arable and one in permanent crop agri-environments.
[b] The minimum and maximum no. of detects calculated by Monte Carlo simulations were (Min / Max): monthly (0 / 1); 14-d (0 / 1); weekly (0 / 2); 3.5-d (0 / 2) in the case of arable crops and (Min / Max): monthly (0 / 1); 14-d (0 / 2); weekly (0 / 3); 3.5-d (0 / 3) in the case of permanent crops.
[c] Defined as the percentage of non-detected insecticide concentrations out of all concentrations available. Calculated as follows: ((Total concentrations available – concentrations detected) / Total concentrations available) x 100.
[d] Despite the fact that one sample per day was taken, only 2 out of 6 (arable crops) and 4 out of 9 (permanent crops) insecticide concentrations (total: 6 out of 15) were detected due to the respective mean exposure durations simulated by FOCUS.
[e] 18 (arable crops) and 22 (permanent crops) samples (total: 40) were considered to be taken by event-triggered sampling assuming three (arable crops) and six (permanent crops) spray events plus 15 (arable crops) and 16 (permanent crops) insecticide entry events potentially occurring due to 15 mm/day irrigation or rainfall as extracted from FOCUS climate documents for the respective scenarios used here.

Beside these implications for surface water surveillance, *Appendix I* also proved that traditional retrospective risk assessment concepts (i.e., deterministic and probabilistic concepts) are inappropriate for a thorough assessment of insecticides` risks. In essence, the deterministic concept ignores the temporal characteristics of exposure and therefore the risks resulting from repeated

insecticide surface water concentrations caused by consecutive entry events (Fig. 5) that are, however, also relevant in terms of adverse ecological effects (Ashauer et al. 2006). Further on, *Appendix I* clearly demonstrates that the probabilistic concept, which evaluates all monitoring data including concentrations < LOD, is in the case of insecticides severely biased by the sampling strategy and specifically the amount of samples taken (i.e., sampling frequencies); in particular, insecticide exposure distributions derived by fixed-interval sampling schemes typically are, due to the highly transient and short-term insecticide exposure characteristics (Fig. 5), dominated by non-detects, i.e., more than 99% of the samples taken do not detect insecticide concentrations (Table 4). It follows that the insecticide contamination existing de facto in the field is of almost no relevance for the threshold level exceedance probability, i.e., the final outcome of the probabilistic risk assessment (Fig. 6a). Even worse, the inclusion of non-detects leads in the case of insecticides to a substantial underestimation of risks and false senses of protectiveness as threshold level excedance probabilities are generally very low due to the predominance of non-detects. Such criticisms are in line with Hart (2001) who claimed that probabilistic risk assessment approaches may yield misleading results if inappropriate data are included.

To overcome these limitations of the deterministic and probabilistic risk assessment concepts, we propose in *Appendix I* the so-called relevance-driven approach for the risk assessment of insecticide monitoring data. In essence, this concept focuses on the de facto existing, and therefore relevant insecticide contamination of agricultural surface waters. The comparison of all actually detected concentrations to the RTL (Fig. 6b) enables the quantification of the risk in terms of exposure incidence frequencies and given ecotoxicological relevance (height of concentration to RTL ratios). Importantly, this approach takes into account the highly specific insecticide exposure pattern characteristics (Fig. 5) by omitting non-detects and thus the fact that it is thus during more than 99% of the time neither feasible nor valid to assess insecticides` risks in the field, i.e., to test the hypothesis if MICs do not exceed their respective RTLs, as none of the data that are needed (i.e., potential insecticide exposure incidences) to verify or falsify this hypothesis do exist. Thus, in the relevance-driven concept, the detection of a de facto present insecticide concentration is essential as an indicator that an insecticide entry event into a surface water body has occurred; these relevant insecticide exposure data provide an informative basis for a thorough risk assessment of insecticide surface water contamination. The relevance-driven approach was consequentially used in this thesis for the risk assessment of insecticide field concentrations and *Appendix I* thus forms an important methodological basis for the outcomes of *Appendices II and III*.

Overall, *Appendix I* evidences that insecticide surface water exposure is characterized by highly specific low frequency/high risk patterns. This publication quantifies the environmental and economic consequences resulting from inappropriate monitoring and risk assessment approaches used for the evaluation of highly transiently occurring pollutants such as insecticides. *Appendix I* defines the requirements for an elaborate, insecticide-specific monitoring design, and proposes the relevance-driven concept as a risk assessment paradigm specifically for a thorough and accurate evaluation of insecticide surface water contamination.

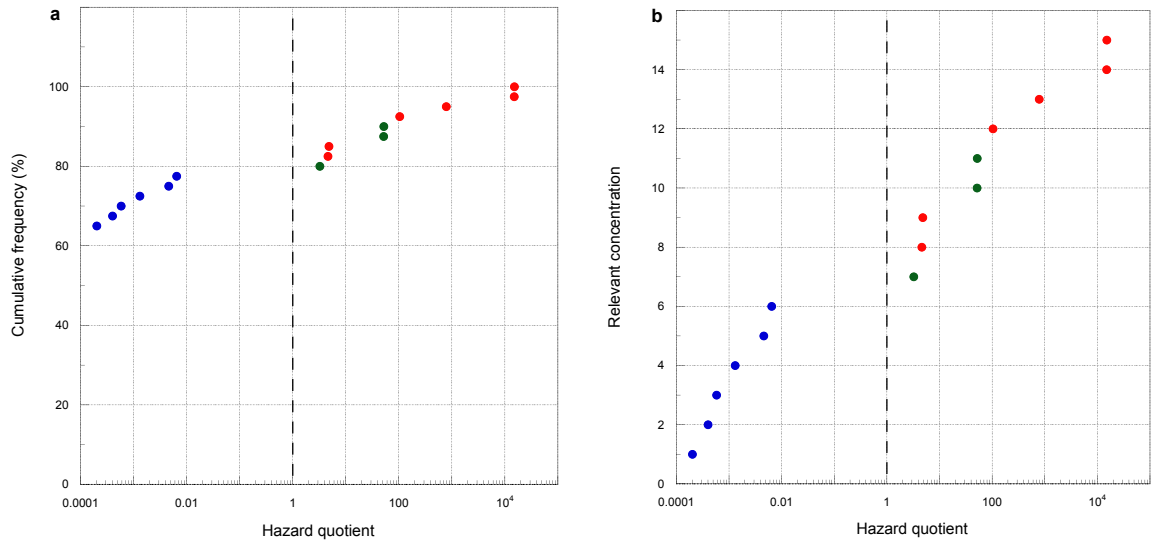

Figure 6 Exemplary risk assessment results using probabilistic (a) and relevance-driven (b) insecticide monitoring data evaluation approaches. Concentrations were normalized by calculating hazard quotients and result from realistic insecticide exposure patterns for two typical agricultural streams located in arable and permanent crop agri-environments (see Fig. 5a and b) constructed using event-triggered sampling (data taken from Table 4). In Fig. 6a, 62.5% of all (n = 40) concentrations were below the LOD (concentrations < LOD not shown in the graph), resulting in an RTL (vertical dashed line) exceedance probability of 22.5% (i.e., 9 out of 40 samples > RTL). In contrast, the relevance-driven risk assessment (b) assesses only insecticide concentrations > LOD, i.e., those which are of ecological relevance. As a result, a high ecological risk is indicated, as 9 out of 15 concentrations exceeded their RTLs. Figure taken from *Appendix I*.

4.2 Insecticide exposure of global surface waters: implications for global freshwater biodiversity and analysis of drivers for risks [RO2 and RO3]

This thesis provides the first global assessment of insecticide surface water contamination using legally accepted RTLs. The overall dataset comprises 11,300 insecticide concentrations measured in 73 countries between 1960 and 2011. However, although a highly comprehensive and exhaustive literature search was performed, MICs were reported in the scientific literature for only approximately 10% of global agricultural areas (Fig. 7). It follows that no scientific data on insecticide surface water exposure are available for approximately 90% of global high-intensity agricultural areas and 122 out of a total of 195 countries with arable land coverage. These figures are alarming considering that more than 400,000 t a.i. of highly biologically active insecticides are applied to global croplands (i.e., 15.3 x 10^6 km^2; Fig. 1) annually without scientific knowledge on the potential environmental consequences for large proportions of these applications. However, Ippolito et al. (2015) recently published global maps depicting based on model predictions that 40% of water bodies worldwide are at risk of insecticide contamination due to runoff; the exposure hotspots identified in this study should thus be used to prioritize future surface water monitoring campaigns.

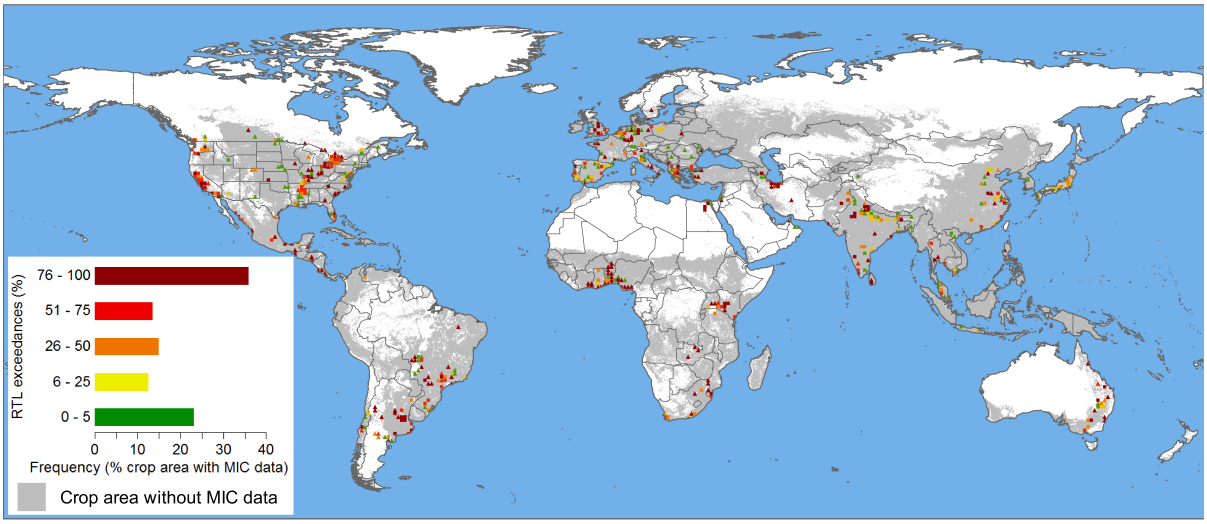

Figure 7 Global crop area and the distribution of regulatory threshold level (RTL) exceedance rates for reported measured insecticide concentrations (MICs, n = 10,659) aggregated in 1° grid cells. Information on insecticide surface water exposure was available for only 1.62 Mio km^2 (10.6%) of the 15.3 x 10^6 km^2 of global croplands (Foley et al. 2011). Rectangles (n = 307) represent subclassified cropped areas with five or more MICs, and triangles (n = 290) display grid cells with fewer than 5 MICs. Please note that 641 MICs could not be allocated to a specific grid cell due to the provision of imprecise location information in the studies. The horizontal bars in the legend illustrate the relative distributions of the respective insecticide RTL exceedance classes among the global cropped area with information on insecticide exposure. Figure taken from *Appendix II*.

However, the most important finding of this thesis is that 52.4% of the 11,300 insecticide concentrations detected, i.e., 5,915 cases distributed globally (Fig. 7), exceeded their RTL. In detail, 40.8% of the directly bioavailable water-phase concentrations (n = 8,166) and 82.5% of the sediment concentrations (n = 3,134), which reflect exposure conditions over longer time spans, exceeded respective threshold levels (Fig. 8a). Importantly, an analysis of the ecological effects resulting from insecticide concentrations > RTL based on field data published by Beketov et al. (2013) clearly illustrates that species richness is reduced at the taxonomic family level by 29% at sites, which are contaminated only slightly above the RTL_{SW} (1.12 x RTL_{SW}) relative to uncontaminated control sites (Fig. 8b). It follows that insecticide concentrations above the RTL lead to severe declines in regional freshwater biodiversity; moreover, even concentrations that were a factor of 10 below the RTLs already triggered clear effects, i.e., a family richness reduction of approximately 12% (Fig. 8b). The observed reductions in taxonomic richness have also been shown in a meta-analysis of field studies that highlights a relationship, which has recently been reported to be present across biomes (Handa et al. 2014), between these reductions and reduced ecosystem functions, such as leaf decomposition (Schäfer et al. 2012). In addition, recent studies (Hautier et al. 2015; Hooper et al. 2012) report that ecosystem biodiversity losses caused by anthropogenic drivers result in long-term decreases of ecosystem productivities and stabilities and thus fundamental ecosystem impairments. The RTL, which was originally defined by regulators as a threshold level that indicates a risk, is thus well suited to indicate substantial pesticide-induced adverse effects on aquatic ecosystems at the regional scale. This thesis, however, evidences for the first time the global extent of insecticide-related freshwater biodiversity impairments resulting from global high-intensity agriculture. It thus augments to our knowledge on the importance of drivers for the global freshwater biodiversity crisis and addresses

current research topics such as: “The worldwide distribution of toxicants is an important yet understudied driver of biodiversity, and the mechanisms relating toxicity to diversity have not been adequately explored.” (De Laender et al. 2014), or the fundamental question raised in *Nature News* by the Canadian toxicologist Keith Solomon whether pesticide adverse effects are restricted to only a few worst-case sites or common in global, agriculturally-influenced surface waters: "It begs the question as to what is happening in all the other streams out there." (Oosthoek 2013). In addition, this thesis responds to the call of 25 of the worlds leading agricultural experts in *Nature* (Sachs et al. 2010) for global data collection “to monitor the effects of agriculture on the environment, across major ecological and climatic zones, worldwide.“

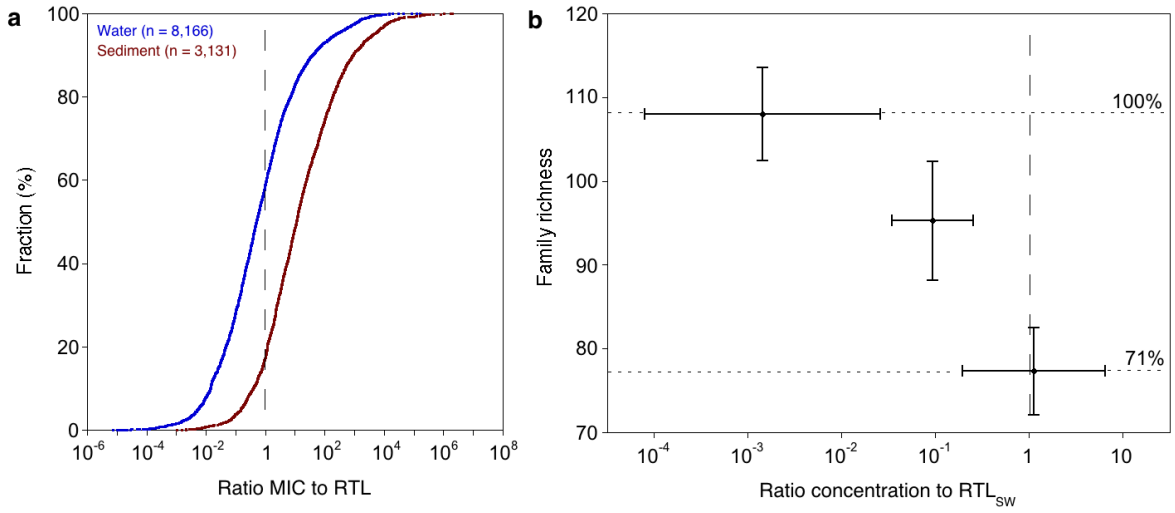

Figure 8 Distribution curves for global reported measured insecticide concentrations (MICs) in water and sediment relative to regulatory threshold levels (RTLs) and observed ecological effects of pesticide exposure on regional surface water biodiversity. (a) Blue represents the concentrations in water relative to the substance-specific RTL_{SW} (n = 8,166), and brown represents the concentrations in sediment relative to the substance-specific RTL_{SED} (n = 3,131). The vertical dashed line indicates the RTL. (b) Dependency of mean macroinvertebrate family richness at 60 agricultural stream sites on mean aqueous pesticide concentration to RTL_{SW} ratios. Data on family richness, pesticide exposure levels and categories were taken from ref. 14. The vertical dashed line indicates the RTL_{SW}, and the error bars denote 95% confidence intervals. Figure taken from *Appendix II*.

However, *Appendix II* reports that there are several aspects that indicate even higher risks for the ecological integrity of global surface waters: (i) the majority (i.e., > 80%) of insecticide concentrations were measured using sampling strategies likely to miss the ecotoxicologically highly relevant exposure peaks (Xing et al. 2013; see, also, 4.1 and specifically *Appendix I*); (ii) aquatic organisms are commonly exposed to mixtures of different pesticides as 81.3% of the samples contained up to 31 additional pesticide compounds; (iii) adverse ecological effects are triggered in the field already at MICs well below the RTL (Schäfer et al. 2012; Beketov et al. 2013; Fig. 8b); and (iv) a risk evaluation based on the more stringent EQS values, which do not tolerate clear (transient) effects on aquatic populations (Crommentuijn et al. 2000), leads to an even higher threshold level exceedance rate of 70.1% (n = 7,821).

Overall, *Appendix II* evidences for the first time that in concert with the more traditional factors such as nutrients and habitat degradation (see 1.4), agricultural insecticides are a major driver for the global freshwater biodiversity crisis. This thesis thus reports timely and important findings for the global environmental sciences community, which is currently about to discover that chemical pollutants need to be considered as key drivers of freshwater deterioration. Beyond that, *Appendix II* evidences that the highly elaborate and increasingly strict pesticide regulatory risk assessment schemes and legislations are ineffective and fail to prevent the global environment from substantial risks caused by agricultural pesticide use. *Appendix II* thus generally challenges the efficacies of current continental (e.g., FIFRA 1947; European Commission 2009) and global (e.g., Stockholm Convention on Persistent Organic Pollutants; Stockholm Convention [2004]) major pesticide laws and regulations. In essence, the findings of this thesis is of major importance for both the scientific and regulatory community, specifically considering that 18 and 24 of the 28 insecticide compounds included in this thesis currently are approved (and their agricultural use thus considered as environmentally justifiable) in highly regulated areas such as the EU and the US, respectively (see also 4.3 for further implications of this thesis for the regulatory risk assessment of pesticides).

Beside the analysis of insecticides` risks for global surface waters, this thesis also identified and quantified important drivers explaining these risks. Pesticide exposure and thus risks for aquatic ecosystems are the result of various interacting processes and factors. However, factors used within site-oriented pesticide exposure modelling (e.g., physicochemical properties, distance between last row of crop and the water edge, pesticide application rates) are already comparably well understood and quantified (Brown et al. 2002; Capri et al. 2005; FOCUS 2001). However, this thesis focuses on a further group of variables, which can only be analysed using a rather large-scale, meta-analytical approach, e.g. temporal trends, insecticide substance class, or country-specific environmental legislations; these variables, including their interactions, denote potentially important drivers for risks. Overall, the statistical analysis of the global insecticide exposure dataset (see *Appendix II*) identified five drivers (i.e., insecticide substance class, environmental regulatory quality, catchment size, sampling interval, sampling date) with a significant effect on the outcome variable MIC_{SW} to RTL_{SW} ratio. In detail, newer-generation insecticides, such as pyrethroids, led to significantly higher RTL_{SW} exceedances (65.8%) compared with both organophosphates (43.7%; $p < 0.001$) and organochlorines (24.4%; $p < 0.001$), and the latter two also differed significantly ($p < 0.001$) (Fig. 9a); the consideration of differences in insecticide classes` bioavailabilities and the ratios between the RTL_{SW} and the LOQ in additional linear model analyses did not alter this finding. This thesis thus is one of the first to report a clear relationship, which is in sharp contrast to the general perception in the scientific literature (e.g., Devine and Furlong 2007; Lamberth et al. 2013): The newer the insecticide substance class, the higher the acute risks for aquatic ecosystems. The main reason for this finding is the steady increase of acute toxicities in the development and market introduction of newer insecticide compounds during the last six decades (Spurlock and Lee 2008; Werner and Hitzfeld 2012). Although organophosphate insecticides are less persistent than organochlorines, their toxicity exceed those of the latter; however, the ban on many uses of these two insecticide classes, as well as the emergence of resistant insect species has led to their gradual replacement with other, even more potent classes of insecticides in recent years, among them particularly pyrethroids and more recently neonicotinoids (Werner and

Hitzfeld 2012; Denholm et al. 2002). Especially pyrethroids are far less persistent than organochlorines and less toxic to mammals than organophosphates, but non-target invertebrates and fish are susceptible already to extremely low concentrations and only very brief periods of exposure (Spurlock and Lee 2008; US EPA 2015c) due to the rapid onset of adverse effects (Schulz and Liess 2001; Lauridsen and Friberg 2005; Heckmann et al. 2005). In addition to the higher ecotoxicological risks for global surface waters proven by this thesis, this also poses new challenges for detection and regulation of these highly toxic and fast-acting newer-generation insecticides and it reveals failures of the pesticide industries` research and development efforts to develop more environmental friendly compounds.

The countries` environmental regulatory quality also affected insecticide risks, i.e. the linear model analysis detected significantly higher MIC_{SW} to RTL_{SW} ratios in countries with a low environmental regulatory quality (LERQ) compared to those with a high environmental regulatory quality (HERQ) (Fig. 9b). Although not unexpected due to less effective regulations (see below) this finding is alarming considering that future agricultural expansion and intensification (including higher pesticide use) is expected to increase mainly in biodiversity-rich tropical LERQ countries (Foley et al. 2011) due to (i) regional availabilities of suitable agricultural land (Tilman et al. 2001; Foley et al. 2011), (ii) raising food demand in the world`s poorest countries (Conway and Toenniessen 2003), (iii) major crop losses due to climate change especially in developing countries (Kiers et al. 2008), and (iv) increase in high-input Green Revolution techniques in regions (e.g., Africa) by now still dominated by traditional, low-input farming systems (Evenson and Gollin, 2003; IAASTD 2009; Ippolito et al. 2015); it overall follows that pesticide-induced environmental impacts are expected to increase considerably in LERQ countries. Green et al. (2005) state that current agricultural effects on wild nature and species are already greatest in developing countries and these authors thus alert that future agricultural intensification may lead to accelerating environmental degradation in those regions. However, the absolute percentage of the detected RTL_{SW} exceedances (39.9%) in the HERQ countries (such as the US, Canada, Germany, Japan, and Australia) is only slightly lower than that observed for the LERQ countries (42.2%) (Fig. 9b); this indicates that the environmental side-effects of the modern, high-intensity agricultural practices of HERQ countries, which rely heavily on pesticide use, are not controlled effectively by increasingly stringent environmental regulations at present (see 4.3 on this topic). Considering that agricultural insecticide use is expected to increase substantially also in HERQ countries (Kattwinkel et al. 2011; Tilman et al. 2001), effective risk mitigation and adaption strategies (see, e.g., Stehle et al. [2011] and Reichenberger et al. [2007] for further information) are needed to stall aquatic ecosystems` deterioration.

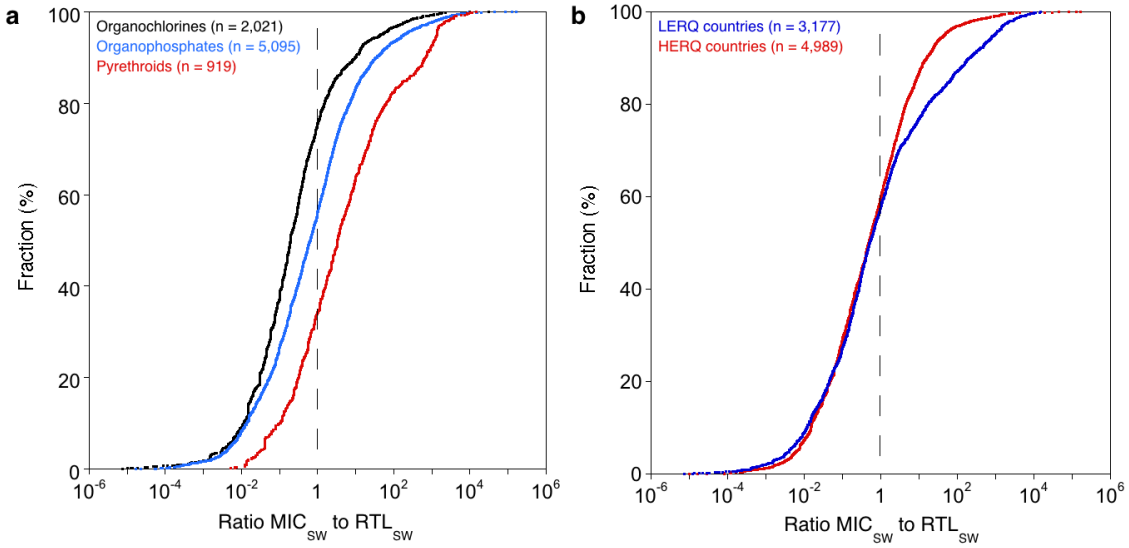

Figure 9 Effect of insecticide class and country environmental regulations on the distribution curves for reported measured insecticide concentrations in the water phase (MIC_{SW}) relative to substance-specific regulatory threshold levels (RTL_{SW}). (a) Black represents data obtained for organochlorine insecticides (n = 2,021), blue represents data obtained for organophosphate insecticides (n = 5,095), and red represents data obtained for pyrethroid insecticides (n = 919); 6.1% of the MIC_{SW} of neonicotinoids (n = 131) exceeded the RTL_{SW} (not displayed in the figure). (b) Distribution curves for MIC_{SW} relative to substance-specific RTL_{SW}. Blue represents concentrations measured in countries with low environmental regulatory quality (LERQ; n = 3,177), and red represents data measured in countries with high environmental regulatory quality (HERQ; n = 4,989). The vertical dashed lines indicate the RTL_{SW}. Figure taken from *Appendix II*.

Beside substance classes and environmental regulatory quality, the linear model analysis identified catchment size, sampling interval, and sampling date as important variables for insecticides` risks. In brief, surface waters with smaller catchments are exposed to higher insecticide concentrations (and consequentially risks) due to close proximities and huge connectivities with surrounding agricultural areas and limited dilution potentials (Karaouzas et al. 2011; Schulz 2004). Regarding the variable sampling interval, the results presented in *Appendix II* support the findings of *Appendix I* (see 4.1) and those of Xing et al. (2013), i.e., the highly transient insecticide exposure peaks (Fig. 5) can only accurately be detected using event-related sampling designs and are underestimated by fixed-interval monitoring campaigns. The three-way interaction among substance class, country regulatory classification, and sampling date derived from the linear model analysis (please see Supporting Information of *Appendix II* for a detailed discussion, the results of the test of simple slopes and the modified Johnson-Neyman technique, as well as a graphical presentation of the three-way interaction) contributes significantly to the variation in the concentration to RTL_{SW} ratios. The interaction results showed, amongst others, that for LERQ countries, the predicted MIC_{SW} to RTL_{SW} ratios for organochlorine and organophosphate insecticides significantly increased over time; this is reasoned by increased insecticide use and simultaneously weak or even non-existent pesticide regulation schemes and farmers' limited knowledge on appropriate pesticide use (Ecobichon 2001; Schreinemachers and Tipraqsa 2012). In opposite, for HERQ countries, the ratios of concentration to RTL_{SW} slightly decreased for all three insecticide classes, presumably due to more stringent pesticide application prescriptions and increasing environmental awareness of farmers. Nevertheless, the

overall results presented in *Appendix II* not only challenge the protectiveness of the current regulatory insecticide risk assessments and management procedures at the global scale but also particularly those currently enforced in HERQ countries as 49.5% (n = 2,681) of the MICs detected in these highly regulated countries after the year 2000 exceeded their respective RTLs, although, for example, major EU and US pesticide legislations were enforced much earlier.

Overall, *Appendix II* provides the first comprehensive field-data based analysis of insecticides` risks to global surface waters. It reveals that current pesticide regulations fail to protect worldwide freshwater ecosystems from elevated contamination levels caused by current high-intensity agricultural practices and conclusively evidences that insecticides are an important driver for the global freshwater biodiversity crisis. Moreover, *Appendix II* proved that the environmental risk increased with the development of newer-generation insecticides and that risks are high even in countries with stringent environmental regulations. This study is thus of major importance for chemical risk assessors and environmental protection agencies worldwide, as well as for the global environmental science community.

4.3 Level of protection, field-relevance, and deficiencies of the current pesticide regulatory risk assessment schemes: a case study for the European Union [RO4]

Plant protection products are the chemicals that have been regulated the longest and they are considered as the most intensively tested and regulated chemicals (ECPA 2003; ECPA 2012; Werner and Hitzfeld 2012). Specifically the European pesticide regulations (e.g., European Commission 2009; EFSA 2013) are, on a worldwide comparison, rather strict and aim to achieve a high level of environmental protection. Highly elaborated and science-based regulatory environmental risk assessment schemes are mandatory prior final pesticide authorisation in the EU. However, *Appendix III* shows that 44.7% (n = 1,566) of the MICs detected in EU surface waters exceeded respective RTLs; this challenges the overall efficacy of EU pesicide legislations and the fulfilment of the general protection goals outlined in Regulation (EC) No. 1107/2009, as well as of the specific protection goals defined by Nienstedt et al. (2012) and the EFSA PPR Panel (EFSA 2010) for the regulatory risk assessment of pesticides in the EU. In addition, we clearly evidence in *Appendix IV* that not only the endpoints of the regulatory effect assessment (i.e., RTL, see *Appendix III*) are exceeded in the field, but also those of the EU regulatory exposure assessment (i.e., PEC); 23% of step 3 and 31% of step 4 standard PECs (i.e., those FOCUS steps most relevant for final insecticide authorisation) were exceeded by respective MICs (Fig. 10). It must therefore overall be concluded based on the findings of *Appendices III* and *IV* that the highly elaborated EU pesticide legislations including the entire regulatory risk assessment as it is conducted at present fail to protect the aquatic environment. These findings thus complement the global results on insecticide risks presented in *Appendix II* by proving that not even the legislations and environmental risk assessment schemes of one of the world's most robust and stringent regulatory system, in which pesticides have undergone extensive reviews based on multi-year testing, are able to prevent excessive insecticide contamination of the environment. Two further critical results of *Appendix III* support this conclusion: first, the RTL exceedances (41.2%) of the 15 insecticide compounds currently authorised in the EU was only slightly lower than those of the

8 compounds, which are no longer approved (45.9%) and a linear model analysis predicting insecticides` risks could not detect a significant explanatory power for the differentiation between authorised and non-authorised compounds. We therefore have to conclude that the cancellation of the authorisation of obsolete active ingredients under Directive 91/414/EEC and Regulation (EC) No. 1107/2009 may have served alternative objectives but it did at least not reduce insecticides` acute risks for surface waters. Second, we identified even higher MIC_{SW} to RTL_{SW} ratios after the enforcement of the Directive 91/414/EEC in 1993 and for more recent sampling dates by the linear model analysis, i.e. independent of the influence of covariates such as increased detections of the more toxic pyrethroids in recent years; this, again, challenges the effectiveness of increasingly strict EU pesticide regulations enforced in recent years. However, other reasons not concerning aquatic organisms (e.g., high mammalian and avian toxicities of organophosphates) presumably led to the withdrawal of hazardous pesticide compounds under Directive 91/414/EEC, so that the overall environmental risks might nonetheless be reduced over time (Cross and Edward-Jones 2011).

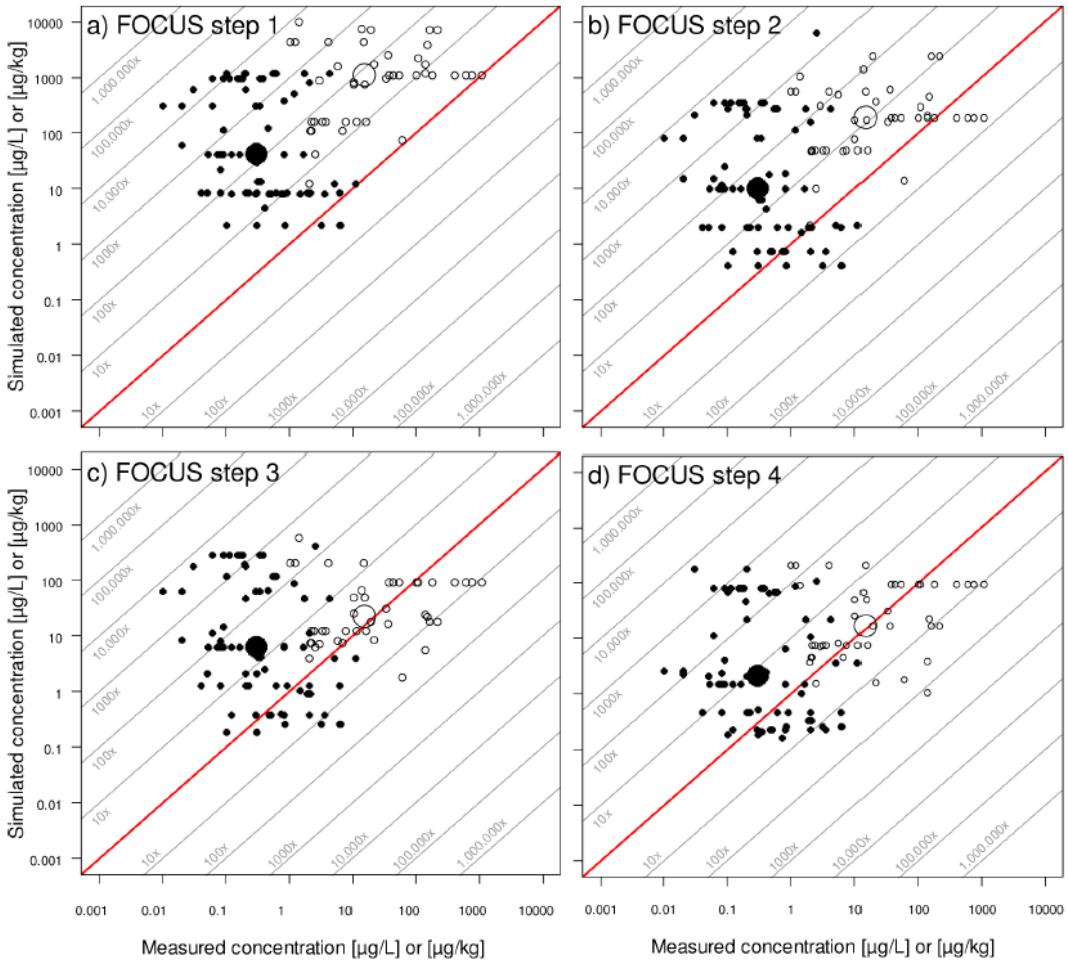

Figure 10 Relationship between simulated and measured insecticide concentrations (MICs) for FOCUS standard scenarios using information from field studies. (•) Water (n = 77); (○) sediment (n = 45); larger circles, overall medians. The 45° line denotes identity between PEC and MIC. The grey lines indicate over- and underestimation by orders of magnitude. The simulated concentrations are displayed on the y-axis so that the MFC overestimations are plotted above the 45° line. Figure taken from *Appendix IV* (modified).

Importantly, *Appendix IV* identified and quantified potential reasons for the occurrence of PEC and RTL exceedances in the field. In detail, a maximum amount of only 8% out of the in total 31% of MICs underpredicted by step 4 PECs (Fig. 10d) could theoretically be linked to farmers` malpractice during insecticide application, whereas 23% (i.e., 74% of step 4 underestimations) have to be attributed to FOCUS exposure model inaccuracies and therefore failures of the prospective regulatory risk assessment. Further on, *Appendix IV* provides important scientific explanations for the high RTL exceedances of newer, increasingly used pyrethroids reported in the *Appendices II and III* as it identified deficiencies of the PRZM runoff model, which is also used for the authorization of pesticide compounds in other countries such as the US (US EPA 2015b), specifically for highly hydrophobic compounds such as pyrethroids.

Beside its overall protectiveness, *Appendix III* also challenges the field-relevance of the EU pesticide regulatory risk assessment. In brief, we found highest RTL exceedances for MICs detected in small edge-of-field water bodies and for those definitively resulting from agricultural nonpoint source entries, i.e. for those cases that are the specific focus of the aquatic EU regulatory risk assessment (EFSA 2013). Even more, *Appendix III* also clearly proved that pesticides typically occur as mixtures in agricultural surface waters; this finding (i) challenges the protectiveness of the RTL, which is defined for single active ingredients only (EFSA 2013) and (ii) proves that current revisions of the EU pesticide regulations (European Commission 2009; EFSA 2013) does not respond to actual situations in the field although this fact has already been well documented in the scientific literature (e.g., Liess et al. 1999; Gilliom 2007; Schäfer et al. 2013; Moschet et al. 2014).

An in-depth analysis of the tiered approach of the EU environmental regulatory risk assessment reveals further deficiencies. In brief, this procedure leads to the contradictory fact that liberal higher tier RTLs (i.e., those RTLs defined by substantially reduced assessment factors [see *Appendix III* for details]) drive the final regulatory risk assessment specifically of extremely toxic insecticide compounds. In detail, these insecticides have a substantially higher intrinsic ecotoxicity potential towards aquatic (standard test) organisms compared to those of compounds authorised using tier I RTL_{SW} (Fig. 11). It follows that the most toxic insecticides are authorised using least conservative RTLs. Considering these high toxicity potentials and that such liberal higher tier RTLs are set with hardly any margin of safety, exceedances of these RTLs in the field should not occur in order to prevent unacceptable adverse effects. *Appendix III*, however, clearly disproves this assumption as 16.4% of MIC_{SW} detected in EU surface waters even exceeded the liberal higher tier RTL_{SW}. This finding is even more alarming considering that recent field studies (Schäfer et al. 2012; Beketov et al. 2013) and a meta-analysis (Peters et al. 2013) reported pesticide-induced adverse effects at concentrations even well below (i.e., 1/10 to 1/100) tier I RTL_{SW}; this evidences that even the conservative tier I RTL_{SW} are potentially not protective in the field, which may thus be even more true for the even less conservative higher tier RTL_{SW}. These findings reported here for insecticide compounds are in accordance with a recent study on aquatic ecosystems and fungicides (Zubrod et al. 2015), which also claimed that the higher tier regulatory EU risk assessment does not provide an adequate level of protection. We overall conclude that in addition to cases with RTL exceedances, the occurrence of unacceptable adverse effects in the field cannot be excluded for MICs complying with conservative tier I RTL_{SW} and are even more likely for the MICs that comply with higher tier RTL_{SW};

this, again, challenges the protectiveness of the presumed highly elaborated EU pesticide risk assessment.

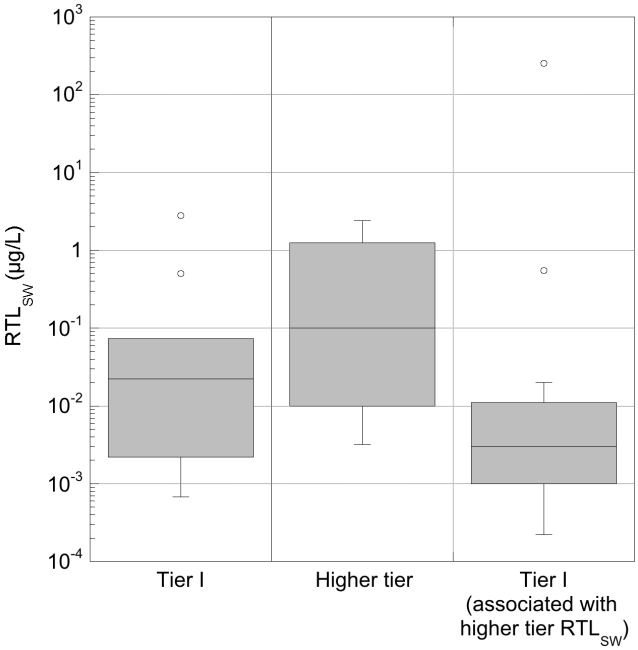

Figure 11 Comparison of the RTL_{SW} levels derived from the different tiers of the official EU pesticide risk assessment (n [insecticides] tier I risk assessment: 10, median RTL_{SW} = 0.02225 µg/L; n [insecticides] higher tier risk assessment: 13, median RTL_{SW} = 0.1 µg/L). The tier I RTL_{SW} associated with higher tier RTL_{SW} (n [insecticides]: 13, median RTL_{SW} = 0.003 µg/L) denote RTL_{SW} derived from the first tier risk assessment for the 13 compounds (central column), which were finally approved using higher tier studies (micro-/mesocosms; see Table 3). Figure taken from *Appendix III* (modified).

In summary, the data presented in the *Appendices III* and *IV* clearly evidence that both the regulatory exposure and the effect assessment as they are conducted at present for the authorisation of pesticide compounds in the highly-regulated EU need to be improved in terms of field-relevance and environmental protectiveness. We therefore propose in *Appendix III* the following five risk assessment amendments, which, however, should also be considered by regulatory agencies outside the EU:

(i) the protectiveness of the regulatory exposure assessment should be increased, e.g. by only considering FOCUS step 1 PECs or by applying safety factors to step 3 and step 4 PECs.

(ii) the uncertainties of the effect assessment should be substantially reduced, and its protectiveness must be increased; in particular, a critical reconsideration of the ecotoxicity endpoints (i.e., magnitude and duration of effects considered acceptable) and assessment factors used in higher tier effect assessment for the RTL derivation and authorisation of highly toxic compounds should thoroughly be addressed. In addition, mixture toxicity should be considered in the prospective assessment of effects, and the implementation of additional hazard-based cut-off criteria such as the new vTfMoA (very Toxic, fast Mode of Action) cut-off criteria proposed in *Appendix III* for extremely toxic compounds (e.g., pyrethroids) should be considered.

(iii) the overall link between the regulatory risk assessment and the actual situation in the field must considerably be strengthened, and findings from field studies on pesticide exposure and effects - like those summarised in the present thesis - be used for a retrospective validation of the current EU

regulatory risk assessment, particularly for its future development. The fundamental rationale of the risk assessment, i.e., to protect aquatic biocoenoses in the field, not in the computer or any sort of artificial test system, must be the driver for all future risk assessment revisions.

(iv) effective risk management measures (e.g., large non-cropped buffer zones between agricultural fields and water bodies) should be mandatory for all pesticide approvals.

(v) an obligatory validation of the risk assessment through targeted chemical and biological post-authorisation monitoring programmes must be implemented for compounds of concern to ensure that their application does not lead to unacceptable effects in the field.

Overall, *Appendices III* and *IV* reveal based on empirical data and official RTLs and PECs critical failures and deficiencies of the current European pre-application risk assessment for pesticides. These two publications evidence that both the regulatory exposure assessment, as well as the effect assessment substantially lack field relevance and protectiveness. These findings thus indicate that a critical reconsideration of the entire pesticide regulatory risk assessment approach is imperatively needed even in highly regulated entities such as the EU and provide important guidance for the future development of sound and protective pesticide regulations and risk assessment concepts.

5 Conclusion

Modern agriculture is essential for global food production and its importance is prospected to increase substantially to meet the challenge of feeding 9 billion people by 2050. However, this thesis alerts that the reliance on current high-intensity agricultural practices fostered in the context of the Green Revolution such as the tremendous use of agrochemicals critically threatens global ecosystems. Considering particularly pesticides, the prevailing perception of very elaborate standards of risk assessment and management for theses highly toxic chemicals has led to the general assumption that their use in agriculture is environmentally safe. The results of this thesis clearly disprove this assumption for the first time at the global scale and evidence that the surface water pollution resulting from current agricultural insecticide use considerably exceeds the limits set by regulatory agencies and constitutes an excessive environmental threat; essentially, insecticides constitute potential key drivers for the global freshwater biodiversity crisis and thus for overall losses of ecosystem productivities (Hooper et al. 2012) and stabilities (Hautier et al. 2015). These findings of global environmental importance have so far been overlooked due to a lack of global integrative assessments of insecticide risks for the worlds surface waters, as well as due to the fact that these risks are triggered by highly transient and short-term periods of exposure. Environmental monitoring is thus in the case of insecticides faced with the challenge to detect very low concentration levels occurring stochastically in time and space, which however, are of high ecotoxicological risks.

However, the results reported here clearly indicate that the increasing worldwide contamination of freshwater systems with highly toxic synthetic chemicals such as pesticides denote a key environmental threat. This thesis thus responds to a request to quantify the “concentrations of [...] pollutants in the global environment” (Rockström et al. 2010; Steffen et al. 2015), made with regard to chemical pollution as one of the two planetary boundaries that have not yet been quantified. The overall insights presented here even exceed this request by furthermore linking the concentrations of pollutants (i.e., insecticides) to the resulting consequences for the aquatic biodiversity and by revealing shortcomings of current regulatory risk assessment concepts; the latter may trigger far-reaching concerns because the regulatory evaluation process for pesticides is widely perceived to be highly elaborated in comparison with the process for many other groups of environmental chemicals, suggesting that the pollution resulting from these other chemicals may also far exceed established limits.

To date, an effective and sustainable global strategy against this mostly unseen contamination of aquatic environments by highly toxic chemicals barely exists (Schwarzenbach et al. 2006; Scheringer 2012). However, this thesis clearly evidences that new frontiers in pollution prevention, such as designing chemicals according to the principles of green chemistry and substitution of hazardous chemicals preferably by nonchemical solutions, as well as new approaches in risk assessment and management of synthetic chemicals are urgently needed. It is critically debated (e.g., Benbrook 2012; Gilbert 2013; Barfoot and Brookes 2014) if at all and to what extent the use of genetically modified crops enable pesticide use reductions; considering the multitude of environmental, human health, sociological, ethical, and economical issues related to this technology (see, for example, the *Nature* special issue [Vol. 497, Issue 7447; (2013)] “GM crops: Promise and Reality” at: http://www.nature.com/news/specials/gmcrops/index.html), a final conclusion on the relevance of

genetic engineering in future agriculture is beyond the scope of this thesis. However, considering particularly pesticides, the high specificities and toxicities designed to disrupt the physiology of specific taxonomic groups makes it nearly impossible to develop a pesticide that is selective for the target species yet nontoxic to phylogenetically related non-target organisms. It follows that the global pesticide treadmill (Turnbull and Hector 2010; Weddle et al. 2009; Lewis et al. 1997) must be resolved by means of a sustainable, second Green Revolution that allows to maintain and even increase the worldwide crop production without exceeding planetary-scale critical boundaries of global ecosystem pollution. Such a fundamental system change, which evolves worldwide agriculture into a sustainable design, can be achieved by reforming conventional agricultural systems and adopting promising approaches from organic farming (Seufert et al. 2012), including the elimination of pesticides wherever applicable, in concert with the closing of yield gaps on underperforming lands (Foley et al. 2011; Mueller et al. 2012), precision agricultural techniques (Gebbers and Adamchuk 2010) and reversing agricultural landscape simplification fostering insect pest pressure (Meehan et al. 2011). Ultimately, a key challenge for mankind in the 21st century will be to secure an adequate food production for current and future generations in a way that reverses the global environmental impacts of agrochemical-based high-intensity agriculture and thus preserves global biodiversity and ecosystem services essential to human existence.

6 References

Adriaanse P, et al. (1997) *Surface water models and EU registration of plant protection products - Dok. 6476/VI/96.* Final report of the work of the regulatory modelling working group of surface water models of FOCUS (FOrum for the Co-ordination of pesticide fate models and their USe).

Aiken LS, West SG (1991) *Multiple regression: Testing and interpreting interactions.* Sage Publications, Thousand Oaks.

Alston JM, Beddow JM, Pardey PG (2009) Agricultural research, productivity, and food prices in the long run. *Science* 325: 1209-1210.

Anderson JC, Dubetz C, Palace VP (2015) Neonicotinoids in the Canadian aquatic environment: A literature review on current use products with a focus on fate, exposure, and biological effects. *Science of the Total Environment* 505: 409-422.

Ashauer R, Boxall A, Brown C (2006) Predicting effects on aquatic organisms from fluctuating or pulsed exposure to pesticides. *Environmental Toxicology and Chemistry* 25: 1899–1912.

Barfoot P, Brookes G (2014). Key global environmental impacts of genetically modified (GM) crop use 1996–2012. *GM Crops & Food: Biotechnology in Agriculture and the Food Chain* 5: 149-160.

Baughman DS, Moore, DW, Scott GI (1989) A comparison and evaluation of field and laboratory toxicity tests with fenvalerate on an estuarine crustacean. *Environmental Toxicology and Chemistry* 8: 417–429.

Beketov MA, Kefford BJ, Schäfer RB, Liess M (2013) Pesticides reduce regional biodiversity of stream invertebrates. *Proceedings of the National Academy of Sciences of the United States of America* 110: 11039–11043.

Benbrook CM (2012) Impacts of genetically engineered crops on pesticide use in the U.S. – the first sixteen years. *Environmental Sciences Europe* 24: 24 (13 pp).

Bereswill R, Streloke M, Schulz R (2013) Current-use pesticides in stream water and suspended particles following runoff: exposure, effects, and mitigation requirements. *Environmental Toxicology and Chemistry* 32: 1254-1263.

Bollmohr S, Schulz R (2009) Seasonal changes of macroinvertebrate communities in a Western Cape river, South Africa, receiving nonpoint-source insecticide pollution. *Environmental Toxicology and Chemistry* 28: 809-817.

Brown CD, Bellamy PH, Dubus IG (2002) Prediction of pesticide concentrations found in rivers in the UK. *Pesticide Management Science* 58: 363-373.

Bundschuh M, Goedkoop W, Kreuger J (2014) Evaluation of pesticide monitoring strategies in agricultural streams based on the toxic-unit concept - Experiences from long-term measurements. *Science of the Total Environment* 484: 84-91.

Capri E, Balderacchi M, Yon D, Reeves G (2005) Deposition and dissipation of chlorpyrifos in surface water following vineyard applications in northern Italy. *Environmental Toxicology and Chemistry* 24: 852-860.

Collen B, et al. (2014) Global patterns of freshwater species diversity, threat and endemism. *Global Ecology and Biogeography* 23: 40-51.

Conway G, Toenniessen G (2003) Science for African food security. *Science* 299: 1187-1188.

Crawford CG (2004) Sampling strategies for estimating acute and chronic exposures of pesticides in streams. *Journal of the American Water Resources Association* 40: 485-502.

Crommentuijn T, Sijm D, de Bruijn J, van Leeuwen K, van de Plassche E (2000) Maximum permissible and negligible concentrations for some organic substances and pesticides. *Journal of Environmental Management* 58: 297-312.

Cross P, Edward-Jones G (2011) Variation in pesticide hazard from arable crop production in Great Britain from 1992 to 2008: An extended time-series analysis. *Crop Protection* 30: 1579-1585.

De Laender F, et al. (2014) The contribution of intra- and interspecific tolerance variability to biodiversity changes along toxicity gradients. *Ecology Letters* 17: 72-81.

Denholm I, Devine GJ, Williamsons MS (2002) Insecticide resistance on the move. *Science* 297: 2222-2223.

De Snoo GR (2003) Variations in agricultural practice and environmental care. In: *Pesticides: Problems, improvements, alternatives.* Eds Den Hond F, Groenewegen P, van Straalen NM. Blackwell, Oxford, UK, pp 100-112.

Devine GJ, Furlong MJ (2007) Insecticide use: Contexts and ecological consequences. *Agriculture and Human Values* 24: 281–306.

DG SANCO (2014) *EU pesticides database*. European Commission, Brussels. Available at: http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=homepage&language=EN.

Dudgeon D, et al. (2006) Freshwater biodiversity: Importance, threats, status and conservation challenges. *Biological Reviews* 81: 163-182.

Dynesius M, Nilsson C (1994) Fragmentation and flow regulation of river systems in the northern third of the world. *Science* 266: 753-762.

Ecobichon DJ (2001) Pesticide use in developing countries. *Toxicology* 160: 27-33.

ECPA (2003) *The ABCs of crop protection: Fast facts for European policy-makers.* European Crop Protection Association (ECPA), Brussels.

ECPA (2012) *Registering plant protection products in the EU.* European Crop Protection Association (ECPA), Brussels.

ECPA (2013) *Pesticides and biodiversity - Agricultural productivity and biodiversity conservation.* European Crop Protection Association (ECPA), Brussels.

Edwards DD, Moore PA (2014) Real exposure: Field Measurement of chemical plumes in headwater streams. *Archives of Environmental Contamination and Toxicology* 67: 413-425.

EFSA (2010) Scientific opinion on the development of specific protection goal options for environmental risk assessment of pesticides, in particular in relation to the revision of the guidance

documents on aquatic and terrestrial ecotoxicology (SANCO/3268/2001 and SANCO/10329/2002). *EFSA Journal* 8: 1821 (55 pp).

EFSA (2013) Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. *EFSA Journal* 11: 3290 (186 pp).

Elbert A, Haas M, Springer B, Thielert W, Nauen R (2008) Applied aspects of neonicotinoid uses in crop protection. *Pesticide Management Science* 64: 1099-1105.

European Commission (2009) Regulation (EC) No 1107/2009 of the European parliament and the council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Official Journal of the European Union* L309: 1–50.

European Commission (2013a) Commission implementing Regulation (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances. *Official Journal of the European Union* L139: 12-26.

European Commission (2013b) Directive 2013/39/EU of the European parliament and the council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. *Official Journal of the European Union* L226: 1-17.

Evenson RE, Gollin D (2003) Assessing the impact of the Green Revolution, 1960 to 2000. *Science* 300: 758-762.

FAO (2014) *The state of food insecurity in the world 2014. Strengthening the enabling environment for food security and nutrition.* Report of the Food and Agriculture Organization of the United Nations (FAO), the International Fund for Agricultural Development (IFAD) and the World Food Programme (WFP), Rome.

Fernandez D, et al. (2014) Calibration and field application of passive sampling for episodic exposure to polar organic pesticides in streams. *Environmental Pollution* 194: 196-202.

FIFRA (1947) *Federal Insecticide, Fungicide and Rodenticide Act*. US Federal Law amended in 1972 and 1988.

Finlayson CM, et al. (2005) Inland water systems. In: *Ecosystems and human well-being: Current state and trends, Volume 1.* Eds Hassan R, Scholes R, Ash N. Island Press, Washington, DC, pp 551-583.

Finley DB, et al. (1999) Case study: ecotoxicological assessment of urban and agricultural nonpoint source runoff effects on the Grass Shrimp, Palaemonetes pugio. In: *Ecotoxicology and risk assessment for wetlands*. Eds Lewis MA, et al. Society of Environmental Toxicology and Chemistry (SETAC), Pensacola, pp 243–273.

Fishel FM (2013a) *Pesticide use trends in the U.S.: Global comparison.* PI-143 Report, Pesticide Information Office, Institute of Food and Agricultural Sciences (IFAS), University of Florida, Gainesville, FL.

Fishel FM (2013b) *The EPA conventional reduced risk pesticide program.* PI-224 Report, Pesticide Information Office, Institute of Food and Agricultural Sciences (IFAS), University of Florida, Gainesville, FL.

FOCUS (2001) *FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC.* Report of the FOCUS working group on surface water scenarios. EC Document Reference SANCO/4802/2001-rev.2.

Foley JA, et al. (2005) Global consequences of land use. *Science* 309: 570-574.

Foley JA, et al. (2011) Solutions for a cultivated planet. *Nature* 478: 337–342.

Gebbers R, Adamchuk VI (2010) Precision agriculture and food security. *Science* 327: 828–831.

Gianessi L, Reigner N (2006) *Pesticide use in U.S. crop production: 2002 - Insecticides & other pesticides*. Crop Life Foundation, Washington, DC.

Giddings JM, Hall LW Jr, Solomon KR (2000) Ecological risks of diazinon from agricultural use in the Sacramento–San Joaquin River basins, California. *Risk Analysis* 20: 545–572.

Gilbert N (2013) A hard look at GM crops. *Nature* 497: 24-26.

Gilliom RJ (2007) Pesticides in U.S. streams and groundwater. *Environmental Science and Technology* 41: 3408-3414.

Gleick PH (1998) The human right to water. *Water Policy* 1: 487–503.

Götz CW, et al. (2010) Targeting aquatic microcontaminants for monitoring: exposure categorization and application to the Swiss situation. *Environmental Science and Pollution Research* 17: 341–354.

Green RE, Cornell SJ, Scharlemann JPW, Balmford A (2005) Farming and the fate of wild nature. *Science* 307: 550-555.

Guzsvany V, Csanádi J, Gaal F (2006) NMR study of the influence of pH on the persistence of some neonicotinoids in water. *Acta Chimica Slovenia* 53: 52–57.

Hall LW (2003) Analysis of diazinon monitoring data from the Sacramento and Feather River watersheds: 1991–2001. *Environmental Monitoring and Assessment* 86: 233–253.

Hallmann CA, Foppen RPB, van Turnhout CAM, de Kroon H, Jongejans E (2014) Declines in insectivorous birds are associated with high neonicotinoid concentrations. *Nature* 511: 341–343.

Handa IT, et al. (2014) Consequences of biodiversity loss for litter decomposition across biomes. *Nature* 509: 218-221.

Hart A (2001) *Probabilistic risk assessment for pesticides in Europe: implementation & research needs.* Report of the European workshop on probabilistic risk assessment for the environmental impacts of plant protection products (EUPRA). Central Science Laboratory, York, UK.

Hautier Y, et al. (2015) Anthropogenic environmental changes affect ecosystem stability via biodiversity. *Science* 348: 336-340.

Heckmann L-H, Friberg N, Ravn HW (2005) Relationship between biochemical biomarkers and pre-copulatory behaviour and mortality in *Gammarus pulex* following pulse-exposure to lambda-cyhalothrin. *Pesticide Management Science* 61: 627-635.

Holvoet K, Seuntjens P, Mannaerts R, De Schepper V, Vanrolleghem PA (2007) The dynamic water–sediment system: Results from an intensive pesticide monitoring campaign. *Water Science and Technology* 55: 177–182.

Hooper DU, et al. (2012) A global synthesis reveals biodiversity loss as a major driver of ecosystem change. *Nature* 486: 105-108.

House WA (1994) Sampling techniques for organic substances in surface waters. *International Journal of Environmental Analytical Chemistry* 57: 207–214.

IAASTD (2009) *Agriculture at a crossroads*. Global Report of the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD), Island Press, Washington, DC.

Ippolito A, et al. (2015) Modeling global distribution of agricultural insecticides in surface waters. *Environmental Pollution* 198: 54-60.

Iwafune T, Yokoyama A, Nagai T, Horio T (2011) Evaluation of the risk of mixtures of paddy insecticides and their transformation products to aquatic organisms in the Sakura River, Japan. *Environmental Toxicology and Chemistry* 30: 1834–1842.

Jergentz S, Mugni H, Bonetto C, Schulz R (2005) Assessment of insecticide contamination in runoff and stream water of small agricultural streams in the main soybean area of Argentina. *Chemosphere* 61: 817–826.

Jeschke P, Nauen R (2008) Neonicotinoids – from zero to hero in insecticide chemistry. *Pesticide Management Science* 64: 1084-1098.

Jeschke P, Nauen R, Schindler M, Elbert A (2011) Overview of the status and global strategy for neonicotinoids. *Journal of Agriculture and Food Chemistry* 59: 2829-2908.

Karaouzas I, Lambropoulou DA, Skoulikidis NT, Albanis TA (2011) Levels, sources and spatiotemporal variation of nutrients and micropollutants in small streams of a Mediterranean River basin. *Journal of Environmental Monitoring* 13: 3064–3074.

Kattwinkel M, Kühne J-V, Foit K, Liess M (2011) Climate change, agricultural insecticide exposure, and risk for freshwater communities. *Ecological Applications* 21: 2068-2081.

Kiely T, Donaldson D, Grube A (2004) *Pesticide industry sales and usages – 2000 and 2001 market estimates.* Report from the Office of Pesticide Programs, US Environmental Protection Agency, Washington, DC.

Kiers ET, et al. (2008) Agriculture at a crossroads. *Science* 320: 320-321.

Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS surface water models fail to predict insecticide concentrations in the field. *Environmental Science and Technology* 46: 8397-8404.

Kreuger J (1995) Monitoring of pesticides in subsurface and surface water within an agricultural catchment in southern Sweden. *British Crop Protection Council Monograph* 62: 81–86.

La N, Lamers M, Bannwarth M, Nguyen V, Streck T (2014) Imidacloprid concentrations in paddy rice fields in northern Vietnam: measurement and probabilistic modelling. *Paddy and Water Environment* 13: 191-203.

Lamberth C, Jeanmart S, Luksch T, Plant A (2013) Current challenges and trends in the discovery of agrochemicals. *Science* 341: 742–746.

Lauridsen RB, Friberg N (2005) Stream macroinvertebrate drift response to pulsed exposure of the synthetic pyrethroid lambda-cyhalothrin. *Environmental Toxicology* 20: 513-521.

Lewis WJ, van Lenteren JC, Phatak SC, Tumlinson JH (1997) A total system approach to sustainable pest management. *Proceedings of the National Academy of Sciences of the United States of America* 94: 12243-12248.

Liess M, Schulz R (2000) Sampling methods in surface waters. In: *Handbook of water analysis.* Eds Nollet LML. Marcel Dekker, New York, pp 1–24.

Liess M, Schulz R, Liess MHD, Rother B, Kreuzig R (1999) Determination of insecticide contamination in agricultural headwater streams. *Water Research* 33: 239–247.

Liess M, von der Ohe PC (2005) Analyzing effects of pesticides on invertebrate communities in streams. *Environmental Toxicology and Chemistry* 24: 954–65.

Line DE, et al. (1997) Nonpoint sources. *Water Environment Research* 69: 844–860.

Lubick N (2010) Endosulfan's exit: U.S. EPA pesticide review leads to a ban. *Science* 328:1466.

Loague K, Corwin DL, Ellsworth TR (1998) The challenge of predicting nonpoint source pollution. *Environmental Science and Technology* 32: 130–133.

Malaj E, et al. (2014) Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. *Proceedings of the National Academy of Science of the United States of America* 111: 9549–9554.

Matson PA, Parton WJ, Power AG, Swift MJ (1997) Agricultural intensification and ecosystem properties. *Science* 277: 504-509.

Meehan TD, Werling BP, Landis DA, Gratton C (2011) Agricultural landscape simplification and insecticide use in the Midwestern United States. *Proceedings of the National Academy of Science of the United States of America* 108: 11500-11505.

Moore MT, Schulz R, Cooper CM, Smith S Jr, Rodgers JH Jr (2002) Mitigation of chlorpyrifos runoff using constructed wetlands. *Chemosphere* 46, 827–835.

Moran KD (2003) *Insecticide market trends and potential water quality implications*. TDC Environmental, LLC Rep., San Mateo, CA.

Morrissey CA, et al. (2015) Neonicotinoid contamination of global surface waters and associated risk to aquatic invertebrates: A review. *Environment International* 74: 291–303.

Moschet C, et al. (2014) How a complete pesticide screening changes the assessment of surface water quality. *Environmental Science and Technology* 48: 5423-5432.

Mueller ND, et al. (2012) Closing yield gaps through nutrient and water management. *Nature* 490: 254–257.

Nienstedt KM, et al. (2012) Development of a framework based on an ecosystem services approach for deriving specific protection goals for environmental risk assessment of pesticides. *Science of the Total Environment* 415: 31–38.

Nilsson C, Reidy CA, Dynesius M, Revenga C (2005) Fragmentation and flow regulation of the world's large river systems. *Science* 308: 405-408.

Oerke E-C (2006) Crop losses to pests. *Journal of Agricultural Sciences* 144: 31-43.

Oosthoek, S (2013) Pesticides spark broad biodiversity loss. *Nature News (17 June 2013).* Available at: http://www.nature.com/news/pesticides-spark-broad-biodiversity-loss-1.13214.

Peters K, Bundschuh M, Schäfer RB (2013) Review on the effects of toxicants on freshwater ecosystem functions. *Environmental Pollution* 180: 324-329.

Pimentel D (2005) Environmental and economic costs of the application of pesticides primarily in the United States. *Environment, Development and Sustainability* 7: 229–252.

Purcell LA, Giberson DJ (2007) Effects of an azinphos-methyl runoff event on macroinvertebrates in the Wilmot River, Prince Edward Island, Canada. *The Canadian Entomologist* 139: 523-533.

Rabiet M, Margoum C, Gouy V, Carluer N, Coquery M (2010) Assessing pesticide concentrations and fluxes in the stream of a small vineyard catchment—effect of sampling frequency. *Environmental Pollution* 158: 737–748.

Rapp J (2011) *Abschätzung der global eingesetzten Insektizidwirkstoffmengen mithilfe eines geografischen Informationssystems.* Diploma thesis at the Institute for Environmental Science, University Koblenz-Landau, Landau.

Reichenberger S, Bach M, Skitschak A, Frede H-G (2007) Mitigation strategies to reduce pesticide inputs into ground- and surface water and their effectiveness: A review. *Science of the Total Environment* 384: 1–35.

Reuters (2008) *Record increase in global pesticides market to accelerate into 2013.* Specialists in Business Information. Available at: www.sbireports.com/about/release.asp?id=1249 (November 24, 2008).

Rockström J, et al. (2009) A safe operating space for humanity. *Nature* 461: 472–475.

Ruth L (2008) Bio or bust? The economic and ecological cost of biofuels. *Embo Reports* 9: 130-133.

Sachs J, et al. (2010) Monitoring the world`s agriculture. *Nature* 446: 558-560.

Sanchez-Bayo F (2014) The trouble with neonicotinoids. *Science* 346: 806-807.

Schäfer RB, et al. (2007) Effects of pesticides on community structure and ecosystem functions in agricultural streams of three biogeographical regions in Europe. *Science of the Total Environment* 382: 272-285.

Schäfer RB, Paschke A, Vrana B, Mueller R, Liess M (2008) Performance of the Chemcatcher© passive sampler when used to monitor 10 polar and semi-polar pesticides in 16 central European streams, and comparison with two other sampling methods. *Water Research* 42: 2707-2717.

Schäfer RB, et al. (2012) Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environmental Science and Technology* 46: 5134–5142.

Schäfer RB, et al. (2013) How to characterize chemical exposure to predict ecologic effects on aquatic communities? *Environmental Science and Technology* 47: 7996-8004.

Schäfer RB, van den Brink PJ, Liess M (2011a) Impacts of pesticides on freshwater ecosystems. In: *Ecological impacts of toxic chemical*s. Eds Sanchez-Bayo F, van den Brink PJ, Mann RM. Bentham Science Publishers Ltd, New York, pp 111-137.

Schäfer RB, von der Ohe PC, Kuhne R, Schüürmann G, Liess M (2011b) Occurrence and toxicity of 331 organic pollutants in large rivers of north Germany over a decade (1994 to 2004). *Environmental Science and Technology* 45: 6167–6174.

Scheringer M (2012) Umweltchemikalien 50 Jahre nach *Silent Spring:* Ein ungelöstes Problem. *GAIA* 21: 210-216.

Schreinemachers P, Tipraqsa P (2012) Agricultural pesticides and land use intensification in high, middle and low income countries. *Food Policy* 37: 616-626.

Schulz R (2001) Rainfall-induced sediment and pesticide input from orchards into the Lourens River, Western Cape, South Africa: Importance of a single event. *Water Research* 35: 1869–1876.

Schulz R (2004) Field studies on exposure, effects, and risk mitigation of aquatic nonpoint-source insecticide pollution: A review. *Journal of Environmental Quality* 33: 419–448.

Schulz R, Liess M (1999) A field study of the effects of agriculturally derived insecticide input on stream macro-invertebrate dynamics. *Aquatic Toxicology* 46: 155–176.

Schulz R, Liess M (2001) Toxicity of aqueous-phase and suspended particle-associated fenvalerate: chronic effects after pulse-dosed exposure of *Limnephilus lunatus* (Trichoptera). *Environmental Toxicology and Chemistry* 20: 185-190.

Schulz R, Peall SKC, Hugo C, Krause V (2001) Concentration, load and toxicity of spraydrift-borne azinphos-methyl at the inlet and outlet of a constructed wetland. *Ecological Engineering* 18: 239–245.

Schulz R, et al. (1998) A qualitative field method for monitoring pesticides in the edge-of-field runoff. *Chemosphere* 36: 3071–3082.

Schwarzenbach RP, et al. (2006) The challenge of micropollutants in aquatic systems. *Science* 313: 1072-1077.

Seufert V, Ramankutty N, Foley JA (2012) Comparing the yields of organic and conventional agriculture. *Nature* 485: 229–232.

Shires SW, Bennett D (1985) Contamination and effects in freshwater ditches resulting from an aerial application of cypermethrin. *Ecotoxicology and Environmental Safety* 9: 145–158.

Smith VH (2003) Eutrophication of freshwater and coastal marine ecosystems. A global problem. *Environmental Science and Pollution Research* 10: 126-139.

Solomon K, Giesy J, Jones P (2000) Probabilistic risk assessment of agrochemicals in the environment. *Crop Protection* 19: 649–655.

Spurlock F (2002) *Analysis of diazinon and chlorpyrifos surface water monitoring and acute toxicity bioassay data, 1991— 2001.* California Department of Pesticide Regulation, Environmental Hazards Assessment Program—Environmental Monitoring Branch, Sacramento, California.

Spurlock F, Bacey J, Starner K, Gill S (2005) A probabilistic screening model for evaluating pyrethroid surface water monitoring data. *Environmental Monitoring and Assessment* 109: 161–179.

Spurlock F, Lee M (2008) Synthetic pyrethroid use patterns, properties, and environmental effects. In: *Synthetic pyrethroids, occurrence and behavior in aquatic environments.* Eds Gan J, Spurlock F, Hendley P, Weston D. American Chemical Society, Washington, DC, pp 3–25.

Starner K, Spurlock F, Kelley K, Goh KS (2011) *Pesticides in surface water from agricultural regions of California 2006–2007*. Report 238, California Environmental Protection Agency, California Department of Pesticide Regulation, Sacramento, California.

Steffen W, et al. (2015) Planetary boundaries: Guiding human development on a changing planet. *Science* 347: 1259855-1.

Stehle S, et al. (2011) Pesticide risk mitigation by vegetated treatment systems: a meta-analysis. *Journal of Environmental Quality* 40: 1068–1080.

Stendera S, et al. (2012) Drivers and stressors of freshwater biodiversity patterns across different ecosystems and scales: A review. *Hydrobiologia* 696: 1-28.

Stockholm Convention (2004) *Stockholm Convention on persistent organic pollutants.* Secretariat of the Stockholm Convention, Chatalaine, Switzerland. Available at: http://chm.pops.int/default.aspx.

Stokstad E (2013) Pesticides under fire for risks to pollinators. *Science* 340: 674-676.

Stone WW, Gilliom RJ, Ryberg KR (2014) Pesticides in U.S. streams and rivers: Occurrence and trends during 1992−2011. *Environmental Science and Technology* 48: 11025-11030.

Strayer DL, Dudgeon D (2010) Freshwater biodiversity conservation: Recent progress and future challenges. *Journal of the North American Benthological Society* 29: 344-358.

Tennekes HA, Sanchez-Bayo F (2011) Time-dependent toxicity of neonicotinoids and other toxicants: Implications for a new approach to risk assessment. *Journal of Environmental and Analytical Toxicology* S4: 1-8.

Tilman D, Cassman KG, Matson PA, Naylor R, Polasky S (2002) Agricultural sustainability and intensive production practices. *Nature* 418: 671-677.

Tilman D, et al. (2001) Forecasting agriculturally driven global environmental change. *Science* 292: 281-284.

Touart LW, Maciorowski AF (1997) Information needs for pesticide registration in the United States. *Ecological Applications* 7: 1086-1093.

Turnbull LA, Hector A (2010) How to get even with pests. *Nature* 466: 36-37.

US EPA (2015a) *Conventional reduced risk pesticide program.* United States Environmental Protection Agency, Washington, DC. Available at: http://www2.epa.gov/pesticide-registration/conventional-reduced-risk-pesticide-program#status.

US EPA (2015b) *Technical overview of ecological risk assessment—analysis phase: Exposure characterization.* US Environmental Protection Agency, Washington, DC. Available at: http://www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_exp.htm.

US EPA (2015c) *ECOTOXicology database system, version 4.0.* US Environmental Protection Agency, Washington, DC. Available at: http://cfpub.epa.gov/ecotox/.

Vörösmarty CJ, et al. (2010) Global threats to human water security and river biodiversity. *Nature* 467: 555–561.

Wauchope RD (1978) The pesticide content of surface water draining from agricultural fields—A review. *Journal of Environmental Quality* 7: 459–472.

Weddle PW, Welter SC, Thomson D (2009) History of IPM in California pears – 50 years of pesticide use and the transition to biologically intensive IPM. *Pesticide Management Science* 65: 1287-1292.

Werner I, Hitzfeld B (2012) 50 years of ecotoxicology since *Silent Spring* – A review. *GAIA* 21: 217-224.

White HD (2009) Scientific communication and literature retrieval. In: *The Handbook of research synthesis and meta-analysis*. Eds Cooper H, Hedges LV, Valentine JC. Russel Sage Foundation, New York, ed. 2, pp 51-71.

Williams RJ, et al. (1995) Pesticide transport to surface waters within an agricultural catchment. *Journal of the Institution of Water and Environmental Management* 9: 72–81.

Woodward G, et al. (2012) Continental-scale effects of nutrient pollution on stream ecosystem functioning. *Science* 336: 1438-1440.

WWF (2014) *Living planet report 2014. Species and spaces, people and places.* WWF International, Gland, Switzerland.

Xing Z, et al. (2013) Influences of sampling methodologies on pesticide-residue detection in stream water. *Archives of Environmental Contamination and Toxicology* 64: 208-218.

Yu SJ (2008) *The toxicology and biochemistry of insecticides.* CRC Press, Boca Raton, Florida.

Zubrod JP, et al. (2015) Does the current fungicide risk assessment provide sufficient protection for key drivers in aquatic ecosystem functioning? *Environmental Science and Technology* 49: 1173-1183.

7 Declaration

I, the undersigned, author of this work, declare that this thesis is my own work and has not been submitted in any form for another degree or diploma at any university or other institution of tertiary education.

Information derived from the published or unpublished work of others has been acknowledged in the text and a list of references is given.

....

Date Signature

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10 Appendices

Appendix I

Stehle S, Knäbel A, Schulz R (2013) Probabilistic Risk Assessment of Insecticide Concentrations in Agricultural Surface Waters: A Critical Appraisal. *Environmental Monitoring and Assessment* 185: 6295-6310

Appendix II

Stehle S, Schulz R (2015) Agricultural Insecticides Threaten Surface Waters at the Global Scale. *Proceedings of the National Academy of Sciences of the United States of America* 112: 5750-5755

Appendix III

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Appendix IV

Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS Surface Water Models Fail to Predict Insecticide Concentrations in the Field. *Environmental Science and Technology* 46: 8397-8404

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Probabilistic risk assessment of insecticide concentrations in agricultural surface waters: a critical appraisal

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Abstract Due to the specific modes of action and application patterns of agricultural insecticides, the insecticide exposure of agricultural surface waters is characterized by infrequent and short-term insecticide concentration peaks of high ecotoxicological relevance with implications for both monitoring and risk assessment. Here, we apply several fixed-interval strategies and an event-based sampling strategy to two generalized and two realistic insecticide exposure patterns for typical agricultural streams derived from FOCUS exposure modeling using Monte Carlo simulations. Sampling based on regular intervals was found to be inadequate for the detection of transient insecticide concentrations, whereas event-triggered sampling successfully detected all exposure incidences at substantially lower analytical costs. Our study proves that probabilistic risk assessment (PRA) concepts in their present forms are not appropriate for a thorough evaluation of insecticide exposure. Despite claims that the PRA approach uses all available data to assess exposure and enhances risk assessment realism, we demonstrate that this concept is severely biased by the amount of insecticide concentrations below detection limits and therefore by the sampling designs. Moreover, actual insecticide exposure is of almost no relevance for PRA threshold level exceedance frequencies and consequential risk assessment outcomes. Therefore, we propose a concept that features a field-relevant ecological risk analysis of agricultural insecticide surface water exposure. Our study quantifies for the first time the environmental and economic consequences of inappropriate monitoring and risk assessment concepts used for the evaluation of short-term peak surface water pollutants such as insecticides.

Keywords Insecticides · Surface water exposure · Monitoring · Risk assessment

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Introduction

Insecticide surface water exposure and consequences for monitoring

Due to their global use and intentional release into the environment, agricultural pesticides have been shown to regularly enter aquatic ecosystems (Schwarzenbach et al. 2006; Schulz 2004). In general, pesticides are characterized by a complex input dynamic, i.e., their release into surface waters is usually coupled to rain events and seasonal use, which results in a discontinuous and complex exposure pattern (Götz et al. 2010; Rabiet et al. 2010). Herbicides and fungicides have relatively slow modes of action and thus must persist in the environment for longer time periods to act against their respective pests. Therefore, these

pesticides are used at comparably high application rates with several consecutive applications per season. In contrast, insecticides often show fast modes of action (Yu 2008) and thus do not need to persist in the environment to be effective against target organisms. This, in combination with the fact that their intrinsic toxicities are often very high (Schäfer et al. 2011; Schulz 2004), leads to discrete insecticide applications at comparably low rates. Concerning exposure and associated risks for aquatic ecosystems, these low application rates, accompanied by short field half lives and high K_{OC} values, result in infrequent and very short-term (i.e., a few hours) exposure events (Spurlock et al. 2005; Kreuger 1995). However, even in surface waters, which may be considered high-risk sites, a single transient insecticide surface water concentration can cause substantial adverse ecological effects (Schulz 2001b; Schulz and Liess 1999; Schulz 2004). When focusing on the ecological risk of agricultural insecticides use, particularly small headwater streams (e.g., catchment areas <100 km^2) may be at risk of pollution, as they have close proximities and huge connectivities with surrounding agricultural areas and limited dilution potentials (Karaouzas et al. 2011; Schulz 2004). All of these specific characteristics and watershed scale effects have to be taken into account when insecticide exposure and risk are evaluated using monitoring data. Static fixed-interval and fixed-station governmental monitoring programs are rather unspecific (Holvoet et al. 2007; House 1994) and tend to emphasize the importance of regularly occurring chemical stressors, such as nutrients and herbicides. They may thus underrate the exposure and risk of rare but potentially toxic contaminants such as insecticides. To overcome these serious shortcomings, Liess and Schulz (2000) and Schulz (2004) noted that the very specific insecticide exposure dynamics, which are driven mainly by distinct rainfall-, irrigation-, and application-related short-term entry events, need to be monitored using an event-triggered sampling design. This is in accordance with Strobl and Robillard (2008), who stated that sampling strategies have to be primarily oriented toward the expected variability of the quality of the water being examined.

Insecticide risk assessment approaches

During regulatory pesticide registration procedures, exposure models are used to predict environmental concentrations, which are subsequently compared to regulatory acceptable concentrations (RACs) using deterministic or probabilistic approaches (U.S. EPA 2011; DG SANCO 2002). However, when a pesticide has been in use, instead of modeling environmental concentrations, actual measured values from monitoring programs can be used for a deterministic or probabilistic risk evaluation. The deterministic risk assessment (DRA) of insecticide monitoring data (e.g., Iwafune et al. 2011; Jergentz et al. 2005; Karaouzas et al. 2011) is performed by comparing a point estimate of exposure to a threshold level within a hazard quotient (HQ) approach. This risk evaluation concept is rather simplified and not conclusive, as usually only the highest exposure incidence is assessed, whereas the full range of insecticide concentrations remains unconsidered (Solomon et al. 2000).

In contrast, probabilistic risk assessment (PRA) approaches focus on the frequencies or likelihoods of insecticide exposure incidences to exceed a specific threshold level (e.g., the RAC) by incorporating both variability and uncertainty into risk estimates. In detail, compilations of insecticide concentrations are used to derive a cumulative frequency distribution, which intentionally includes monitoring values below the limit of detection (LOD) (Solomon et al. 2000). Such PRA methods rapidly gained acceptance and have been used for the ecological risk assessment of insecticide surface water concentrations by several researchers (e.g., Giddings et al. 2000; Hall 2003) and regulatory agencies (e.g., Starner et al. 2011; Spurlock 2002) over the past decade. However, despite being more comprehensive, concerns were raised that probabilistic monitoring data evaluation approaches may yield misleading results if inappropriate data are included (Hart 2001). Here, we evaluate whether PRA methods are adequate for a thorough risk assessment of insecticide monitoring data by applying these to generalized and realistic insecticide exposure data.

The following three objectives were addressed:

(a) The derivation of two generalized and two realistic insecticide exposure patterns for small agricultural surface waters and their verification using real-world field studies
(b) The implications of insecticide exposure pattern characteristics for different sampling strategies commonly used in monitoring campaigns
(c) The consequences arising from insecticide exposure patterns in agricultural surface waters for

their environmental risk assessment using monitoring data and PRA, DRA, and relevance-driven risk assessment (RRA) concepts

Materials and methods

Derivation of a typical model insecticide and selection of real insecticides

A typical "model insecticide" was specified that typifies the median physicochemical properties, application rates, acute ecotoxicity, and LOD of all synthetic insecticide compounds (n=50, comprising 20 insecticide classes) currently listed on Annex I of the 91/414/EEC EU Pesticide Directive (DG SANCO 2008) (see Table S1 in electronic supplementary material (ESM) for all model insecticide parameters). Therefore, median values of physicochemical properties retrieved from the Footprint pesticide properties database (PPDB 2011) and official pesticide registration documents for all 50 synthetic insecticide compounds were calculated. In addition, the organophosphorous insecticide malathion, the neonicotinoid acetamiprid, and the pyrethroid deltamethrin were selected as examples of real insecticide compounds. These three compounds cover the three most important insecticide classes (Wirtz et al. 2009), are currently approved for and highly used in European (DG SANCO 2008) and US agriculture (Gianessi and Reigner 2006), and cover a wide range of physicochemical properties and application rates (see Table S1, ESM), which are important in determining the pesticide exposures of surface water systems (FOCUS 2001).

We derived a conservative RAC for the model insecticide and the three real compounds by calculating Tier I Uniform Principle (UP) criteria, which are commonly used for the ecotoxicological evaluation of insecticide monitoring data (e.g., Schäfer et al. 2012). In detail, the median EC_{50} (*Daphnia magna*) value retrieved from the Footprint pesticide properties database (PPDB 2011) for the 50 insecticide compounds listed on Annex I and the actual toxicity values for the three real insecticide compounds were divided by a safety factor of 100 (DG SANCO 2002; Table S1, ESM). The RAC, which is defined as part of the legal pesticide registration procedure, describes a concentration level that must not be exceeded to exclude adverse environmental effects (Brock et al. 2006). In addition, a representative LOD for the model insecticide was obtained by calculating the median value of all detection limits for insecticide compounds (n=22) analyzed in the USGS NAWQA monitoring campaign (Gilliom et al. 2006). This median LOD was in good accordance with LOD values typically observed for different insecticide compounds in monitoring campaigns (e.g., Pichon et al. 1998; Lepom et al. 2009). As no LOD values were available in the work of Gilliom et al. (2006) for deltamethrin and acetamiprid, the calculated median value was also used for these insecticides, whereas the actual LOD reported by Gilliom et al. (2006) was used for malathion (Table S1, ESM).

FOCUS simulations

Two generalized and two realistic insecticide exposure patterns were simulated for arable and permanent crops using the standardized forum for the coordination of pesticide fate models and their use (FOCUS) modeling approach for surface waters in Europe, which considers all non-point source entry routes (i.e., spray drift, runoff, drainage) potentially resulting in the exposure of surface waters to insecticides (FOCUS 2001). Predicted environmental concentrations (PECs) induced by spray drift during pesticide application or rainfall events were calculated using the FOCUS step 3 "realistic worst-case" surface water scenarios (FOCUS 2001) and the physicochemical properties of the model and the three real insecticides (Table S1, ESM). For arable crops, model and realistic insecticide PECs were simulated for eight model years using four out of six drainage scenarios (D1, D2, D4, and D5) and all runoff scenarios (R1–R4). Drainage scenarios D3 and D6 were excluded because no streams are associated with these scenarios. Concerning permanent crops, PECs were simulated for six model years using all available FOCUS stream scenarios, i.e., D4, D5, and R1–R4. We focused here on small streams (e.g., catchment areas <100 km^2), as these are by far the most abundant streams in Europe (European Environment Agency 2007) and the USA (Allan and Castillo 2007) and they are the most vulnerable to agricultural non-point source pollution (Schulz 2004; Karaouzas et al. 2011). In addition, the PECs calculated by FOCUS for streams included pesticide exposure from a 20-ha field in the upstream catchment, considerably increasing the field relevance and realism of the exposure simulations (FOCUS 2001).

For arable crops, winter cereals were selected as crops in the four drainage scenarios, and maize was selected in the four runoff scenarios, while pomes (apples) were chosen for the FOCUS drainage and runoff scenarios for permanent crops. The selection of all crops was based on (a) their importance for European agriculture in terms of cultivated area, as cereals and maize are the two most important arable crops and pomes are the second most important permanent crop (Eurostat 2007); (b) their importance in terms of insecticide use in European agriculture, as cereals, maize, and pomes require the highest volumes of insecticide among arable and permanent crops, respectively (European Commission 2000); and (c) the associations of crops and scenarios, as winter cereal is the only crop selectable for all drainage scenarios, maize is the most important arable crop available for all runoff scenarios, and most FOCUS scenarios for permanent crops are available for pomes (FOCUS 2001). The model insecticide application rates for winter cereals, maize, and pomes were extracted from Eurostat (2007) for the years 1992 to 2003 (see Table S1, ESM). However, as the amount of insecticides applied to cereals was only specified as <0.1 kg a.i./ha for each year, a conservative average of 0.09 kg a.i./ha was used for FOCUS calculations. With regard to malathion and acetamiprid, application rates for the different crops were obtained from official EU and US EPA pesticide registration documents, while those for deltamethrin were obtained from the official product label. The model insecticide was applied three times per growing season to winter cereals and maize and six times to pomes in each scenario. For malathion, acetamiprid, and deltamethrin, one application to winter cereals and maize (in total, three applications per season) and two to pomes (in total, six applications per season) were simulated. All insecticide application dates, intervals, and numbers were selected to be representative for real agricultural insecticide use (Ewald and Aebischer 2000; Schulz and Liess 1999; Süss et al. 2006).

Data aggregation, derivation, and verification of generalized and realistic insecticide exposure patterns

The results of the FOCUS calculations were combined into two generalized insecticide exposure patterns using the model insecticide results for arable and permanent crops to generate representative insecticide exposure patterns not influenced by individual compound properties. In addition, we synthesized two realistic insecticide exposure patterns using FOCUS simulation results for the application of the three real compounds to arable and permanent crops. In detail, the average application dates, the average number of days with PECs > LOD per year, the associated exposure durations (hourly resolution), and the average concentration heights, as well as the average exposure dates relative to the application dates, were calculated from the respective scenarios and model years for arable and permanent crops. Subsequently, we merged all these data into four synthesis graphics to create generalized and realistic annual insecticide exposure patterns for arable and permanent crops and a typical agricultural stream. Furthermore, ecotoxicological evaluations of these insecticide exposure profiles were performed by comparing aggregated concentrations to the RACs of the model insecticide and real compounds.

Evaluation of different sampling strategies

We reviewed 56 US governmental monitoring reports and compiled information on typical sampling strategies most frequently used for regulatory insecticide monitoring (see Table S2 in ESM). As a result, 97 % of the 2,775 measured insecticide concentrations were sampled using one of the following six sampling intervals: event-based sampling, daily, 3.5 days, weekly, 14 days, and monthly. Subsequently, these sampling intervals were applied to the generalized and realistic insecticide exposure patterns synthesized from FOCUS stream scenarios using Monte Carlo simulations (Crawford 2004). A program written in R (www.r-project.org; version 2.11.1 (R 2011)) was used to randomly sample from the population of model insecticide concentrations using the fixed monthly, 14 days, weekly, and 3.5-day sampling intervals. The date of the first sample in the first sampling period (e.g., first month, first week, etc.) to be taken in the model year was selected randomly using the R-function "sample()" (sampling of a random number with replacement). Subsequent samples were drawn at approximately fixed intervals. The exact intervals were allowed to vary randomly within a specified amount of time to simulate the variability inherent in water quality sampling programs because of logistic restrictions. The variations ranged from 1 day for weekly sampling up to 3 days for monthly sampling (14-day interval: ±2 days;

3.5-day interval: random sequence of 3- or 4-day intervals). A total of 100,000 Monte Carlo simulations were run for each of these sampling strategies, and the mean, minimum, and maximum numbers of insecticide detections per model year were computed. In addition, we considered the average exposure durations simulated by FOCUS for the model and realistic insecticide concentrations in the evaluation of all fixed interval sampling strategies.

In contrast, event-based sampling (Liess and Schulz 2000; Harmel et al. 2003) followed no fixed intervals but was triggered in a twofold manner: (a) spray drift-related pesticide entries were sampled manually during pesticide application (e.g., Schulz 2001a; Dabrowski et al. 2006), and (b) a runoff sample was taken by an automatic water sampler (e.g., Harmel et al. 2003; Jergentz et al. 2005) if a rainfall intensity of 15 mm/day occurred, which denotes a typical threshold level for moderate to heavy precipitation events leading to erosion events on agricultural land (Boardman et al. 1990; Bocheva et al. 2009). This rainfall intensity was also used as a trigger value for event-related runoff sampling in pesticide monitoring campaigns (Pedersen et al. 2006). We extracted the number of days exceeding 15 mm of irrigation or rainfall from FOCUS climate documents (FOCUS 2001) for each of the runoff and drainage scenarios for arable and permanent crops (see Table S3 in ESM) and subsequently applied the average number to the generalized and realistic yearly insecticide exposure patterns. Consequently, simulated event-driven runoff samples originated from the population of post-rainfall data points simulated by FOCUS.

For the overall evaluation of sampling strategies, we assumed that the two typical agricultural streams located in arable and permanent crop agri-environments were monitored within one sampling campaign. To facilitate an economic evaluation of all sampling strategies, we determined total costs of $300 per sample, which is composed of $200 of analytical cost per sample and $100 in additional costs for sample collection and preparation, travel costs, and equipment/supplies (California EPA 2006). However, no costs for the monitoring plan, data evaluation, quality assurance, or the reporting of monitoring results were included in this amount. For event-triggered sampling, in addition to $300 per sample, yearly costs of $1,500 were assumed, comprising $10,000 in acquisition costs for the automatic water sampler and $5,000 in maintenance charges over an expected service life of 10 years.

The field relevance of the simulated insecticide monitoring results was compared to real-world insecticide monitoring studies. We reviewed and compiled field studies reporting insecticide concentrations in small agricultural streams located in the same geographic regions as those covered by the FOCUS simulations used here (i.e., D1, D2, D4, D5 and R1–R4, see above) and compared these real-world sampling results to findings from Monte Carlo simulations conducted in this study.

Risk assessment procedures

Monitoring results derived from Monte Carlo simulations applied to generalized and realistic insecticide exposure patterns were subsequently evaluated using the following three risk assessment procedures:

(a) DRA, i.e., comparison of a single maximum exposure value to an RAC within an HQ approach
(b) PRA, i.e., comparing the cumulative frequency distribution of all monitoring data, including values below the LOD, to the RAC to achieve RAC-exceedance percentages. Given the fact that at least six concentrations > LOD are considered necessary to characterize a concentration frequency distribution (Giddings et al. 2000) and that the total number of insecticide exposure incidences are actually known in our study, we did not create centile ranks of concentrations and use regression analyses for the calculation of RAC-exceedance probabilities (e.g., Solomon et al. 2000), but rather we calculated PRA results by dividing the number of insecticide concentrations > RAC detected by a given sampling strategy by the amount of samples taken
(c) RRA, defined as the comparison of all insecticide concentrations > LOD to the RAC

Although it is not a typical practice, we performed the risk assessments not separately for each of the three realistic insecticide compounds but for all insecticide concentrations normalized by their RACs (i.e., normalization using HQ). This procedure does not bias risk assessment outcomes, yet it overcomes the restrictions of the small number of concentrations of individual real insecticide compounds available for exemplary risk assessments.

Results and discussion

Generalized and realistic insecticide exposure patterns in small agricultural streams

The generalized exposure patterns simulated for arable and permanent crops and a typical agricultural stream revealed the occurrence of 11 and 16 distinct model insecticide concentrations above the LOD, respectively (Fig. 1a, b, see Table S4 in ESM for detailed FOCUS scenario results). Considering the mean simulated model insecticide surface water exposure durations of 10.7 h in arable and 12.7 h in permanent crop scenarios, insecticide concentrations were detectable during only 1.3 % (117.7 h/year) and 2.3 % (203.2 h/year) of the time, respectively. Correspondingly, no concentrations were observed during the remainder of the model year, i.e., for 354 (arable crops) and 349 (permanent crops) out of 365 days. For real insecticides, applications resulted in six (0.62 % of the time; mean exposure duration, 9.1 h) and nine (0.97 % of the time; mean exposure duration, 9.7 h) individual surface water concentrations for arable and permanent crop scenarios, respectively (Fig. 1c, d; Table S5, ESM). Again, no concentrations were observed during most of the days of the model year, i.e., for 359 (arable crops) and 356 (permanent crops) out of 365 days. In contrast to the model insecticide results, which also indicated exposure incidences in October and November, simulations using real insecticide compounds resulted only in surface water exposures within the respective insecticide application periods, i.e., May to July for arable crops and June to August for permanent crops (Fig. 1). Generally, the highest concentrations for the model and real insecticides occurred via spray drift entries, while the subsequent exposure incidences due to drainage and runoff entries led to lower concentrations. However, nine out

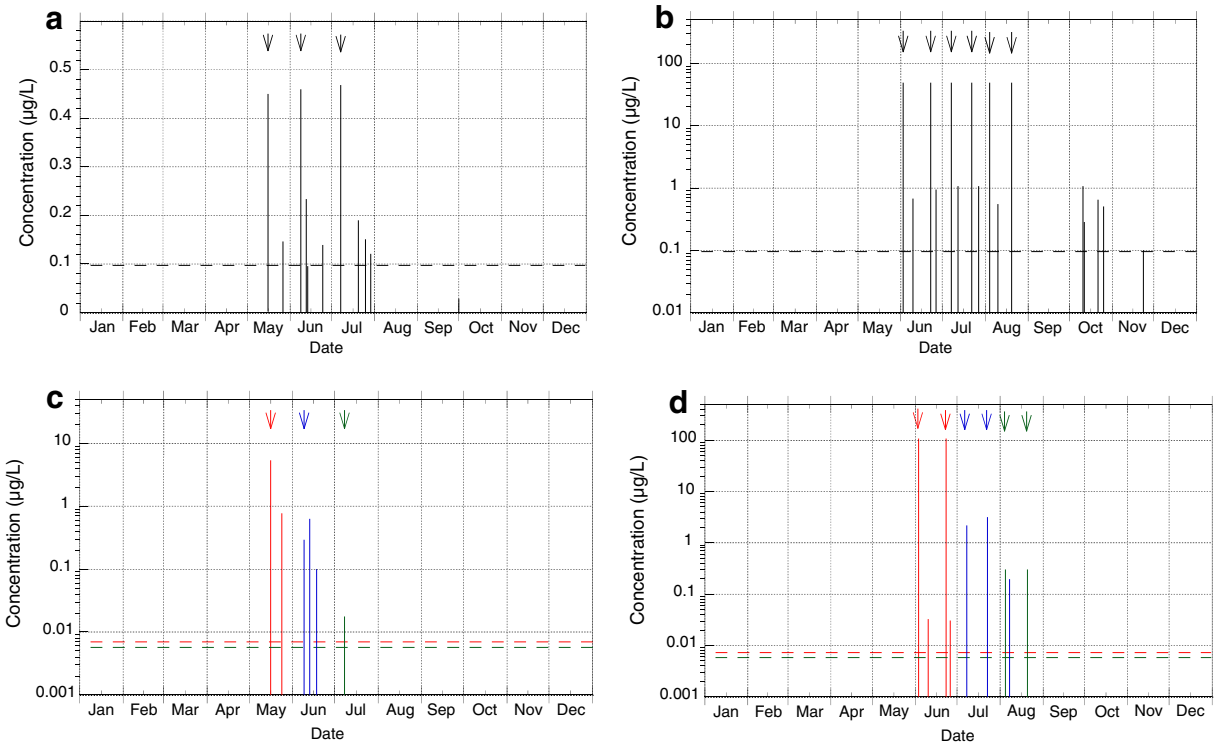

Fig. 1 Generalized (**a**, **b**) and realistic (**c**, **d**) insecticide (*red bars* malathion; *blue bars* acetamiprid; *green bars* deltamethrin) exposure profiles in a stream receiving agricultural non-point source pollution as synthesized from respective FOCUS surface water scenarios (see Table S4 and Table S5 in ESM for detailed FOCUS scenario results). **a**, **c** Arable crops with three insecticide applications (*arrows above bars*, application dates 16.5.; 9.6.; 7.7.); **b**, **d** six applications to permanent crops (application dates: 3.6.; 23.6.; 7.7.; 22.7.; 4.8.; 20.8.). The *dashed horizontal lines* indicate the RAC for the model insecticide (*black dashed line* in **a** and **b**, RAC=0.0995 µg/L) and the *red* (malathion, RAC=0.007 µg/L) and *green* (deltamethrin, RAC=0.0056 µg/L) *dashed horizontal lines* indicate the RAC for the real insecticides. The RAC for acetamiprid (498 µg/L) is not shown here

of 11 and 15 out of 16 model insecticide concentrations, as well as three out of six and six of nine real insecticide concentrations, exceeded their particular RACs in arable and permanent crop scenarios, respectively (Fig. 1).

The FOCUS model is currently used for regulatory pesticide surface water exposure predictions in the EU. Although a broad generalization of modeled insecticide concentration patterns for the variety of all real-world situations is challenging, recent reports (Ashauer and Brown 2007; Brock et al. 2008) confirmed that FOCUS predictions adequately reproduce the general pattern of pesticide surface water exposure, as comparisons between measured and simulated data showed broad correspondences with respect to overall concentration patterns, peak intervals, and decreases in peak concentration heights for successive pesticide exposure events. However, the frequency of insecticide concentration peaks in the field is potentially even lower than that calculated by FOCUS. Numerous field investigations in small agricultural streams showed, on average, a maximum of five insecticide inputs associated with one insecticide application period (e.g., Liess et al. 1999; Williams et al. 1995; Jergentz et al. 2005; Barra et al. 1995; Schulz et al. 1998). In addition to exposure frequencies, the mean exposure durations of 9.1 to 12.7 h are most likely overrated by FOCUS simulations, as various field studies clearly demonstrated a rapid decrease of insecticide concentrations to below the LOD within 3 to 4 h following inputs to small agricultural streams (Kreuger 1995; Spurlock et al. 2005; Crossland et al. 1982). These overestimations are due to several realistic worst-case assumptions, which determine simulated pesticide exposure in surface waters within the FOCUS modeling (FOCUS 2001). However, although the overall characteristics (i.e., the occurrence of few discrete insecticide concentrations) are comparable, a comparison of the simulated insecticide exposure patterns (Fig. 1) to those described in real-world monitoring studies confirms that there is a higher degree of realism for the realistic (Fig. 1c, d) compared to the generalized insecticide exposure profiles (Fig. 1a, b). Therefore, we focus in subsequent chapters on the realistic insecticide exposure patterns. Nevertheless, the generalized exposure patterns derived using a model insecticide, which is unbiased by physicochemical properties or application rates of individual compounds, clearly indicate that the occurrence of few, transient short-term peak concentration incidences in small agricultural streams is a specific exposure feature typical for all modern insecticides.

Despite their rare occurrences, the high intrinsic acute toxicity potentials of insecticides, accompanied by their fast modes of action (Yu 2008), lead to a higher ecotoxicological risk for aquatic ecosystems compared to herbicides and fungicides (Schäfer et al. 2011). The few available field studies on aquatic insecticide effects measured under normal farming practices (Table 1) indicate that insecticide concentrations > RAC indeed led to severe ecological effects (e.g., changes in community structure or function, changes in invertebrate dynamics, fish kills) in the affected aquatic ecosystems. Transferred to results concerning the realistic simulated exposure patterns (Fig. 1), this means that, although only very few insecticide exposure incidences are expected to occur in agricultural surface waters, these in fact constitute a high ecological risk (Table 2). It follows that there are urgent needs to adequately address these low-frequency/high-risk insecticide exposure patterns in monitoring campaigns and risk assessment concepts. Although one can argue that the Tier I UP criteria denote rather conservative RACs and other toxicity thresholds (e.g., those derived from species sensitivity distributions or mesocosm data) would presumably result in more realistic and less stringent RACs, evidence exists that the occurrence of insecticide concentrations well below (i.e., 1/10 to 1/100) their respective Tier I UP criteria already leads to unacceptable effects in stream ecosystems (Schäfer et al. 2012). It follows that the evaluation of the observed (Table 1) and simulated (Table 2) insecticide field concentrations using less stringent RACs would potentially result in substantial underestimations of ecological risks.

Implications for monitoring

All fixed-interval sampling regimes (i.e., monthly, 14 days, weekly, 3.5 days, daily) detected less than 50 % of the concentrations simulated for the realistic insecticide exposure patterns, as shown in Fig. 1c, d, resulting in peak detection errors of 60 to 100 % for the two typical agricultural streams (Table 3; see Table S6 in ESM for individual results for arable and permanent crops). The same holds true if the detection frequencies of RAC-exceeding concentrations are considered (Table 5), indicating that fixed-interval monitoring programs are unbiased with respect to time but seriously biased with respect to risk when highly

Table 1 Field studies reporting effects caused by insecticide exposure of small agricultural surface waters (adapted from Schulz (2004)) and related hazard quotients based on RAC

Insecticide	Observed field concentration (μg/L)	RAC[a] (μg/L)	HQ[b] (RAC[a])	Observed effect size and endpoint	Species	Source
Azinphos-methyl	0.87	0.011	**79**	46 % in situ mortality	*Chironomus* spec.	Schulz et al. (2001)
Chlorpyrifos	1.3	0.001	**1,300**	46 % in situ mortality	*Chironomus* spec.	Moore et al. (2002)
Cypermethrin	0.03	0.003	**10**	90 % abundance reduction	Various invertebrate species	Shires and Bennett (1985)
Endosulfan	1.44	4.4	0.33	Die-off	Various fish species	Finley et al. (1999)
Fenvalerate	0.11	0.0003	**367**	55 % in situ mortality	Shrimp (*P. pugio*)	Baughman et al. (1989)
Parathion-ethyl	6	0.025	**240**	100 % mortality	Various invertebrate species	Schulz and Liess (1999)

RAC regulatory acceptable concentration, *HQs* hazard quotients

[a] The Uniform Principle criterion was calculated by dividing the respective median LC50 (*D. magna*) values for the respective insecticide by a safety factor of 100 (see DG SANCO (2002) for details) and subsequently used here as the regulatory acceptable concentration

[b] Hazard quotients were calculated by dividing the observed insecticide concentrations by the RACs. HQs>1 are displayed in bold

Table 2 Simulated insecticide field concentrations, hazard quotients based on the RAC, and related expected effects in agricultural surface waters

Insecticide	Simulated field concentration (μg/L)	RAC[a] (μg/L)	HQ[b] (RAC[a])	Expected effect size	Date	Crop
Malathion	5.47	0.007	**782**	Very strong	16.5.	Arable
Malathion	0.729	0.007	**104**	Very strong	24.5.	Arable
Acetamiprid	0.29	498	0.0006	No effects	9.6.	Arable
Acetamiprid	0.65	498	0.0013	No effects	13.6.	Arable
Acetamiprid	0.1	498	0.0002	No effects	18.6.	Arable
Deltamethrin	0.018	0.0056	**3.23**	Strong	7.7.	Arable
Malathion	104.8	0.007	**14,976**	Extreme	3.6.	Permanent
Malathion	0.034	0.007	**4.83**	Strong	10.6.	Permanent
Malathion	105.4	0.007	**15,059**	Extreme	23.6.	Permanent
Malathion	0.032	0.007	**4.6**	Strong	27.6.	Permanent
Acetamiprid	2.28	498	0.0046	No effects	7.7.	Permanent
Acetamiprid	3.22	498	0.0065	No effects	22.7.	Permanent
Acetamiprid	0.199	498	0.0004	No effects	7.8.	Permanent
Deltamethrin	0.29	0.0056	**51.9**	Strong	4.8.	Permanent
Deltamethrin	0.29	0.0056	**51.9**	Strong	20.8.	Permanent

Insecticide exposure data were derived from realistic exposure patterns simulated by FOCUS exposure modeling (see Fig. 1c, d) for three real insecticide compounds

RAC regulatory acceptable concentration, *HQs* hazard quotients

[a] The Uniform Principle criterion was calculated by dividing the median LC50 (*D. magna*) values for the respective insecticides by a safety factor of 100 (see DG SANCO (2002) for details) and subsequently used here as the regulatory acceptable concentration

[b] Hazard quotients were calculated by dividing the simulated insecticide concentrations by the RACs. HQs>1 are displayed in bold

Table 3 Effectiveness and costs associated with different sampling strategies

Interval (no. of samples[a])	Mean[d] no. of detects (peak detection error[e] (%))	Mean[d] no. of non-detects	Percentage of non-detects	Costs per detection ($)	Total costs per year ($)
Monthly (24)	0 (100)	24	100	n/a	7,200
14 days (52)	0 (100)	52	100	n/a	15,600
Weekly (104)	1 (93.3)	103	99	31,200	31,200
3.5 days (208)	2 (86.6)	206	99	31,200	62,400
Daily[b] (730)	6 (60)	724	99.2	36,500	219,000
Event[c] (40)	15 (0)	25	62.5	1,000	15,000

Values were calculated and combined by applying Monte Carlo simulations to realistic insecticide exposure patterns synthesized from FOCUS exposure model calculations (Fig. 1c, d) for two typical agricultural streams located in arable and permanent crop agri-environments

[a] No. of samples refers to two typical agricultural streams, where one is located in arable and one in permanent crop agri-environments (see Table S6 in ESM for detailed results separated by crops)

[b] Despite the fact that one sample per day was taken, only two out of six (arable crops) and four out of nine (permanent crops) insecticide concentrations (total: six out of 15) were detected due to the respective mean exposure durations simulated by FOCUS

[c] Eighteen (arable crops) and 22 (permanent crops) samples (total 40) were considered to be taken by event-triggered sampling assuming three (arable crops) and six (permanent crops) spray events plus 15 (arable crops) and 16 (permanent crops) insecticide entry events potentially occurring due to 15 mm/day irrigation or rainfall as extracted from FOCUS climate documents (see Table S3, ESM) for the respective scenarios used here

[d] The minimum and maximum no. of detects calculated by Monte Carlo simulations were (min/max): monthly (0/1); 14 days (0/1); weekly (0/2); 3.5 days (0/2) in the case of arable crops and (min/max): monthly (0/1); 14 days (0/2); weekly (0/3); 3.5 days (0/3) in the case of permanent crops

[e] Defined as the percentage of non-detected insecticide concentrations out of all concentrations available. Calculated as follows: ((Total concentrations available − concentrations detected)/Total concentrations available) × 100

transient but very toxic insecticide concentrations are to be evaluated. However, with higher temporal resolutions of fixed-interval sampling strategies, the mean number of non-detects increased considerably in parallel with the increasing mean number of detections and decreasing peak detection errors. All sampling strategies based on fixed intervals resulted in high percentages of non-detects (99 to 100 %; Table 3), which compares well with findings from the generalized insecticide exposure pattern (Table S7, ESM) and from real-world monitoring studies (97.9 % non-detects in regular sampling programs, Table 4). This further confirms that fixed-interval sampling schemes are generally inappropriate for insecticide exposure assessment irrespective of particular insecticide properties and application schemes. This is alarming considering that small streams are those aquatic habitats most likely to be exposed to agricultural non-point source insecticide pollution (Schulz 2004) and that governmental monitoring predominantly relies on fixed-interval sampling (Holvoet et al. 2007; House 1994; see also Table S2, ESM). Our results further demonstrate that even the employment of a more flexible and sophisticated fixed-interval sampling strategy (i.e., increasing the sampling frequency from monthly to weekly or daily during insecticide application periods) would not improve insecticide monitoring results (Table 3), but only substantially increase monitoring program costs (see below).

In contrast, event-based sampling detected all insecticide concentrations with a peak detection error of 0 % (Table 3) and therefore also detected all RAC-exceedance incidences (Table 5). Thorough field monitoring of the typical low-frequency/high-risk insecticide exposure pattern thus inevitably requires an event-controlled sampling design. This is of particular importance because 50 % (arable crops) and 66.6 % (permanent crops) of the simulated realistic insecticide concentrations exceeded their RACs (Fig. 1), which underlines the high risk to aquatic communities (Table 2). Regarding the sampling of spray drift events, we acknowledge that this is a challenging approach, with both implications for logistics and manpower requirements, especially when targeting on the landscape level. However, the consideration of insecticide application recommendations as released by official

Table 4 Number of samples with insecticide concentrations < LOD (non-detects) extracted from real-world monitoring studies conducted in small agricultural surface waters

Reference	Region/ FOCUS scenario	No. of insecticides analyzed	Total no. of samples	No. (%) of non-detects	Sampling regime	Total program costs (costs per detection) ($)
Kreuger and Brink (1988)	Sweden; D1	5	378	361 (95.5)	14 days–monthly	113,400 (6,671)
Crawford (2004)	Ohio, USA; D1, D4	1	3,956	3,818 (96.5)	Event–3.5 days[a]; weekly–14 days[b]	1,186,800 (8,600)
Turnbull et al. (1995)	UK; D2	1	10	7 (70)	Event	4,500 (1,500)
Gregoire et al. (2010)	France; D4, R1	1	41	37 (90.2)	Event	13,800 (3,450)
Schäfer et al. (2007)	France; D5	4	16	5 (31.3)	Event	6,300 (573)
Sturm et al. (2000)	Germany; R1	4	85	78 (91.8)	Event	27,000 (4,500)
Tauler et al. (2001)	Portugal; R2, R4	3	256	230 (89.8)	Monthly[a]	76,800 (2,954)
Wilson and Foos (2006)	Florida, USA; R3	14	789	783 (99.2)	Daily	236,700 (39,450)
Senseman et al. (1997)	Arkansas, USA; R3	3	485	484 (99.7)	Regular intervals	145,500 (145,500)
Carter and Capri (2004)	Italy, Spain; R3, R4	1	4,640	4,611 (99.4)	n/a	1,392,000 (48,000)
Aguilar et al. (1999)	Spain; R4	2	20	20 (100)	Monthly[a]	6,000 (n/a)
Total		27	10,676	10,434 (97.4)		3,208,800 (13,260)

All FOCUS scenarios used for the syntheses of generalized and realistic exposure patterns (Fig. 1) were covered by these field studies

n/a no information available

[a] Sampling interval during application period

[b] Sampling interval during non-application period

extension services in the planning of monitoring programs for a particular study area, as well as the cooperation with local farmers, could provide a targeted approach for the effective sampling of spray drift-related exposure events. The necessity of employing event-based sampling for the detection of insecticides in the field has also been recognized in the scientific literature (e.g., Schulz et al. 1998; Liess and Schulz 2000; Schulz 2004). This study quantifies the general implications for the first time.

In addition to the fact that the information obtained for water quality management must be questioned when insecticide contamination is monitored using fixed-interval sampling, a cost–benefit analysis also highlights the deficiencies of this approach. As shown in Table 3, costs were more than a factor of 30 higher for positive detections by fixed-interval sampling compared to event-based sampling. Again, the economic analyses of both real-world monitoring studies (Table 4) and simulation results (Table 3) support this conclusion, as on average $14,549 and $32,966, respectively, had to be spent to detect one insecticide concentration > LOD in the field using fixed intervals, whereas only $2,506 and $1,000, respectively, were spent in the case of event sampling. Excepting monthly sampling, which did not detect any exposure incidences, the simulated total yearly surveillance costs were also substantially lower for event-based than for fixed-interval sampling strategies (Table 3).

Generally, water quality monitoring targets are characterized by multiple objectives and need multi-objective optimization (Kollat and Reed 2006). These objectives are usually conflicting and optimality must be defined in the context of objectives trade-offs, often by finding Pareto-optimal solutions, i.e., the improvement in one objective (e.g., an increased number of insecticide detections through more frequent sampling) is accompanied by disadvantages for another objective (e.g., higher monitoring costs) (Kollat and Reed 2006). However, in contrast to fixed-interval sampling, these trade-offs do not exist for event-based sampling of insecticide concentrations in small streams, as this approach results in a maximum of information (i.e., detection of all insecticide concentrations) at a minimum cost (Table 3). Overall, these findings may become increasingly relevant considering the extent of

Table 5 Risk assessment results for deterministic, probabilistic, and relevance-driven data evaluation approaches

Interval (no. of samples)	Mean[a] no. of RAC-exceeding concentrations detected (%)	Deterministic risk assessment: comparison of peak concentration to RAC	Probabilistic risk assessment based on RAC exceedance frequencies[c] (%)	Relevance-driven risk assessment: no. of relevant concentrations > RAC
Monthly (24)	0 (0)	n/a[b]	0	n/a[b]
14 days (52)	0 (0)	n/a[b]	0	n/a[b]
Weekly (104)	1 (11.1)	1 of 1	0.96	1 of 1
3.5 days (208)	2 (22.2)	1 of 1	0.96	1 of 2
Daily (730)	4 (44.4)	1 of 1	0.55	4 of 6
Event (40)	9 (100)	1 of 1	22.5	**9 of 15**
Theoretical concept		Based on the highest concentration	Based on all concentrations, including non-detects	Based on relevant concentrations, i.e., those > LOD

Data were combined from realistic insecticide exposure patterns for typical streams located in arable and permanent crop agro-ecosystems (Fig. 1c, d; Table 3). The actual ecological risks of insecticide concentrations can only be obtained by the relevance-driven evaluation of insecticide concentrations detected by event-triggered sampling (bold, see text for details)

DRA deterministic risk assessment, *PRA* probabilistic risk assessment, *RRA* relevance-driven data evaluation approaches, *RAC* regulatory acceptable concentration

[a] Mean no. of insecticide concentrations > RAC refers to 100,000 Monte Carlo simulations applied to a realistic insecticide exposure pattern considering mean exposure durations of 9.1 h (arable crops) and 9.4 h (permanent crops) (see Fig. 1 and Table 3 for details).

[b] No risk assessment results are available for monthly and 14-day sampling because no concentrations > LOD were detected

[c] Calculated by dividing the number of insecticide concentrations > RAC for each sampling interval by the amount of samples taken

the current economic crisis in the EU and the US and the associated budget restrictions in the governmental sector (Marshall 2008).

Implications for risk assessment

In the DRA approach, only the highest insecticide concentration is compared to the RAC. As a result, all monitoring findings derived from sampling strategies with one concentration > RAC indicate a risk independent of the actual number of RAC exceedances (Table 5). Overall, the deterministic concept ignores the temporal characteristics of exposure and therefore ignores the risks resulting from repeated insecticide concentrations caused by consecutive spray drift and runoff events that are relevant in terms of adverse ecological effects (Ashauer et al. 2006; Table 2). However, if DRA is perceived only as a risk screening tool, that is if one HQ>1 indicates unacceptable risk (e.g., Iwafune et al. 2011; Karaouzas et al. 2011), and subsequent risk mitigation measures are implemented, this concept may be protective. Nevertheless, DRA appears unsuitable for a realistic and thorough retrospective risk assessment of highly variable insecticide exposure.

The PRA concept uses all data points of insecticide monitoring programs to estimate ecological risks in terms of threshold level exceedance frequencies (Solomon et al. 2000; Hall 2003). Therefore, all risk estimates based on fixed-interval sampling regimes indicated extremely low RAC exceedance frequencies (Table 5) and, consequently, low ecological risks (see Table S8 in ESM for risk assessment results separated for arable and permanent crops and Table S9 in ESM for model insecticide risk assessment results). For instance, 99 to 100 % of samples taken at fixed intervals were below the LOD (Table 3), corresponding to RAC exceedance frequencies between 0 and 0.96 % (Table 5). In contrast, the application of an event-based sampling strategy and subsequent probabilistic data evaluation to the identical insecticide exposure data results in a completely different ecological risk assessment outcome, with 22.5 % of the samples exceeding RACs (Fig. 2a; Table 5). This large discrepancy in the outcomes of PRA clearly shows that, in contrast to DRA and RRA results (see below), the RAC exceedance probability depends, in the case of insecticides, almost exclusively on the amount of samples taken and not on the actual concentrations present in surface waters. An increase of a

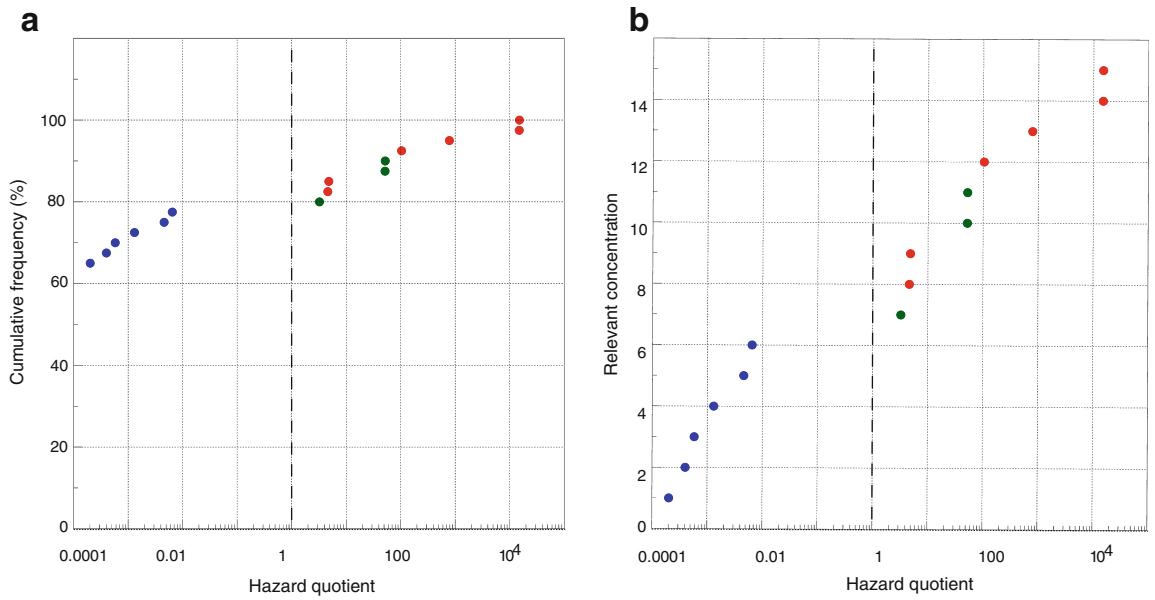

Fig. 2 Exemplary risk assessment results using probabilistic (**a**) and relevance-driven (**b**) insecticide monitoring data evaluation approaches. Concentrations were normalized by calculating hazard quotients and result from realistic insecticide exposure patterns for two typical agricultural streams located in arable and permanent crop agri-environments (see Fig. 1c, d, data taken from Tables 2, 3, and 5) constructed using event-triggered sampling. In Fig. 2a, 62.5 % of all (n=40) concentrations were below the LOD, resulting in an RAC (*vertical dashed line*) exceedance probability of 22.5 % (i.e., 9 out of 40 samples > RAC). In contrast, the relevance-driven risk assessment (**b**) assesses only insecticide concentrations > LOD, i.e., those which are of ecological relevance. As a result, a high ecological risk is indicated, as nine out of 15 concentrations exceeded their RACs

regular sampling frequency (e.g., from weekly to daily) disproportionally increases the number of non-detects (Table 3) and therefore results in a greater arbitrary decrease in the threshold level exceedance rate, even though a greater number of insecticide concentrations > RAC were detected (Table 5). In conclusion, if no considerations are made as to how accurate and complete available insecticide monitoring data are, PRA creates a false sense of certainty and protection. Overall, our simulated risk assessment results clearly demonstrate that a probabilistic evaluation of monitoring data including concentrations < LOD is unsuitable for contaminants characterized by a low frequency and extreme short-term peak exposure pattern such as insecticides. Although the PRA approach uses more information (data) compared to DRA, it introduces "new uncertainties" (Verdonck et al. 2007) into insecticide ecological risk assessment in that outcomes rely substantially on available input data, which, in turn, are ultimately determined by the methods (i.e., sampling intervals) used to acquire these data. This is alarming because PRA is already used for insecticide risk assessment for regulatory purposes. Presumably, no risk management options would be considered based on PRA applied to the data used here (Table 5), despite the fact that nine insecticide concentrations above mandatory threshold levels occurred in the field (Fig. 1) and potentially led to severe ecological effects (Tables 1 and 2), indicating that risk mitigation measures (e.g., no-spray buffer zones, constructed wetlands) would be strongly advisable (Stehle et al. 2011).

Relevance-driven risk assessment evaluates the actual, existing, and therefore potentially relevant insecticide contamination of an agricultural stream by comparing each detected concentration to the RAC within an HQ. It follows that RRA focuses on all insecticide exposure characteristics that are pertinent for adverse ecological effects, that is, the number of exposure incidences, concentration, and toxicity levels (Fig. 1). The hazard of insecticide exposure in small streams can therefore be quantified in terms of incidence frequencies and given ecotoxicological relevance (height of HQs) (Fig. 2b). This information also allows the RRA to rank surface water sites according to their insecticide exposure-related risks (e.g., Table S8, ESM), which, however, is

not fully possible for either deterministic or probabilistic approaches. Based on RRA outcomes, complementary and unbiased insecticide risk management decisions can be made. However, sampling is also a critical factor for relevance-driven risk assessment, as fixed-interval measurements led to inaccurate risk assessment results, with non-conformance increasing with larger sampling intervals (Table 5).

Overall, our results demonstrate that the RRA approach, which focuses on insecticide concentrations actually present, is appropriate for the specific low-frequency/high-risk insecticide exposure patterns in small streams. The combination of event-related insecticide monitoring with such a relevance-driven data evaluation concept constitutes a risk assessment approach that is not biased by methodological artifacts but is only driven by exposure features relevant for aquatic ecosystems.

Conclusions

Insecticide concentrations have very high toxic potentials and thus pose a great threat to the ecological integrities of agricultural surface waters. It is therefore important that monitoring programs accurately detect insecticide exposure incidences. Due to the very transient natures of insecticide exposures, this inevitably requires an event-based sampling design. Traditionally operated fixed-interval sampling regimes fail to accurately depict the typical low-frequency/high-risk exposure patterns of insecticides. As a consequence, risk assessment must be further improved for insecticides by considering the generation and interpretation of monitoring data. PRA concepts in particular potentially underestimate risks, as these do not address the substantial uncertainties arising from the extremely high variabilities of insecticide exposure data. An important paradigm for a realistic insecticide risk assessment must therefore be to focus on the environmental relevance of insecticide exposure, i.e., on the actually present and thus relevant ecological impacts of insecticides. Ultimately, the RRA concept demonstrated here for insecticides implies a general change of the focus of pesticide risk assessment from generalizations across all pesticide groups (herbicides, insecticides, fungicides) to an assessment accounting for pesticide property- and application-specific exposure assessment and from rigid reliance on occurrence probabilities to relevance-driven analyses that elucidate the actual ecological risks in the field.

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References

Aguilar, C., Ferrer, I., Borrull, F., Marce, R. M., & Barcelo, D. (1999). Monitoring of pesticides in river water based on samples previously stored in polymeric cartridges followed by on-line solid-phase extraction liquid chromatography diode array detection and confirmation by atmospheric pressure chemical ionization mass spectrometry. *Analytica Chimica Acta, 386*, 237–248.

Allan, J. D., & Castillo, M. M. (2007). *Stream ecology—structure and functioning of running waters* (2nd ed.). Dordrecht: Springer.

Ashauer, R., Boxall, A., & Brown, C. (2006). Predicting effects on aquatic organisms from fluctuating or pulsed exposure to pesticides. *Environmental Toxicology and Chemistry, 25*, 1899–1912.

Ashauer, R., & Brown, C. D. (2007). *Comparison between FOCUS output for pesticide concentrations over time and field observations*. University of York report for Defra project PS2231.

Barra, R., Vighi, M., & Di Guardo, A. (1995). Prediction of surface water input of chloridazon and chlorpyrifos from an agricultural watershed in Chile. *Chemosphere, 30*, 485–500.

Baughman, D. S., Moore, D. W., & Scott, G. I. (1989). A comparison and evaluation of field and laboratory toxicity tests with fenvalerate on an estuarine crustacean. *Environmental Toxicology and Chemistry, 8*, 417–429.

Boardman, J., Evans, R., Favis-Mortlock, D. T., & Harris, T. M. (1990). Climate change and soil erosion on agricultural land in England and Wales. *Land Degradation & Rehabilitation, 2*, 95–106.

Bocheva, L., Marinova, T., Simeonov, P., & Gospodinov, I. (2009). Variability and trends of extreme precipitation events over Bulgaria (1961–2005). *Atmospheric Research, 93*, 490–497.

Brock, T., Alix, A., Brown, C., Capri, E., Gottestbüren, B., Heimbach, F., et al. (2008). *ELINK—linking aquatic exposure and effects in the registration procedure of plant protection products*. Boca Raton: CRC.

Brock, T. C. M., Arts, G. H. P., Maltby, L., & Van den Brink, P. J. (2006). Aquatic risk of pesticides, ecological protection goals, and common aims in European Union Legislation. *Integrated Environmental Assessment and Management, 2*, e20–e46.

California Environmental Protection Agency (EPA). (2006). Amendments to the water quality control plan for the

Sacramento River and San Joaquin River basins for the control of diazinon and chlorpyrifos runoff into the Sacramento–San Joaquin Delta. Appendix D—Cost calculations. Final Staff Report.

Carter, A., & Capri, E. (2004). Exposure and effects of chlorpyrifos following use under southern European conditions, Catania (Italy), 9–10 April 2003. *Outlooks on Pest Management, 15*, 24–28.

Crawford, C. G. (2004). Sampling strategies for estimating acute and chronic exposures of pesticides in streams. *Journal of the American Water Resources Association, 40*, 485–502.

Crossland, N. O., Shires, S. W., & Benett, D. (1982). Aquatic toxicology of cypermethrin. III. Fate and biological effects of spray drift deposits in fresh water adjacent to agricultural land. *Aquatic Toxicology, 2*, 253–270.

Dabrowski, J. M., Bennett, E. R., Bollen, A., & Schulz, R. (2006). Mitigation of azinphos-methyl in a vegetated stream: comparison of runoff- and spray-drift. *Chemosphere, 62*, 204–212.

DG SANCO. (2002). Guidance document on aquatic ecotoxicology—in the context of the Directive 91/414/EEC. Sanco/3268/2001 rev.4 (final), Working Document. European Commission Health & Consumer Protection Directorate-General.

DG SANCO. (2008). EU pesticide database. http://ec.europa.eu/sanco_pesticides/public/index.cfm2011. Accessed 27 May 2011.

Commission, E. (2000). *Plant protection in the EU—consumption of plant protection products in the European Union (Data 1992–1996)*. Luxembourg: Office for Official Publications of the European Communities.

European Environment Agency. (2007). *Briefing small water bodies*. *Report prepared by European Topic Centre on water*. (EEA/ADS/06/001—Water).

Eurostat. (2007). *The use of plant protection products in the European Union—data 1992–2003*. Luxembourg: Office for Official Publications of the European Commission.

Ewald, J. A., & Aebischer, N. J. (2000). Trends in pesticide use and efficacy during 26 years of changing agriculture in southern England. *Environmental Monitoring and Assessment, 64*, 493–529.

Finley, D. B., Scott, G. I., Daugomah, J. W., Layman, S. L., Reed, L., Sanders, M., et al. (1999). Case study: ecotoxicological assessment of urban and agricultural nonpoint source runoff effects on the Grass Shrimp, *Palaemonetes pugio*. In M. A. Lewis, F. L. Mayer, R. L. Powell, M. K. Nelson, S. I. Klaine, & M. G. Henry (Eds.), *Ecotoxicology and risk assessment for wetlands* (pp. 243–273). Pensacola: Society of Environmental Toxicology and Chemistry (SETAC).

FOCUS (2001). *FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC*. *Report of the FOCUS Working Group on Surface Water Scenarios*. EC Document Reference SANCO/4802/2001-rev.2.

Gianessi, L., & Reigner, N. (2006). *Pesticide use in U.S. crop production: 2002—insecticides & other pesticides*. Washington: CropLife Foundation.

Giddings, J. M., Hall, L. W., Jr., & Solomon, K. R. (2000). Ecological risks of diazinon from agricultural use in the Sacramento–San Joaquin River basins, California. *Risk Analysis, 20*, 545–572.

Gilliom, R. J., Barbash, J. E., Crawford, C. G., Hamilton, P. A., Martin, J. D., Nakagaki, N., et al. (2006). *The quality of our nation's waters—pesticides in the nation's streams and ground water, 1992–2001. U.S. Geological Survey Circular 1291*. Reston: U.S. Geological Survey.

Götz, C. W., Stamm, C., Fenner, K., Singer, H., Scharer, M., & Hollender, J. (2010). Targeting aquatic microcontaminants for monitoring: exposure categorization and application to the Swiss situation. *Environmental Science and Pollution Research International, 17*, 341–354.

Gregoire, C., Payraudeau, S., & Domange, N. (2010). Use and fate of 17 pesticides applied on a vineyard catchment. *International Journal of Environmental Analytical Chemistry, 90*, 406–420.

Hall, L. W. (2003). Analysis of diazinon monitoring data from the Sacramento and Feather River watersheds: 1991–2001. *Environmental Monitoring and Assessment, 86*, 233–253.

Harmel, R. D., King, K. W., & Slade, R. M. (2003). Automated storm water sampling on small watersheds. *Applied Engineering in Agriculture, 19*, 667–674.

Hart, A. (2001). *Probabilistic risk assessment for pesticides in Europe: implementation & research needs*. Sand Hutton: Central Science Laboratory.

Holvoet, K., Seuntjens, P., Mannaerts, R., De Schepper, V., & Vanrolleghem, P. A. (2007). The dynamic water–sediment system: results from an intensive pesticide monitoring campaign. *Water Science and Technology, 55*, 177–182.

House, W. A. (1994). Sampling techniques for organic substances in surface waters. *International Journal of Environmental Analytical Chemistry, 57*, 207–214.

Iwafune, T., Yokoyama, A., Nagai, T., & Horio, T. (2011). Evaluation of the risk of mixtures of paddy insecticides and their transformation products to aquatic organisms in the Sakura River, Japan. *Environmental Toxicology and Chemistry, 30*, 1834–1842.

Jergentz, S., Mugni, H., Bonetto, C., & Schulz, R. (2005). Assessment of insecticide contamination in runoff and stream water of small agricultural streams in the main soybean area of Argentina. *Chemosphere, 61*, 817–826.

Karaouzas, I., Lambropoulou, D. A., Skoulikidis, N. T., & Albanis, T. A. (2011). Levels, sources and spatiotemporal variation of nutrients and micropollutants in small streams of a Mediterranean River basin. *Journal of Environmental Monitoring, 13*, 3064–3074.

Kollat, J. B., & Reed, P. M. (2006). Comparing state-of-the-art evolutionary multi-objective algorithms for long-term groundwater monitoring design. *Advances in Water Resources, 29*, 792–807.

Kreuger, J. (1995). Monitoring of pesticides in subsurface and surface water within an agricultural catchment in southern Sweden. *British Crop Protection Council Monograph No. 62*, *Pesticide Movement to Water*, 81–86.

Kreuger, J. K., & Brink, N. (1988). Losses of pesticides from agriculture. In IEAE (Ed.), *Pesticides: food and environmental implications* (pp. 101–112). Vienna: International Atomic Energy Agency.

Lepom, P., Brown, B., Hanke, G., Loos, R., Quevauviller, P., & Wollgast, J. (2009). Needs for reliable analytical methods for monitoring chemical pollutants in surface water under the European Water Framework Directive. *Journal of Chromatography. A, 1216*, 302–315.

Liess, M., & Schulz, R. (2000). Sampling methods in surface waters. In L. M. L. Nollet (Ed.), *Handbook of water analysis* (pp. 1–24). New York: Marcel Dekker.

Liess, M., Schulz, R., Liess, M. H.-D., Rother, B., & Kreuzig, R. (1999). Determination of insecticide contamination in agricultural headwater streams. *Water Research, 33*, 239–247.

Marshall, E. (2008). Breakdown of the year—financial meltdown. *Science, 322*, 1772.

Moore, M. T., Schulz, R., Cooper, C. M., Smith, S., Jr., & Rodgers, J. H., Jr. (2002). Mitigation of chlorpyrifos runoff using constructed wetlands. *Chemosphere, 46*, 827–835.

Pedersen, J. A., Yeager, M. A., & Suffet, J. H. M. (2006). Organophosphorus insecticides in agricultural and residential runoff: field observations and implications for total maximum daily load development. *Environmental Science and Technology, 40*, 2120–2127.

Pichon, V., Charpak, M., & Hennion, M. C. (1998). Multiresidue analysis of pesticides using new laminar extraction disks and liquid chromatography and application to the French priority list. *Journal of Chromatography. A, 795*, 83–92.

PPDB (2011). The Pesticide Properties Database (PPDB) developed by the Agriculture & Environment Research Unit (AERU), University of Hertfordshire, funded by UK National Sources and the EU-funded Footprint Project (FP6-SSP-022704). http://sitem.herts.ac.uk/aeru/footprint/index2.htm2011.

R Development Core Team. (2011). R: a language and environment for statistical computing, reference index version 2.11.1. http://www.r-project.org. Accessed 29 June 2011.

Rabiet, M., Margoum, C., Gouy, V., Carluer, N., & Coquery, M. (2010). Assessing pesticide concentrations and fluxes in the stream of a small vineyard catchment—effect of sampling frequency. *Environmental Pollution, 158*, 737–748.

Schäfer, R. B., Caquet, T., Siimes, K., Mueller, R., Lagadic, L., & Liess, M. (2007). Effects of pesticides on community structure and ecosystem functions in agricultural streams of three biogeographical regions in Europe. *Science of the Total Environment, 382*, 272–285.

Schäfer, R. B., von der Ohe, P. C., Kuhne, R., Schüürmann, G., & Liess, M. (2011). Occurrence and toxicity of 331 organic pollutants in large rivers of north Germany over a decade (1994 to 2004). *Environmental Science & Technology, 45*, 6167–6174.

Schäfer, R. B., von der Ohe, P. C., Rasmussen, J., Kefford, B. J., Beketov, M. A., Schulz, R., & Liess, M. (2012). Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environmental Science & Technology, 46*, 5134–5142.

Schulz, R. (2001a). Comparison of spraydrift- and runoff-related input of azinphos-methyl and endosulfan from fruit orchards into the Lourens River, South Africa. *Chemosphere, 45*, 543–551.

Schulz, R. (2001b). Rainfall-induced sediment and pesticide input from orchards into the Lourens River, Western Cape, South Africa: importance of a single event. *Water Research, 35*, 1869–1876.

Schulz, R. (2004). Field studies on exposure, effects and risk mitigation of aquatic nonpoint-source insecticide pollution—a review. *Journal of Environmental Quality, 33*, 419–448.

Schulz, R., Hauschild, M., Ebeling, M., Nanko-Drees, J., Wogram, J., & Liess, M. (1998). A qualitative field method for monitoring pesticides in the edge-of-field runoff. *Chemosphere, 36*, 3071–3082.

Schulz, R., & Liess, M. (1999). A field study of the effects of agriculturally derived insecticide input on stream macroinvertebrate dynamics. *Aquatic Toxicology, 46*, 155–176.

Schulz, R., Peall, S. K. C., Hugo, C., & Krause, V. (2001). Concentration, load and toxicity of spraydrift-borne azinphos-methyl at the inlet and outlet of a constructed wetland. *Ecological Engineering, 18*, 239–245.

Schwarzenbach, R. P., Escher, B. I., Fenner, K., Hofstetter, T. B., Johnson, C. A., von Gunten, U., et al. (2006). The challenge of micropollutants in aquatic systems. *Science, 313*, 1072–1077.

Senseman, S. A., Lavy, T. L., Mattice, J. D., Gbur, E. E., & Skulman, B. W. (1997). Trace level pesticide detections in Arkansas surface waters. *Environmental Science & Technology, 31*, 395–401.

Shires, S. W., & Bennett, D. (1985). Contamination and effects in freshwater ditches resulting from an aerial application of cypermethrin. *Ecotoxicology and Environmental Safety, 9*, 145–158.

Solomon, K., Giesy, J., & Jones, P. (2000). Probabilistic risk assessment of agrochemicals in the environment. *Crop Protection, 19*, 649–655.

Spurlock, F. (2002). *Analysis of diazinon and chlorpyrifos surface water monitoring and acute toxicity bioassay data, 1991—2001*. Sacramento: California Department of Pesticide Regulation, Environmental Hazards Assessment Program—Environmental Monitoring Branch

Spurlock, F., Bacey, J., Starner, K., & Gill, S. (2005). A probabilistic screening model for evaluating pyrethroid surface water monitoring data. *Environmental Monitoring and Assessment, 109*, 161–179.

Starner, K., Spurlock, F., Kelley, K., & Goh, K. S. (2011). *Pesticides in surface water from agricultural regions of California 2006–2007. Report 238*. Sacramento: California Environmental Protection Agency, California Department of Pesticide Regulation.

Stehle, S., Elsaesser, D., Gregoire, C., Imfeld, G., Niehaus, E., Passeport, E., et al. (2011). Pesticide risk mitigation by vegetated treatment systems: a meta-analysis. *Journal of Environmental Quality, 40*, 1068–1080.

Strobl, R. O., & Robillard, P. D. (2008). Network design for water quality monitoring of surface freshwaters: a review. *Journal of Environmental Management, 87*, 639–648.

Sturm, A., Wogram, J., Segner, H., & Liess, M. (2000). Different sensitivity to organophosphates of acetylcholinesterase from three-spined stickleback (*Gaterosteus aculeatus*). *Environmental Toxicology and Chemistry, 19*, 1607–1615.

Süss, A., Bischoff, G., Mueller, A. C. W., & Buhr, L. (2006). Chemisch-biologisches Monitoring zu Pflanzenschutzmittelbelastungen und Lebensgemeinschaften in den Gräben des Alten Landes. *Nachrichtenblatt Deutscher Pflanzenschutzdienst, 58*, 28–42.

Tauler, R., Azevedo, D. D., Lacorte, S., Cespedes, R., Viana, P., & Barcelo, D. (2001). Organic pollutants in surface waters from Portugal using chemometric interpretation. *Environmental Technology, 22*, 1043–1054.

Turnbull, A., Harrison, R., DiGuardo, A., Mackay, D., & Calamari, D. (1995). An assessment of the behavior of selected pesticides at ADAS Rosemaund. *BCPC, 62*, 87–92.

U.S. Environmental Protection Agency (EPA). (2011). Initiative to revise the ecological assessment process for pesticides—about ecological risk assessment. http://www.epa.gov/oppefed1/ecorisk/. Accessed 5 Dec 2011.

Verdonck, F. A. M., Souren, A., van Asselt, M. B. A., Van Sprang, P. A., & Vanrolleghem, P. A. (2007). Improving uncertainty analysis in European Union risk assessment of chemicals. *Integrated Environmental Assessment and Management, 3*, 333–343.

Williams, R. J., Brooke, D., Matthiesen, P., Mills, M., Turnbull, A., & Harrison, R. M. (1995). Pesticide transport to surface waters within an agricultural catchment. *Journal of the Institution of Water and Environmental Management, 9*, 72–81.

Wilson, P. C., & Foos, J. F. (2006). Survey of carbamate and organophosphorous pesticide export from a south Florida (U.S.A.) agricultural watershed: implications of sampling frequency on ecological risk estimation. *Environmental Toxicology and Chemistry, 25*, 847–2852.

Wirtz, K., Bala, S., Amann, A., & Elbert, A. (2009). A promise extended—future role of pyrethroids in agriculture. *Bayer CropScience Journal, 62*, 145–158.

Yu, S. J. (2008). *The toxicology and biochemistry of insecticides*. Boca Raton: CRC.

Electronic Supplementary Material

Probabilistic Risk Assessment of Insecticide Concentrations in Agricultural Surface Waters: A Critical Appraisal

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Table S1 Parameters for the model insecticide and three real insecticides used for FOCUS calculations and the derivations of generalized and realistic insecticide exposure patterns. The parameters for the model insecticide were synthesized from all synthetic insecticide compounds (n = 50) currently listed on Annex I of the 91/414/EEC EU pesticide directive (DG SANCO 2008)

Parameter	**Unit**	**Model insecticide**	**Malathion**	**Acetamiprid**	**Deltamethrin**
Insecticide class[a]		-	OP	Neo	Pyr
Molar mass	g/mol	351.68	330.36	222.67	505.2
Vapor pressure	Pa	9.3×10^{-7}	0.0031	1.73×10^{-7}	1.24×10^{-8}
Solubility	mg/L	1.13	148	2,950	0.0002
K_{OC}	ml/g	3,916	1,800	200	10,240,000
Freundlich isotherm (1/n)		0.95	0.94	0.9	1.1
DT_{50} water	d	5.85	0.4	4.7	17
DT_{50} soil	d	18	0.17	3	13
DT_{50} sediment	d	24.5	0.4	42.3	65
Application rates for cereals	kg/ha	0.09	1.12	0.05	0.005625
Application rates for maize	kg/ha	0.099	1.12	0.07	0.0075
Application rates for permanent crops (pomes)	kg/ha	0.792	1.8	0.055	0.00875
LOD		0.0095	0.014	0.0095	0.0095
48-h EC_{50} (*Daphnia magna*)	µg/L	9.95	0.7	49,800	0.56
Tier I UP criterion (RAC)	µg/L	0.0995	0.007	498	0.0056

[a] OP: organophosphorous insecticide; Neo: neonicotinoid; Pyr: pyrethroid.

Table S2 Sampling intervals extracted from 56 US governmental monitoring reports. In total, 3,049 insecticide surface water concentrations were reported (time span: 1976 – 2008), with sampling interval information available for 2,775 insecticide concentrations. Bold sampling intervals denote common sampling strategies applied to generalized and realistic insecticide exposure patterns within the present study

Sampling interval	**No. of concentrations (percentages) measured by a specific sampling interval**
Yearly	7 (0.25%)
Biannual (180 d)	12 (0.43%)
90 d	8 (0.29%)
60 d	18 (0.65%)
Monthly (30 d)	427 (15.4%)
21 d	13 (0.47%)
14-d	408 (14.7%)
Weekly	766 (27.6%)
3.5- or 4-d	202 (7.3%)
2-d	25 (0.9%)
Daily	370 (13.3%)
Event	519 (18.7%)
n/a[a]	274

[a] No information available.

Table S3 Number of irrigation and rainfall events exceeding 15 mm per day for the different runoff and drainage scenarios and crop combinations. Values were extracted from FOCUS climate documents (FOCUS 2001)

Scenario	Crop	No. of irrigation and rainfall events > 15 mm/day per year
D1	Winter cereals	6
D2	Winter cereals	5
D4	Winter cereals	6
D5	Winter cereals	4
R1	Maize	8
R2	Maize	33
R3	Maize	24
R4	Maize	32
Mean (arable crops)		**15**
D4	Pomes	6
D5	Pomes	4
R1	Pomes	8
R2	Pomes	33
R3	Pomes	15
R4	Pomes	30
Mean (permanent crops)		**16**

Table S4 Detailed results of FOCUS step 3 calculations for the model insecticide used to derive a generalized insecticide concentration pattern (see Materials and Methods for details)

Scenario[a]	Location	Application dates	No. of exposure events (route of entries[b])	Days (percentage) with concentration > LOD[c]
Arable crops (3 applications)				
D1	Sweden	25.04.; 14.05.; 17.06.	3 (3 s)	3 (0.8%)
D2	UK	07.05.; 11.05.; 02.06.	3 (3 s)	10 (2.7%)
D4	Denmark	25.04.; 05.05.; 01.06.	3 (3 s)	3 (0.8%)
D5	France	25.04.; 11.05.; 31.05.	3 (3 s)	3 (0.8%)
R1	Germany	01.06.; 11.07.; 20.08.	26 (3 s; 23 r)	26 (7.1%)
R2	Portugal	04.06.; 16.07.; 05.08.	4 (3 s; 1 r)	4 (1.1%)
R3	Italy	02.06.; 06.07.; 01.08.	15 (3 s; 12 r)	15 (4.1%)
R4	France	01.06.; 03.07.; 07.08.	19 (3 s; 16 r)	20 (5.5%)
Permanent crops (6 applications)				
D4	Denmark	01.06.; 04.07.; 18.07.; 01.08.; 13.08.; 27.08.	11 (6 s; 5 d)	11 (3%)
D5	France	09.06.; 09.07.; 21.07.; 04.08; 17.08.; 29.08.	6 (6 s)	12 (3.3%)
R1	Germany	01.06.; 18.06.; 30.06.; 12.07.; 27.07.; 20.08.	10 (6 s; 4 r)	10 (2.7%)
R2	Portugal	02.06.; 14.06.; 06.07.; 18.07.; 30.07.; 11.08.	16 (6 s; 10 r)	18 (4.9%)
R3	Italy	01.06.; 18.06.; 01.07.; 26.07.; 07.08.; 19.08.	15 (6 s; 9 r)	23 (6.3%)
R4	France	01.06.; 15.06.; 27.06.; 09.07.; 25.07.; 11.08.	22 (6 s; 16 r)	23 (4.9%)

[a] Arable crops: winter cereals in D scenarios and maize in R scenarios. Permanent crops: pomes (apples) in D and R scenarios.
[b] Routes of entry: s: spray drift; r: rainfall- or irrigation-induced runoff; d: drainage.
[c] Limit of detection.

Table S5 Detailed results of FOCUS step 3 calculations for three real insecticide compounds used to derive a realistic insecticide concentration pattern (see Materials and Methods for details)

Scenario[a]	Location	Insecticide	Application dates	No. of exposure events (route of entries[b])	Sum[c] of days (percentage) with concentration > LOD[d]
Arable crops (3 applications)					
D1	Sweden	Malathion	25.04.	1 (1 s)	3 (0.82)
		Acetamiprid	14.05.	1 (1 s)	
		Deltamethrin	17.06.	1 (1 s)	
D2	UK	Malathion	07.05.	1 (1 s)	14 (3.8%)
		Acetamiprid	11.05.	3 (1 s; 2 d)	
		Deltamethrin	02.06.	1 (1 s)	
D4	Denmark	Malathion	25.04.	1 (1 s)	3 (0.82)
		Acetamiprid	05.05.	1 (1 s)	
		Deltamethrin	01.06.	1 (1 s)	
D5	France	Malathion	25.04.	1 (1 s)	3 (0.82)
		Acetamiprid	11.05.	1 (1 s)	
		Deltamethrin	31.05.	1 (1 s)	
R1	Germany	Malathion	01.06.	1 (1 s)	4 (1.1%)
		Acetamiprid	11.07.	2 (1 s; 1 r)	
		Deltamethrin	20.08.	1 (1 s)	
R2	Portugal	Malathion	04.06.	1 (1 s)	3 (0.82)
		Acetamiprid	16.07.	1 (1 s)	
		Deltamethrin	05.08.	1 (1 s)	
R3	Italy	Malathion	02.06.	1 (1 s)	6 (1.6%)
		Acetamiprid	06.07.	4 (1 s; 3 r)	
		Deltamethrin	01.08.	1 (1 s)	
R4	France	Malathion	01.06.	2 (1 s; 1 r)	7 (1.9%)
		Acetamiprid	03.07.	4 (1 s; 3 r)	
		Deltamethrin	07.08.	1 (1 s)	
Permanent crops (6 applications)					
D4	Denmark	Malathion	01.06.; 04.07.	2 (2 s)	6 (1.6%)
		Acetamiprid	18.07.; 01.08.	2 (2 s)	
		Deltamethrin	13.08.; 27.08.	2 (2 s)	
D5	France	Malathion	09.06.; 09.07.	2 (2 s)	8 (2.2%)
		Acetamiprid	21.07.; 04.08.	2 (2 s)	
		Deltamethrin	17.08.; 29.08.	2 (2 s)	
R1	Germany	Malathion	01.06.; 18.06.	3 (2 s; 1 r)	9 (2.5%)
		Acetamiprid	30.06.; 12.07.	4 (2 s; 2 r)	
		Deltamethrin	27.07.; 20.08.	2 (2 s)	
R2	Portugal	Malathion	02.06.; 14.06.	2 (2 s)	8 (2.2%)
		Acetamiprid	06.07.; 18.07.	2 (2 s)	
		Deltamethrin	30.07.; 11.08.	2 (2 s)	
R3	Italy	Malathion	01.06.; 18.06.	3 (2 s; 1 r)	11 (3%)
		Acetamiprid	01.07.; 26.07.	4 (2 s; 2 r)	
		Deltamethrin	07.08.; 19.08.	2 (2 s)	
R4	France	Malathion	01.06.; 15.06.	5 (2 s; 3 r)	13 (3.6%)
		Acetamiprid	27.06.; 09.07.	6 (2 s; 4 r)	
		Deltamethrin	25.07.; 11.08.	2 (2 s)	

[a] Arable crops: winter cereals in D scenarios and maize in R scenarios. Permanent crops: pomes (apples) in D and R scenarios.
[b] Routes of entry: s: spray drift; r: rainfall- or irrigation-induced runoff; d: drainage.

[c] Sum of all days (and percentages) with concentration > LOD for all three insecticide compounds.
[c] Limit of detection.

Table S6 Implications for monitoring: Detailed results for the real insecticides. Mean number of detects and non-detects of insecticides resulting from different sampling strategies, costs per one detection, and total costs per year. Data are shown separately for the two streams located in arable crop (3 applications; 6 concentrations > LOD; mean exposure duration: 9.1 h) and permanent crop (6 applications; 9 concentrations > LOD; mean exposure duration: 9.4 h) agri-environments. Values were calculated by applying Monte Carlo simulations to realistic insecticide exposure patterns for arable and permanent crops synthesized from FOCUS exposure model calculations (Fig. 1c and Fig. 1d)

Interval (No. of samples)	Mean[a] no. of detects (peak detection error[b] (%))	Mean[a] no. of non-detects	Percentage of non-detects	Costs per detection ($)	Total costs per year ($)
Arable crops					
Monthly (12)	0 (100)	12	100%	n/a	3,600
14-d (26)	0 (100)	26	100%	n/a	7,800
Weekly (52)	0 (100)	52	100%	n/a	15,600
3.5-d (104)	1 (83.3)	103	99%	31,200	31,200
Daily[c] (365)	2 (66.7)	363	99.5%	54,750	109,500
Event[d] (18)	6 (0)	12	66.7%	1,150	6,900
Permanent crops					
Monthly (12)	0 (100)	12	100%	n/a	3,600
14-d (26)	0 (100)	26	100%	n/a	7,800
Weekly (52)	1 (88.9)	51	98.1%	15,600	15,600
3.5-d (104)	1 (88.9)	103	99%	31,200	31,200
Daily[c] (365)	4 (55.6)	361	98.9%	27,375	109,500
Event[d] (22)	9 (0)	13	59.1%	900	8,100

[a] The minimum and maximum no. of detects calculated by Monte Carlo simulations were (Min / Max): monthly (0 / 1); 14-d (0 / 1); weekly (0 / 2); 3.5-d (0 / 2) in the case of arable crops and (Min / Max): monthly (0 / 1); 14-d (0 / 2); weekly (0 / 3); 3.5-d (0 / 3) in the case of permanent crops.
[b] Defined as percentage of non-detected insecticide concentrations out of all concentrations available. Calculated as follows: ((Total concentrations available – concentrations detected) / Total concentrations available) x 100.
[c] Despite the fact that one sample per day was taken, only 2 out of 6 (arable crops) and 4 out of 9 (permanent crops) insecticide concentrations were detected, due to the respective mean exposure durations simulated by FOCUS.
[d] Totals of 18 (arable crops) and 22 (permanent crops) samples were considered as taken by event-triggered sampling, assuming three (arable crops) and six (permanent crops) spray events plus 15 (arable crops) and 16 (permanent crops) insecticide entry events potentially occurring due to 15 mm/day irrigation or rainfall, as extracted from FOCUS climate documents (see Table S3) for the respective scenarios used here.

Table S7 Implications for monitoring: Detailed results for the model insecticide. Mean number of detects and non-detects of insecticide concentrations resulting from different sampling strategies, costs per one detection, and total costs per year. Data are shown separately for the two streams located in arable crop (3 applications; 11 concentrations > LOD; mean exposure duration: 10.7 h) and permanent crop (6 applications; 16 concentrations > LOD; mean exposure duration: 12.7 h) agri-environments. Values were calculated by applying Monte Carlo simulations to the generalized model insecticide exposure patterns for arable and permanent crops synthesized from FOCUS exposure model calculations (Fig. 1a and Fig. 1b)

Interval (No. of samples)	Mean[a] no. of detects (peak detection error[b] (%))	Mean[a] no. of non-detects	Percentage of non-detects	Costs per detection ($)	Total costs per year ($)
Arable crops					
Monthly (12)	0 (100)	12	100%	n/a	3,600
14-d (26)	0 (100)	26	100%	n/a	7,800
Weekly (52)	1 (90.9)	51	98.1%	15,600	15,600
3.5-d (104)	1 (90.9)	103	99%	31,200	31,200
Daily[c] (365)	5 (54.5)	360	98.6%	21,900	109,500
Event[d] (18)	11 (0)	7	38.9%	627	6,900
Permanent crops					
Monthly (12)	0 (100)	12	100%	n/a	3,600
14-d (26)	1 (93.8)	25	96.2%	7,800	7,800
Weekly (52)	1 (93.8)	51	98.1%	15,600	15,600
3.5-d (104)	1 (93.8)	103	99%	31,200	31,200
Daily[c] (365)	8 (50)	357	97.8%	13,688	109,500
Event[d] (22)	16 (0)	6	27.3%	506	8,100

The minimum and maximum no. of detects calculated by Monte Carlo were (Min / Max): monthly (0 / 1); 14-d (0 / 3); weekly (0 / 3); 3.5-d (0 / 4) in the case of arable crops and (Min / Max): monthly (0 / 3); 14-d (0 / 4); weekly (0 / 5); 3.5-d (0 / 4) in the case of permanent crops.

[b] Defined as percentage of non-detected insecticide concentrations out of all concentrations available. Calculated as follows: ((Total concentrations available – concentrations detected) / Total concentrations available) x 100.

[c] Despite the fact that one sample per day was taken, only 5 out of 11 (arable crops) and 8 out of 16 (permanent crops) insecticide concentrations were detected due to the respective mean exposure durations simulated by FOCUS.

[d] Totals of 18 (arable crops) and 22 (permanent crops) samples were considered as taken by event-triggered sampling assuming three (arable crops) and six (permanent crops) spray events plus 15 (arable crops) and 16 (permanent crops) insecticide entry events potentially occurring due to 15 mm/day irrigation or rainfall, as extracted from FOCUS climate documents (see Table S3) for the respective scenarios used here.

Table S8 Implications for risk assessment: Detailed results for the real insecticides. Risk assessment results for deterministic (DRA), probabilistic (PRA), and relevance-driven (RRA) data evaluation approaches based on mean numbers and percentages of realistic insecticide exposure incidences and concentrations > RAC detected by different sampling strategies. Data are separately shown for two typical streams located in arable (3 out of 6 concentrations > RAC) and permanent crop (6 out of 9 concentrations > RAC) agroecosystems. A profound risk assessment result (bold) can only be obtained by the relevance-driven evaluation of insecticide concentrations detected by event-triggered sampling (see text for details)

Interval (No of samples)	Mean[a] no. of RAC[b]-exceeding concentrations detected (percentages)	Deterministic risk assessment: Comparison of peak concentration to the RAC[b]	Probabilistic risk assessment based on RAC[b] exceedance frequencies[c]	Relevance-driven risk assessment: No. of relevant concentrations > RAC[b]
Arable crops				
Monthly (12)	0 (0%)	n/a[d]	0%	n/a
14-d (26)	0 (0%)	n/a[d]	0%	n/a
Weekly (52)	0 (0%)	n/a[d]	0%	n/a
3.5-d (104)	1 (33.3%)	1 of 1	0.96%	1 of 1
Daily (365)	1 (33.3%)	1 of 1	0.27%	1 of 2
Event (18)	3 (100%)	1 of 1	16.6%	**3 of 6**
Permanent crops				
Monthly (12)	0 (0%)	n/a[d]	0%	n/a
14-d (26)	0 (0%)	n/a[d]	0%	n/a
Weekly (52)	1 (16.6%)	1 of 1	1.9%	1 of 1
3.5-d (104)	1 (16.6%)	1 of 1	0.96%	1 of 1
Daily (365)	3 (50%)	1 of 1	0.82%	3 of 4
Event (22)	6 (100%)	1 of 1	27.3%	**6 of 9**
Theoretical concept		Based on highest concentration	Based on all concentrations, including non-detects	Based on relevant concentrations, i.e., those > LOD

[a] Mean nos. of insecticide concentrations > RAC refer to 100,000 Monte Carlo simulations applied to a realistic insecticide exposure pattern with mean exposure durations of 9.1 hours (arable crops) and 9.4 hours (permanent crops).
[b] Regulatory Acceptable Concentration (RAC).
[c] Calculated by dividing the number of insecticide concentrations > RAC for each sampling interval by the amount of samples taken.
[d] No risk assessment results are available for monthly, 14-d, and weekly sampling intervals for arable crops or for monthly and 14-d sampling intervals for permanent crops because no concentrations > LOD were detected.

Table S9 Implications for risk assessment: Detailed results for the model insecticide. Risk assessment results for deterministic (DRA), probabilistic (PRA), and relevance-driven (RRA) data evaluation approaches based on mean numbers and percentages of model insecticide exposure incidences and concentrations > RAC detected by different sampling strategies. Data are separately shown for two typical streams located in arable (9 out of 11 concentrations > RAC) and permanent crop (15 out of 16 concentrations > RAC) agroecosystems. A profound risk assessment result (bold) can only be obtained by the relevance-driven evaluation of insecticide concentrations detected by event-triggered sampling (see text for details)

Interval (No. of samples)	Mean[a] no. of RAC[b]-exceeding concentrations detected (percentages)	Deterministic risk assessment: Comparison of peak concentration to the RAC[b]	Probabilistic risk assessment based on RAC[b] exceedance frequencies[c]	Relevance-driven risk assessment: No. of relevant concentrations > RAC[b]
Arable crops				
Monthly (12)	0 (0%)	n/a[d]	0%	n/a
14-d (26)	0 (0%)	n/a[d]	0%	n/a
Weekly (52)	1 (11.1%)	1 of 1	1.9%	1 of 1
3.5-d (104)	1 (33.3%)	1 of 1	0.96%	1 of 1
Daily (365)	4 (44.4%)	1 of 1	1.1%	4 of 5
Event (18)	9 (100%)	1 of 1	50%	**9 of 11**
Permanent crops				
Monthly (12)	0 (0%)	n/a[d]	0%	n/a
14-d (26)	1 (6.7%)	1 of 1	3.8%	1 of 1
Weekly (52)	1 (6.7%)	1 of 1	1.9%	1 of 1
3.5-d (104)	1 (6.7%)	1 of 1	0.96%	1 of 1
Daily (365)	8 (53.3%)	1 of 1	2.2%	8 of 8
Event (22)	15 (100%)	1 of 1	68.2%	**15 of 16**
Theoretical concept		Based on highest concentration	Based on all concentrations, including non-detects	Based on relevant concentrations, i.e., those > LOD

[a] Mean nos. of insecticide concentrations > RAC refer to 100,000 Monte Carlo simulations applied to generalized insecticide exposure patterns with mean exposure durations of 10.7 hours (arable crops) and 12.7 hours (permanent crops).
[b] Regulatory Acceptable Concentration (RAC).
[c] Calculated by dividing the number of insecticide concentrations > RAC for each sampling interval by the amount of samples taken.
[d] No data are available for monthly and 14-d sampling intervals for arable crops or for monthly sampling intervals for permanent crops because no concentrations > LOD were detected.

References

DG SANCO. (2008). EU pesticide database. http://ec.europa.eu/sanco_pesticides/public/index.cfm2011. Accessed 27 May 2011.

FOCUS (2001). *FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC*. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev.2.

Agricultural insecticides threaten surface waters at the global scale

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Compared with nutrient levels and habitat degradation, the importance of agricultural pesticides in surface water may have been underestimated due to a lack of comprehensive quantitative analysis. Increasing pesticide contamination results in decreasing regional aquatic biodiversity, i.e., macroinvertebrate family richness is reduced by ∼30% at pesticide concentrations equaling the legally accepted regulatory threshold levels (RTLs). This study provides a comprehensive metaanalysis of 838 peer-reviewed studies (>2,500 sites in 73 countries) that evaluates, for the first time to our knowledge on a global scale, the exposure of surface waters to particularly toxic agricultural insecticides. We tested whether measured insecticide concentrations (MICs; i.e., quantified insecticide concentrations) exceed their RTLs and how risks depend on insecticide development over time and stringency of environmental regulation. Our analysis reveals that MICs occur rarely (i.e., an estimated 97.4% of analyses conducted found no MICs) and there is a complete lack of scientific monitoring data for ∼90% of global cropland. Most importantly, of the 11,300 MICs, 52.4% (5,915 cases; 68.5% of the sites) exceeded the RTL for either surface water (RTL_{SW}) or sediments. Thus, the biological integrity of global water resources is at a substantial risk. RTL_{SW} exceedances depend on the catchment size, sampling regime, and sampling date; are significantly higher for newer-generation insecticides (i.e., pyrethroids); and are high even in countries with stringent environmental regulations. These results suggest the need for worldwide improvements to current pesticide regulations and agricultural pesticide application practices and for intensified research efforts on the presence and effects of pesticides under real-world conditions.

global surface waters | insecticide contamination | agriculture | regulatory risk assessment | biodiversity

At present, 15.3×10^6 km^2 of available croplands (Fig. 1) are cultivated worldwide; thus, agriculture (croplands and pasture) constitutes the world's largest terrestrial biome (1). Agricultural expansion and intensification led to a >750% increase in pesticide production between 1955 and 2000 (2). Moreover, pesticides represent a US$50 billion market worldwide (3). However, agricultural pesticide use leads to the exposure of nontarget ecosystems such as surface waters (4, 5). In this study, we focused on insecticides because they exhibit a high potential toxicity to aquatic organisms (6) that are crucial for ecosystem functions (7), and we analyzed exposure data obtained for surface waters because these waters are likely to be exposed to agricultural insecticide inputs (4, 5, 8) while providing essential environmental and human health-related ecosystem services (9).

Although the importance of nutrient levels and habitat degradation for surface water impairment is well understood (9), the same cannot be said for insecticides or pesticides in general (5, 9) (Fig. 1). A recent study (10) showed that in Europe, organic chemicals and pesticides specifically threaten freshwater integrity. Based on model predictions, another study (8) identified river fragmentation and nutrient loading as greater threats to aquatic biodiversity than pesticides; however, this study did not consider differences in pesticide toxicities. In response to the inherent toxicity of pesticides and their intentional release into the environment, elaborate environmental risk assessment procedures (*SI Appendix*, *SI Discussion*) (11, 12) defining a legally accepted regulatory threshold level (RTL) for each compound (see *SI Appendix*, Table S1 for the RTLs of the 28 insecticides considered here) have been developed; thus, pesticides are among the most intensively tested and regulated chemicals (13) (*SI Appendix*, Table S2), possibly contributing to the general perception of their environmental safety.

A recent study (14) using field data obtained from Germany, France, and Australia showed that elevated pesticide levels affect regional freshwater invertebrate biodiversity. This analysis ruled out confounding factors and used exposure data based on methods reflecting short-term pesticide concentrations. Transferring the standard toxicity values used in this study into RTLs clearly illustrates that species richness is reduced at the taxonomic family level by ∼30% at the RTL and by ∼12% at a factor of 10 below the RTL (Fig. 2*A*). Field studies (15, 16) reporting measured insecticide concentrations (MICs) up to 250 times RTL detected decreases in family richness of up to 63%. Any exceedance of the RTL thus indicates a risk of incurring clearly unacceptable effects on aquatic biodiversity. The overarching question now is how widespread and common this risk is, i.e., do MICs exceed their RTLs in the surface waters globally?

The few large-scale studies of insecticide exposure in surface waters have either examined sites in spatially restricted areas (10, 17, 18); lacked a quantitative data analysis (4); or followed other, rather specific objectives (18, 19) (*SI Appendix*, *SI Discussion*). However, the results obtained in these studies suggest that exceedances of threshold values occur, particularly for insecticides. These studies also showed that insecticides are only present for very short periods

Significance

Agricultural systems are drivers of global environmental degradation. Insecticides, in particular, are highly biologically active substances that can threaten the ecological integrity of aquatic and terrestrial ecosystems. Despite widespread insecticide application to croplands worldwide, no comprehensive field data-based evaluation of their risk to global surface waters exists. Our data show, for the first time to our knowledge at the global scale, that more than 50% of detected insecticide concentrations (n = 11,300) exceed regulatory threshold levels. This finding indicates that surface water pollution resulting from current agricultural insecticide use constitutes an excessive threat to aquatic biodiversity. Overall, our analysis suggests that fundamental revisions of current regulatory procedures and pesticide application practices are needed to reverse the global environmental impacts of agrochemical-based high-intensity agriculture.

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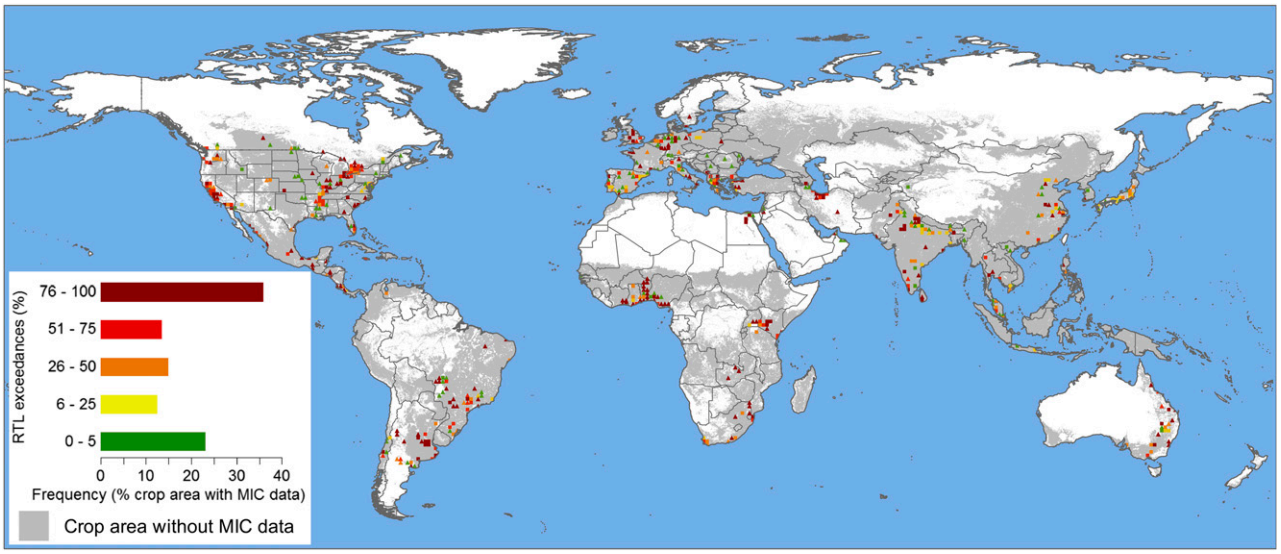

Fig. 1. Global crop area and the distribution of regulatory threshold level (RTL) exceedance rates for reported measured insecticide concentrations (MICs, $n = 10{,}659$) aggregated in 1° grid cells. Information on insecticide surface water exposure was available for only 1.62 million km^2 (10.6%) of the 15.3 million km^2 of global croplands (1). Rectangles ($n = 307$) represent subclassified cropped areas with five or more MICs, and triangles ($n = 290$) display grid cells with fewer than 5 MICs. Please note that 641 MICs could not be allocated to a specific grid cell due to the provision of imprecise location information in the studies. The horizontal bars in the legend illustrate the relative distributions of the respective insecticide RTL exceedance classes among the global cropped area with information on insecticide exposure.

(i.e., less than 1% of the year) in agriculturally influenced surface waters. It follows that most traditionally operated, fixed interval-based sampling campaigns inherently miss insecticide exposure (20). To avoid bias resulting from an excessive number of samples without quantifiable insecticide levels, exposure assessments of insecticides using monitoring data must be based solely on quantifiable concentrations in aquatic environments, i.e., those above the limit of quantification (LOQ) (*SI Appendix*, *SI Discussion*) (20).

Based on prior investigations (4, 10, 17, 18), we hypothesized that MICs in surface waters exceed their RTLs at dimensions underestimated by regulators and the general public. We tested this first hypothesis using a metaanalysis of global insecticide monitoring data from international peer-reviewed publications (*Methods*).

The majority of the 28 insecticides included in our analysis (*SI Appendix*, Table S1) are currently approved in the United States and the European Union. They represent all major insecticide classes and those compounds that are important for global agriculture in terms of annual application rates (*SI Appendix*, *SI Methods*). A total of 11,300 MICs [representing an estimated 2.6% of the population of analyses conducted (*SI Appendix*, *SI Discussion*)] caused by agricultural nonpoint source pollution from 838 studies published between 1962 and 2012 were compared with their respective RTLs for surface water (RTL_{SW}; $n = 8{,}166$) or sediment (RTL_{SED}; $n = 3{,}134$). Specifically, we used the RTL_{SW} derived from the official US Environmental Protection Agency's regulatory risk assessment for the evaluation of MIC_{SW} detected

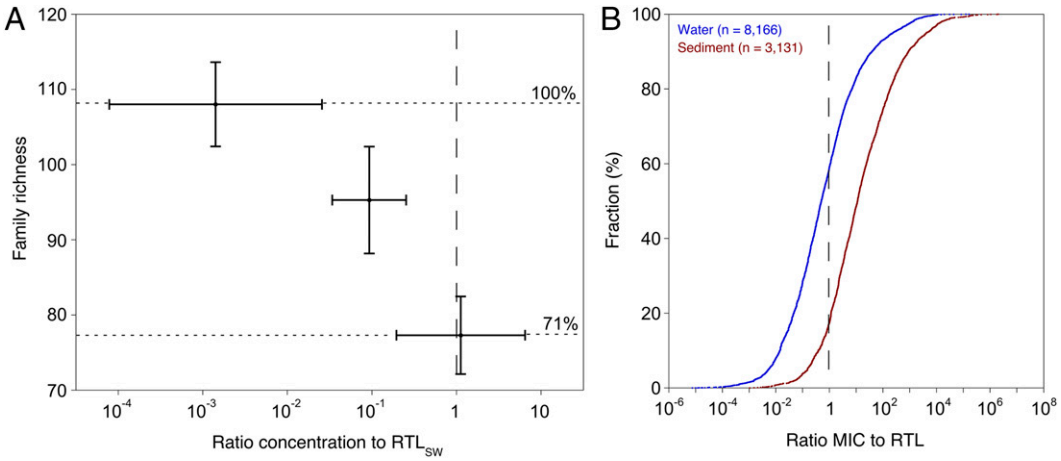

Fig. 2. Observed ecological effects of pesticide exposure on regional surface water biodiversity and distribution curves for global reported measured insecticide concentrations (MICs) in water and sediment relative to regulatory threshold levels (RTLs). (*A*) Dependency of mean macroinvertebrate family richness at 60 agricultural stream sites on mean aqueous pesticide concentration to RTL_{SW} ratios. Data on family richness, pesticide exposure levels, and categories were taken from ref. 14. The vertical dashed line indicates the RTL_{SW}, and the error bars denote 95% confidence intervals. (*B*) Blue represents the concentrations in water relative to the substance-specific RTL_{SW} ($n = 8{,}166$), and brown represents the concentrations in sediment relative to the substance-specific RTL_{SED} ($n = 3{,}131$). The vertical dashed line indicates the RTL.

in the United States and Canada, the official European RTL_{SW} for the evaluation of MIC_{SW} detected in European Union member states, and the average of the two values for the evaluation of MIC_{SW} detected in other parts of the world (*SI Appendix*, Table S1 and *Methods*). Notably, the United States' and European Union's RTL_{SW} values do not differ consistently, i.e., some individual RTL_{SW} values are higher in the United States or the European Union. Our analysis is based on more than 2,500 surface water sites located in 73 countries worldwide (Fig. 1 and *SI Appendix*, Fig. S1 and *SI Discussion*) and includes freshwater (n = 9,910 concentrations) and estuarine (n = 1,390 concentrations) systems with catchment sizes between 0.002 and 3,400,000 km^2 (*SI Appendix*, Table S3).

Results and Discussion

Our global analysis shows that no scientific investigations of insecticide surface water exposure exist for large portions (i.e., ∼90%) of high-intensity agricultural areas (Fig. 1). For example, no MICs were reported for Russia or several other post-Soviet states or from large parts of Africa or northwestern South America, although croplands dominate large areas in these regions. The most important outcome of our study is that among the 11,300 insecticide concentrations detected, 52.4% exceeded their specific threshold levels. Approximately 40.8% of the MIC_{SW} values (which are considered directly bioavailable due to their presence in the water phase) (21, 22) were above their respective RTL_{SW} values (Fig. 2*B*). Thus, our results demonstrate that in at least 3,331 cases distributed globally (Fig. 1), the regional biodiversity of surface waters is at risk for impairment due to insecticide contamination (Fig. 2 *A* and *B*) (14). Importantly, these risks were defined only for individual compounds, without considering the potential effects of mixture toxicity (see below on this topic). The application of only the United States (54% RTL_{SW} exceedances) or European Union (35.1% RTL_{SW} exceedances) RTL_{SW} to global MIC_{SW} did not alter the overall findings of our metaanalysis. When the dataset was rigorously restricted based on land use and entry routes to only those exposure incidents that were definitely linked to agricultural nonpoint entries (*SI Appendix*, *SI Discussion*), the results were even more striking (49.7% RTL_{SW} exceedance; *SI Appendix*, Table S4).

The 82.5% RTL_{SED} exceedances (2,584 cases) reported herein (Fig. 2*B*) also signify remarkable environmental risks. Sediment samples reflect exposure conditions over longer time spans compared with those of water samples, and the high exceedance levels (*i*) support the data reported for water, (*ii*) are likely due to the high hydrophobicity of many insecticides, (*iii*) imply long-term (chronic) risks to sediment-dwelling organisms (23), and (*iv*) indicate that both major aquatic ecosystem components are at risk.

Overall, the data regarding insecticide exposure (Fig. 2*B*) and their attributable ecological effects (Fig. 2*A*) reveal for the first time to our knowledge at the global scale that, in concert with nutrients and habitat degradation, agricultural insecticide use is likely a driver for biodiversity loss in agriculturally impacted aquatic ecosystems (8, 9, 24). This synthesis responds to a request to quantify the "concentrations of [. . .] pollutants in the global environment" (25), made with regard to pollution as one of the two planetary boundaries that have not yet been quantified. Our approach is based on an extended version of the approach used in ref. 8 as it analyzes empirical monitoring data and employs for the first time to our knowledge a global risk-based evaluation that considers the fact that individual insecticide toxicities span several orders of magnitude. Applying the available insecticide monitoring results to areas that currently lack information on insecticide exposure (i.e., ∼90% of global cropland) reveals that the surface waters located in ∼65% of global cultivated areas are at risk for exposure to insecticide RTL exceedance rates of more than 25% (Fig. 1). However, future studies are needed to quantify the uncertainty related to extending the present risk predictions to all global cropland.

Please note that there are a number of aspects that require further consideration in the assessment of insecticide risks. First, the published insecticide monitoring results to which we refer in our analysis most likely underestimate the actual exposure levels because it is extremely difficult to capture transient insecticide peak concentrations; ∼84.4% of the reported water-phase concentrations were measured using sampling strategies likely to miss the short-term insecticide peaks (20). Highly transient exposures are, according to ref. 20, typical for insecticides in agricultural surface waters. Even considerably contaminated sites regularly exhibit detectable insecticide concentrations for only a few (i.e., 3–4) hours during ∼4–6 d/y coinciding with typical application patterns (e.g., in the spring/summer). Organisms present at such sites receive their entire annual insecticide exposure dose during these short time periods during which short-term peak exposure incidents occur, and these incidents may cause long-term ecological perturbations (4, 14) due to the high intrinsic toxicity of insecticides (6, 26). Therefore, environmental science is faced with the challenge of being able to detect very low absolute levels of insecticides occurring stochastically in time and space that lead to negative ecological impacts. It is thus likely that insecticides are regularly underestimated in their importance as a driver of aquatic biodiversity decline. Second, an in-depth evaluation of the field studies underlying this metaanalysis showed that the majority of sites received either repeated contamination peaks over short periods or concurrent exposure to a number of different pesticides. For example, 81.3% of the samples that were analyzed for the presence of additional compounds (n = 4,198) contained up to 31 additional pesticides; this finding indicates that although disregarded in the regulatory risk assessment (11, 27), overall pesticide effects in the field are driven by repetitive exposure peaks and mixture toxicity (the simultaneous exposure of organisms to a multitude of different compounds). Third, unacceptable ecological effects on aquatic organisms are likely to occur in the field at concentrations well below the RTL (Fig. 2*A*) (7, 14). Applied to the data compiled here, this consideration means that in virtually all cases where an insecticide had been detected (ratio MIC to RTL $\geq 10^{-3}$; Fig. 2*B*), the consequence is a negative impact on regional biodiversity (Fig. 2*A*).

Based on these three considerations, both the actual insecticide contamination of surface waters and the resulting ecological risks are, in reality, even greater than indicated in this study based on the assessed literature and current regulatory procedures for insecticide risk assessment. In this context, the comparison of MIC_{SW} to other established threshold levels such as science-based environmental quality standards (EQSs) [which, in contrast to RTLs, do not tolerate (transient) clear effects on aquatic organisms], leads to an even higher threshold level exceedance rate of 70.1% (n = 7,821; *SI Appendix*, *SI Methods*). However, a concentration exceeding the RTL measured at a given site does not necessarily indicate that large stretches of the associated surface water are exposed and therefore harbor risks to aquatic fauna. For example, aquatic vegetation can reduce the negative impacts of pesticides (26). Nonetheless, the fact that RTL exceedances are so widespread and lead to detectable biodiversity reductions clearly highlights the global problem we are facing as a result of insecticide use in agriculture.

In addition to improving the efficiency of insecticides and reducing insect/pest resistance, the research and development (R&D) of insecticide compounds have focused on being more environmentally friendly, with the intention of reducing risks to surface waters as nontarget ecosystems (28, 29). However, a recent study (18) showed that the FOCUS model, used for the regulatory exposure assessment in the European Union, underpredicts field concentrations of newer, increasingly used insecticides such as hydrophobic pyrethroids. Specifically, the ratio of the predicted insecticide surface water concentrations to the MIC_{SW} was significantly lower for pyrethroids than for organochlorines and organophosphorus insecticides. The authors partially attributed these

results to the inadequacies of the runoff model termed "pesticide root zone model" (PRZM), which is also used for the authorization of pesticide compounds in other countries such as the United States (30). Therefore, our second hypothesis was that newer, more recently developed and registered insecticide classes (*SI Appendix*, Table S5) show higher RTL exceedances.

Contemporary insecticides, such as pyrethroids, showed a significantly higher percentage of RTL_{SW} exceedance (65.8%) compared with both organophosphates (43.7%; $P < 0.001$) and organochlorines (24.4%; $P < 0.001$), and the latter two also differed significantly ($P < 0.001$; Fig. 3*A* and *SI Appendix*, Table S6). Although first introduced to the global crop protection market in 1973 (*SI Appendix*, Table S5), pyrethroids have gained prominence in part due to concerns over organophosphates and human health. In our comparison of insecticide classes, we specifically considered differences in bioavailability and the ratios between the RTL_{SW} and the LOQ in additional linear model analyses; neither aspect altered the general picture of significant differences among the compound classes. In particular, considering only the freely dissolved [and therefore directly bioavailable (31)] fraction analyzed in water samples of the highly hydrophobic [organic carbon/water partitioning coefficients (K_{OC}) of 10^5–10^7 (32)] pyrethroids did not reduce their concentration to RTL_{SW} ratios (*SI Appendix*, Table S7 and *SI Discussion*). This finding indicates that the significantly higher RTL_{SW} exceedance frequency for highly sorptive pyrethroids is not biased by potential bioavailability limitations. In addition, considering the lower RTL_{SW} of pyrethroids associated with their comparably higher toxicity to aquatic organisms, and thus lower distances between RTL_{SW} and LOQs (*SI Appendix*, Table S8), did not disprove our findings; however, the discrepancies among insecticide classes were reduced (*SI Appendix*, Table S9 and *SI Discussion*).

Overall, we conclude that the environmental risk is even higher for newer-generation insecticides, such as pyrethroids, compared with older-generation insecticides. Further, these increased risks indicate a failure of R&D efforts to develop more environmentally friendly insecticides to improve surface water protection. Current risk management obligations and application practices for pyrethroids in agriculture obviously do not result in surface water exposure levels that adhere to the strict RTLs triggered by their extremely high invertebrate toxicities (6). However, in contrast to pyrethroids, a valid conclusion for neonicotinoid MIC_{SW} (RTL_{SW} exceedances: 6.1%; $n = 131$) is hindered due to insufficient data. Nonetheless, recent studies (19, 33) on agricultural neonicotinoid use reveal environmental concerns for both aquatic and terrestrial ecosystems.

Our third hypothesis is that countries with a high environmental regulatory quality (HERQ) should exhibit markedly less frequent RTL exceedances than those with a low environmental regulatory quality (LERQ) (*SI Appendix*, Table S10). RTL_{SW} exceedances were indeed significantly more frequent in the LERQ countries ($P < 0.001$; *SI Appendix*, Table S6). This pattern also holds true when accounting for differences in RTL/LOQ ratios (*SI Appendix*, Table S9). Although not unexpected, this finding is alarming considering that recent and anticipated future agricultural expansion and intensification have occurred and will occur in biodiversity-rich tropical LERQ countries (1). In these countries, pesticide regulations are insufficiently enforced (5, 34) (*SI Appendix*, *SI Discussion*) and surface waters are already exposed to numerous other stressors (9). The absolute percentage of the detected RTL_{SW} exceedance (39.9%) in the HERQ countries (such as the United States, Canada, Germany, Japan, and Australia), is only slightly lower than that in the LERQ countries (42.2%; Figs. 1 and 3*B*). Therefore, our data show that the actual extent to which surface waters are contaminated with insecticides is not controlled effectively by increasingly stringent environmental regulations at present. However, in the LERQ countries, substantially larger surface water systems and longer sampling intervals were considered in the monitoring campaigns (*SI Appendix*, Table S11), decreasing the likelihood of determining insecticide peak exposure incidences (*SI Appendix*, Table S6) (20). The application of more targeted insecticide sampling strategies (20) is needed in the future to adequately reflect the risks to the surface waters of LERQ countries.

Overall, RTL exceedances depend on multiple factors, including insecticide classes, environmental regulatory standards, catchment size, sampling regime, and sampling date (*SI Appendix*, Table S6). We identified a significant interaction among insecticide class, the quality of countries' regulatory standards, and sampling date (*SI Appendix*, Tables S6, S12, and S13, Fig. S2, and *SI Discussion*).

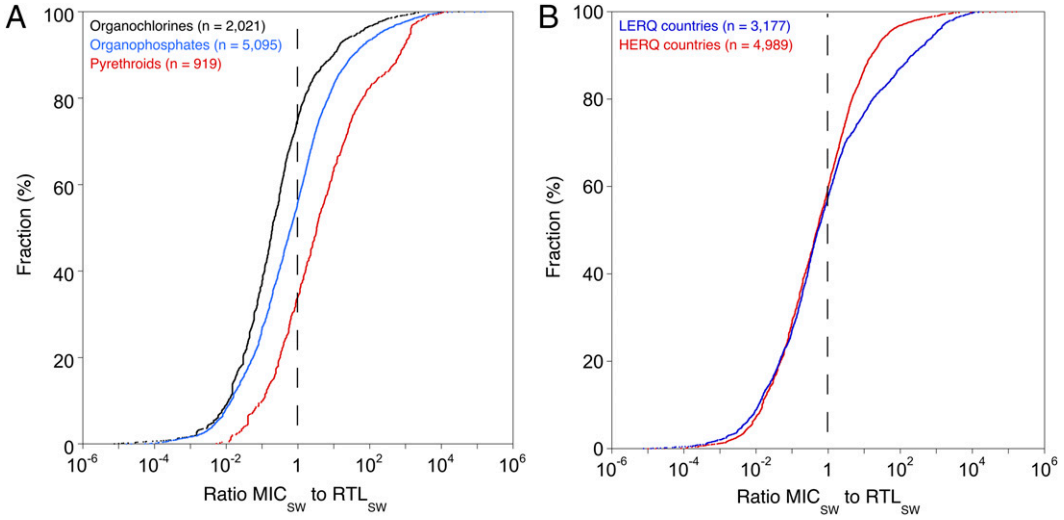

Fig. 3. Effect of insecticide class and country environmental regulations on the distribution curves for reported measured insecticide concentrations in the water phase (MIC_{SW}) relative to substance-specific regulatory threshold levels (RTL_{SW}). (*A*) Black represents data obtained for organochlorine insecticides (n = 2,021), blue represents data obtained for organophosphate insecticides (n = 5,095), and red represents data obtained for pyrethroid insecticides (n = 919); 6.1% of the MIC_{SW} of neonicotinoids (n = 131) exceeded the RTL_{SW} (not displayed). (*B*) Distribution curves for MIC_{SW} relative to substance-specific RTL_{SW}. Blue represents concentrations measured in countries with low environmental regulatory quality (LERQ; n = 3,177), and red represents data measured in countries with high environmental regulatory quality (HERQ; n = 4,989). The vertical dashed lines indicate the RTL_{SW}.

Unlike in HERQ countries, the risks of organochlorine and organophosphorus insecticide exposure in LERQ countries have increased over the last three decades due to increased insecticide use and simultaneously weak or even nonexistent pesticide regulation schemes.

Taken together, our results seriously challenge the protectiveness of the current regulatory insecticide risk assessments and management procedures at the global scale. Although, for example, major EU and US pesticide legislations were already enforced at the beginning of the 1990s (*SI Appendix*, Table S2), 54.2% (n = 4,686; and 49.5%, n = 2,681 when considering HERQ countries only) of the MICs reported since 2000 have exceeded their respective RTLs (*SI Appendix*, Fig. S3 *A* and *B*). Targeted postregistration monitoring schemes and regulatory actions are needed, considering that 18 and 24 of the 28 insecticide compounds included in our metaanalysis are currently approved in EU countries and in the United States, respectively. The high numbers of threshold exceedances worldwide are caused by failures of either regulatory exposure assessment (18) or farmers' adherence to prescribed risk management obligations (35).

Edge-of-field runoff was an important route of entry for insecticides in our dataset, comprising 72.4% of cases for which an entry route was specified (*SI Appendix*, Table S3). In addition to application patterns and geographical and meteorological conditions, the physicochemical properties of an insecticide (such as its hydrophobicity) are crucial components of its potential to enter a surface water via runoff (36, 37). Empirical studies (38, 39) suggest that lower runoff losses to surface waters occur for strongly sorbed compounds. This potential provides opportunities for the more efficient use of insecticides based on modeling of their runoff potential. However, the potential risks of insecticide surface water impairments are driven not only by the respective entry pathways and probabilities of exposure but also by the intrinsic toxicity, which varies considerably among different classes of insecticides (40). Thus, any risk mitigation attempt must consider both entry probability and toxicity.

To date, agriculture occupies ∼40% of the world's land surface and agricultural production is forecast to undergo substantial intensification (1, 2). This situation leads to the projection that future agricultural activities may rival climate change in their environmental impacts (2). Reforming conventional agricultural systems and adopting promising approaches from organic farming (41), including the elimination of pesticides wherever applicable, in concert with the closing of yield gaps on underperforming lands (1, 42) and precision agricultural techniques (43), are possible ways to meet the twin challenges of providing sufficient food for a growing human population and reversing the global environmental impacts of agrochemical-based high-intensity agriculture.

Methods

We conducted a comprehensive literature search of multiple databases to identify scientific studies in eight different languages reporting on agricultural insecticide concentrations in global surface waters. We evaluated more than 200,000 database entries and examined ∼20,000 articles in greater detail. The studies had to meet the following selection criteria to be included in our meta-analysis: (*i*) only peer-reviewed studies were considered to ensure that minimum scientific standards were met; (*ii*) the studies had to be written in one of the following eight languages: Chinese, English, French, German, Japanese, Russian, Spanish, and Portuguese; and (*iii*) the MICs reported resulted from agricultural nonpoint source pollution (excluding urban, industrial, and public health activities; aquaculture; atmospheric deposition; forest application; sheep dipping; golf course applications; accidental spills; intentional water contamination; and in-crop use) and were detected in perennial freshwater or estuarine surface water bodies (*SI Appendix, SI Methods*).

Regulatory threshold levels were applied as follows to assess the ecological importance of reported insecticide exposure data (*SI Appendix, SI Methods*, and Table S1): aqueous concentrations measured in the United States, Canada, or the European Union were compared with the respective regulatory threshold levels (RTL_{SW}), which are defined as part of the US (differentiated further into freshwater and estuarine RTL_{SW}) or EU pesticide legal registration procedures; and aqueous concentrations measured in other parts of the world were compared with the average values of the US and EU RTL_{SW} (*SI Appendix*, Table S1), as both regulatory risk assessments are considered highly elaborated and science based. Sediment or suspended-particle exposure was evaluated using the respective RTL_{SED}. The concentration of each insecticide was compared with its respective RTL, irrespective of how many compounds were measured in a given sample. To focus on the potential ecological risks of the highly relevant short-term exposure peaks of insecticides in surface waters, and considering that insecticide exposure occurs less than 1% of the time per year, we used only insecticide concentrations above the LOQ, as suggested by ref. 20 (see also *SI Appendix, SI Discussion* for further details). The aggregate exceedance frequencies for all studies considered were computed across multiple sites and plotted as distribution curves.

In addition to information on insecticide concentrations, we collected information on several covariates (i.e., sampling location, catchment size, sampling interval, and sampling date) that might influence insecticide exposure and used these data in a linear model analysis (*SI Appendix, SI Methods*) with the logarithm of the MIC_{SW} to RTL_{SW} ratio as the dependent variable to test for differences among specific insecticide classes (organochlorines, organophosphates/carbamates, and pyrethroids) and between countries' environmental regulatory standards (HERQ vs. LERQ countries, classified based on environmental, regulatory, and economic indices) (*SI Appendix, SI Methods*). We also evaluated the effects of the organic carbon/water partitioning coefficient (K_{OC}), the bioavailability of highly sorptive pyrethroids, and the differences in the RTL_{SW}/LOQ ratios on the concentration to RTL_{SW} ratios using two additional linear model analyses (*SI Appendix, SI Discussion*).

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1. Foley JA, et al. (2011) Solutions for a cultivated planet. *Nature* 478(7369):337–342.
2. Tilman D, et al. (2001) Forecasting agriculturally driven global environmental change. *Science* 292(5515):281–284.
3. Specialists in Business Information (November 24, 2008) Record increase in global pesticides market to accelerate into 2013. Available at www.sbireports.com/about/release.asp?id=1249. Accessed February 12, 2013.
4. Schulz R (2004) Field studies on exposure, effects, and risk mitigation of aquatic nonpoint-source insecticide pollution: A review. *J Environ Qual* 33(2):419–448.
5. Schwarzenbach RP, et al. (2006) The challenge of micropollutants in aquatic systems. *Science* 313(5790):1072–1077.
6. US Environmental Protection Agency (2014) ECOTOXicology Database System, Version 4.0. Available at http:/cfpub.epa.gov/ecotox/. Accessed March 18, 2013.
7. Schäfer RB, et al. (2012) Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environ Sci Technol* 46(9):5134–5142.
8. Vörösmarty CJ, et al. (2010) Global threats to human water security and river biodiversity. *Nature* 467(7315):555–561.
9. Finlayson CM, et al. (2005) *Inland Water Systems. Ecosystems and Human Well-Being: Current State and Trends*, eds Hassan R, Scholes R, Ash N (Island Press, Washington, DC), Vol 1, pp 551–583.
10. Malaj E, et al. (2014) Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. *Proc Natl Acad Sci USA* 111(26):9549–9554.
11. European Commission (2009) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Off J Eur Union L* 309(1):1–50.
12. FIFRA (1947) Federal Insecticide, Fungicide and Rodenticide Act, U.S. Federal Law amended in 1972 and 1988.
13. European Crop Protection Association (2003) *The ABCs of Crop Protection: Fast Facts for European Policy-Makers* (ECPA, Brussels).
14. Beketov MA, Kefford BJ, Schäfer RB, Liess M (2013) Pesticides reduce regional biodiversity of stream invertebrates. *Proc Natl Acad Sci USA* 110(27):11039–11043.
15. Schulz R, Liess M (1999) A field study of the effects of agriculturally derived insecticide input on stream macroinvertebrate dynamics. *Aquat Toxicol* 46(3-4):155–176.

16. Bollmohr S, Schulz R (2009) Seasonal changes of macroinvertebrate communities in a Western cape river, South Africa, receiving nonpoint-source insecticide pollution. *Environ Toxicol Chem* 28(4):809–817.
17. Gilliom RJ (2007) Pesticides in U.S. streams and groundwater. *Environ Sci Technol* 41(10):3408–3414.
18. Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS surface water models fail to predict insecticide concentrations in the field. *Environ Sci Technol* 46(15):8397–8404.
19. Morrissey CA, et al. (2015) Neonicotinoid contamination of global surface waters and associated risk to aquatic invertebrates: A review. *Environ Int* 74:291–303.
20. Stehle S, Knäbel A, Schulz R (2013) Probabilistic risk assessment of insecticide concentrations in agricultural surface waters: A critical appraisal. *Environ Monit Assess* 185(8):6295–6310.
21. Weston DP, Lydy MJ (2010) Urban and agricultural sources of pyrethroid insecticides to the Sacramento-San Joaquin Delta of California. *Environ Sci Technol* 44(5): 1833–1840.
22. Spurlock F, Bacey J, Starner K, Gill S (2005) A probabilistic screening model for evaluating pyrethroid surface water monitoring data. *Environ Monit Assess* 109(1-3): 161–179.
23. Du J, Pang J, You J (2013) Bioavailability-based chronic toxicity measurements of permethrin to *Chironomus dilutus*. *Environ Toxicol Chem* 32(6):1403–1411.
24. Pimm SL, et al. (2014) The biodiversity of species and their rates of extinction, distribution, and protection. *Science* 344(6187):1246752.
25. Rockström J, et al. (2009) A safe operating space for humanity. *Nature* 461(7263): 472–475.
26. Stehle S, et al. (2011) Pesticide risk mitigation by vegetated treatment systems: a meta-analysis. *J Environ Qual* 40(4):1068–1080.
27. US Environmental Protection Agency (2015) Technical Overview of Ecological Risk Assessment—Analysis Phase: Ecological Effects Characterization. Available at www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_eco.htm. Accessed February 12, 2015.
28. Lamberth C, Jeanmart S, Luksch T, Plant A (2013) Current challenges and trends in the discovery of agrochemicals. *Science* 341(6147):742–746.
29. Devine GJ, Furlong MJ (2007) Insecticide use: Contexts and ecological consequences. *Agric Human Values* 24(3):281–306.
30. US Environmental Protection Agency (2015) Technical Overview of Ecological Risk Assessment—Analysis Phase: Exposure Characterization. Available at www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_exp.htm. Accessed February 13, 2015.
31. Yang W, Spurlock F, Liu W, Gan J (2006) Inhibition of aquatic toxicity of pyrethroid insecticides by suspended sediment. *Environ Toxicol Chem* 25(7):1913–1919.
32. Laskowski DA (2002) Physical and chemical properties of pyrethroids. *Rev Environ Contam Toxicol* 174:49–170.
33. Hallmann CA, Foppen RPB, van Turnhout CAM, de Kroon H, Jongejans E (2014) Declines in insectivorous birds are associated with high neonicotinoid concentrations. *Nature* 511(7509):341–343.
34. Ecobichon DJ (2001) Pesticide use in developing countries. *Toxicology* 160(1-3):27–33.
35. De Snoo GR (2003) Variations in agricultural practice and environmental care. *Pesticides: Problems, Improvements, Alternatives*, eds Den Hond F, Groenewegen P, van Straalen NM (Blackwell, Oxford), pp 100–112.
36. Capel PD, Larson SJ, Winterstein TA (2001) The behaviour of 39 pesticides in surface waters as a function of scale. *Hydrol Processes* 15(7):1251–1269.
37. Reichenberger S, Bach M, Skitschak A, Frede H-G (2007) Mitigation strategies to reduce pesticide inputs into ground- and surface water and their effectiveness: A review. *Sci Total Environ* 384(1-3):1–35.
38. Riise G, Lundekvam H, Wu QL, Haugen LE, Mulder J (2004) Loss of pesticides from agricultural fields in SE Norway—runoff through surface and drainage water. *Environ Geochem Health* 26(2-3):269–276.
39. Patakioutas GI, Karras G, Hela D, Albanis TA (2002) Pirimiphos-methyl and benalaxyl losses in surface runoff from plots cultivated with potatoes. *Pest Manag Sci* 58(12): 1194–1204.
40. Spurlock F, Lee M (2008) Synthetic pyrethroid use patterns, properties, and environmental effects. *Synthetic Pyrethroids, Occurrence and Behavior in Aquatic Environments*, eds Gan J, Spurlock F, Hendley P, Weston D (American Chemical Society, Washington, DC), pp 3–25.
41. Seufert V, Ramankutty N, Foley JA (2012) Comparing the yields of organic and conventional agriculture. *Nature* 485(7397):229–232.
42. Mueller ND, et al. (2012) Closing yield gaps through nutrient and water management. *Nature* 490(7419):254–257.
43. Gebbers R, Adamchuk VI (2010) Precision agriculture and food security. *Science* 327(5967):828–831.

Supporting Information

for

Agricultural Insecticides Threaten Surface Waters at the Global Scale

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SI Methods

Literature search and selection criteria

We performed an exhaustive literature search (1), using multiple search criteria, e.g., "(insecticide* or pesticide* or organophos* or organochlori* or carbamat* or pyrethroid* or neonicotinoid*) and (stream* or ditch* or lake* or pond* or river* or creek)", of online databases, including ISI Web of Science (1945–June 2012), Biological Abstracts (1926–June 2012), BIOSIS Previews (1926–June 2012), CAB Abstracts (1910–June 2012), CAB Reviews (2003–June 2012), Food Science and Technology Abstracts (1969–June 2012), and Zoological Records (1864–June 2012). To overcome a database coverage bias (2), that is, the systematic exclusion of articles written in languages other than English, we considered articles written in the following eight languages in our literature research: Chinese, English, French, German, Japanese, Russian, Spanish, and Portuguese.

A total of 203,431 database entries resulting from 60 search queries were evaluated in the first step, which was based on the article titles. In the second step, approximately 20,000 articles were checked in greater detail based on the abstract contents, keywords, and, if considered potentially relevant, the main text. Additional studies were identified by footnote chasing (3), i.e., consulting the reference lists of empirical and review papers. This literature search was conducted between June 2006 and June 2012.

For each study considered, the measured insecticide concentration (MIC) reported therein had to meet a series of criteria to be included in the meta-analysis. Specifically, the MIC had to (i) result from agricultural nonpoint sources, which excluded the often extremely high concentrations related to point sources, urban, industrial, and public health activities (e.g., mosquito control, Tse-Tse fly control), aquaculture, atmospheric deposition (long-range transport), forest application, sheep dipping, golf course applications, accidental spills, intentional water contamination (e.g., fishing, waste dumping), and in-crop use (rice fields, cranberry bogs, etc.); (ii) originate from perennial freshwater or estuarine surface water bodies (concentrations measured in edge-of-field runoff or ephemeral channels were excluded); (iii) be above the limit of quantification (LOQ, i.e., those concentrations actually detected and quantified) applicable to the respective study to avoid a bias due to artificially high numbers of data points without quantifiable insecticide levels typical for insecticide surface water monitoring (*SI Discussion*) (4); and (iv) be written in one of the languages specified above.

This literature search procedure resulted in the identification of 838 peer-reviewed

publications containing insecticide exposure concentrations, which were included in the present meta-analysis. The meta-analysis is based on peer-reviewed studies to ensure a certain level of data quality, which cannot be claimed to an equal extent for non-peer-reviewed sources, e.g., proceedings or governmental reports (5).

To serve as a quality-control measure for the entire literature search procedure described above, a further independent literature review was performed externally by the scientific literature search service of the "FIZ Karlsruhe" research institution (see http://www.fiz-karlsruhe.de/search_service.html?&L=1). FIZ Karlsruhe performed several search queries in the STN databases AQUALINE (1960–July 2012) and AQUASCI (1978–July 2012) (see http://www.stn-international.de/index.php?id=123). In total, 885 bibliographic references, including keywords and abstracts, were provided and analyzed as described above. This independent literature search did not identify any additional relevant articles that had not been identified already in our own literature search.

Each data point consisted of the insecticide's name, its concentration in water (μg/L), sediment or suspended particles (μg/kg), the sampling location (including a distinction between a freshwater and an estuarine surface water location), the catchment size, the sampling interval, the sampling date, the LOQ, a classification concerning the certainty that it resulted from an agricultural nonpoint source entry, and the quantity of additional pesticides present in the specific sample. We acknowledge that in very few cases sediment and water samples were taken concurrently at a specific sampling location, which in our analysis, however, constitutes exposure data for different compartments of the aquatic systems under investigation. In cases in which more than one concentration of the same compound resulting from the same insecticide entry event was identified in a certain compartment (e.g., insecticide surface water exposure caused by rainfall-induced runoff or spray drift events sampled with high temporal resolution), we used only one data point (the peak value) to include this event. This step was taken to avoid replicate values that were not independent of one another because such an overlap would have resulted in an overestimation of the total number of independent exposure events. Moreover, we ensured that the equivalent values reported in a number of studies were included only once in the meta-analysis.

We considered endosulfan in our analysis because it is among the only organochlorine insecticides still in agricultural use in many countries (6). Furthermore, we considered a total of six organophosphate insecticides and carbofuran as a carbamate insecticide, which are important insecticides in terms of application rates (7). Finally, all pyrethroid esters (8) and neonicotinoid insecticides were considered, which is justified by the fact that the use of these

two classes of insecticides has increased greatly in recent years to fill the market gaps created by regulatory restrictions on other types of insecticides (9, 10). The concentrations of 16 pyrethroid compounds and four neonicotinoid insecticides measured in agriculturally influenced surface waters were identified and incorporated in the meta-analysis (Table S1).

Regulatory threshold levels for water (RTL_{SW}) and sediment (RTL_{SED})

The insecticide concentrations in water or sediment identified in our meta-analysis were compared with their respective threshold levels. The "regulatory threshold level" (RTL) was used to evaluate the water-phase (RTL_{SW}) and sediment (RTL_{SED}) insecticide concentrations, defining the ecotoxicity endpoint, which allowed for transient adverse ecological effects but was assumed to be ecologically acceptable within the official regulatory insecticide registration procedures (*SI Discussion*).

The RTL_{SW} for North American countries (the US and Canada) were generally derived from the US EPA insecticide registration procedure, whereas the RTL_{SW} applied to European Union member states originated from the European insecticide risk assessment. Both procedures are described in more detail below. The RTL_{SW} used for the evaluation of insecticide concentrations measured in countries outside the US, Canada, or the EU were obtained by calculating the average values of the RTL_{SW} officially used in the US and European risk assessments. These two geographic entities were considered to have rather strict and science-based regulatory procedures for pesticides that could be used for the evaluation of insecticide exposure worldwide. Generally, the concentration of each insecticide was compared with its respective RTL, regardless of how many compounds were measured in a given sample, and the aggregated exceedance frequencies for all studies considered here were computed across multiple sites.

The RTL_{SW} (Table S1) applied to concentrations measured in the US and Canada were derived from the most recent publically available US EPA Office of Pesticide Programs risk assessments for the specific insecticides, e.g., the US EPA's pesticide Reregistration Eligibility Decision (RED) documents (11), which summarize the acute and chronic toxicity endpoints used in ecological risk assessment for aquatic organisms. In the US acute risk assessments, an estimated environmental concentration is divided by the lowest acute toxicity endpoint (EC_{50} or LC_{50}) for freshwater and estuarine invertebrates or fish to obtain a risk quotient (RQ). This RQ is then compared with a level of concern (LOC), as defined by the EPA, which is 0.5 for acute aquatic risk. In cases in which the RQ exceeds the LOC, risks exist and appropriate risk mitigation measures must be applied or else no registration will be

granted (for details, see ref. 12). Within the EPA ecological risk assessment, the RTL_{SW} (as used herein) is calculated by multiplying the lowest relevant acute toxicity endpoint by the LOC of 0.5. Apart from insecticide concentrations measured in the EU (see below), we compared concentrations measured in freshwater systems to freshwater RTL_{SW} and those measured in estuarine surface waters to estuarine RTL_{SW} (Table S1). As no US EPA risk assessment documents were available for fenvalerate, the same EPA risk assessment procedure described above was applied using the most sensitive freshwater or estuarine toxicity endpoint, which is provided by core and supplemental studies in the OPP Pesticide Ecotoxicity Database (13). This database contains the currently known ecotoxicity endpoints for registered pesticides used in the US. The toxicity data included in the database are compiled from actual studies reviewed by the EPA in conjunction with pesticide registration or reregistration procedures and have been deemed acceptable for use in ecological risk assessment processes.

In the EU's pesticide risk assessment procedure, the relevant toxicity endpoint is divided by the predicted environmental concentration, resulting in a toxicity exposure ratio (TER). The TER is then compared with trigger values of 100 for the lowest acute toxicity data of the standard freshwater test species or 1 to 10 for the NOEC, NOEAEC, or EAC from a chronic laboratory or higher-tier aquatic micro- or mesocosm study (14, 15). A risk is indicated if the TER is below the relevant trigger value.

For the RTL_{SW} (Table S1) applied to concentrations measured in EU member states, official European pesticide registration documents (16, 17) were evaluated concerning the relevant ecotoxicity endpoints considered within the aquatic risk assessment context. If no documents were available for a certain insecticide at the EU level, the relevant toxicity endpoints and associated trigger values used by the German Federal Office of Consumer Protection and Food Safety (BVL) were used (18). For endosulfan, fenpropathrin, fenvalerate, and permethrin, no Europe-wide ecological risk assessment endpoints were available, and the relevant German ecotoxicological effect concentrations and safety factors were applied as European RTL_{SW}. Generally, estuarine or marine organisms are not assessed within the official European pesticide environmental risk assessment so that freshwater RTL_{SW} were applied to all insecticide concentrations measured in the EU irrespective of the type of surface water (Table S1).

In addition to the RTL_{SW} described above, we also evaluated MIC_{SW} using environmental quality standards (EQS). The EQS values (taken from refs. 19-21) were available for 18 insecticide compounds with a corresponding total number of 7,821 MIC_{SW}.

RTL_{SED} are not determined by default for all insecticide compounds within the official US or EU insecticide risk assessment procedures. RTL_{SED} were available from official regulatory risk assessment documents for the following six insecticide compounds: carbofuran, bifenthrin, cypermethrin, cypermethrin-alpha, lambda-cyhalothrin, and tefluthrin (Table S1). The RTL_{SED} derivation is comparable to that described above for RTL_{SW}, with an LOC of 0.5 (in the US EPA risk assessment procedure) and trigger values of 10 (in the EU risk assessment procedure). The insecticide exposure levels detected in sediments or suspended particles for which no sediment RTL_{SED} were available were evaluated by applying maximum permissible concentrations (MPC), as compiled in ref. 19 (Table S1). MPCs (referred to as RTL_{SED} in the main text and the *SI Appendix*) determine the insecticide concentrations in the aquatic environment above which the risk of adverse effects is considered unacceptable provided that the entire aquatic community is taken into account (19). If no MPC was available from ref. 19, we adopted the modified EPA method for aquatic ecosystems, according to which fixed assessment factors were applied to convert acute toxicity data into MPC values for sediment or suspended particles (19, 22). The ecotoxicological endpoints used to apply the modified EPA method originated from the published scientific literature (Table S1). RTL_{SED} were generally applied to all insecticide concentrations in sediments, regardless of their geographic origin.

Further details and corresponding references regarding the RTL derivation of each insecticide considered within this meta-analysis are specified in Table S1.

Insecticide classes

The observed exceedances of RTL_{SW} using aqueous-phase exposure data were compared based on a classification of compounds into three generations of insecticide classes (organochlorines, organophosphates and carbamates, and pyrethroids) included in our meta-analysis. We denote the insecticide class "organophosphates and carbamates" as "organophosphates" in the main text and in the *SI Appendix*. The insecticide generations are defined as classes of insecticides that have been on the market for different periods of time (23) and as insecticide classes that differ with regard to their ecotoxicological mode of action (Table S5) (8). We combined organophosphate and carbamate insecticides into one class because they have been on the market for almost the same amount of time and exhibit the same mode of action (Table S5). For the neonicotinoid insecticide class, only 131 surface water concentrations were available in the peer-reviewed literature. Due to the very small number of cases available, which was further reduced to 72 concentrations available for linear

model analyses (see below), this insecticide class was excluded from all statistical analyses of RTL_{SW} exceedance comparisons for the different insecticide generations.

Classification of countries according to their environmental regulatory quality

To evaluate the influence of the country-specific regulatory standards on global surface water insecticide exposure, we analyzed the data collected for our meta-analysis with regard to differences in observed RTL_{SW} exceedances across countries. We distinguished between countries with well-developed risk assessment and management procedures (referred to here as High Environmental Regulatory Quality or HERQ countries) and those with less well-developed risk assessment procedures and environmental regulatory regimes (Low Environmental Regulatory Quality or LERQ countries) (Table S10). The classification procedure was based on the following three environmental regulatory quality indicators: (i) the "Environmental Regulatory Regime Index" (ERRI) score (24), which is based on, among other factors, the stringency of environmental standards and environmental regulatory structure and enforcement; (ii) the countries' regulatory quality percentile rank as one of the World Bank's global governance indicators (25); and (iii) the World Bank's main criterion for classifying economies, namely, the gross national income (GNI) per capita (26). According to ref. 24, high levels of per capita income and economic development show a significant correlation with high environmental regulatory quality.

A country's environmental regulatory quality was categorized as high if (i) the ERRI score of the particular country exceeded one (24) or if (ii) the ERRI score of a particular country was positive or not specified and a country's regulatory quality rank fell in the upper 25th percentile worldwide (25) and that particular country was classified as a high-income economy with a GNI per capita of $12,476 or more (26). All other countries were classified as LERQ countries (Table S10).

Statistical analyses: linear model

A linear model analysis was conducted with the logarithm of the aqueous phase measured insecticide concentration to RTL_{SW} ratio as the dependent variable. To determine the effects of the countries' environmental regulatory quality (Table S10) and the three insecticide classes (Table S5) on the dependent variable, the following independent variables were entered in the analysis using a complete-case approach (27): log sampling interval, log catchment size, sampling date, and the dummy-coded categorical variables for country regulatory classification (HERQ countries ["0"] vs. LERQ countries ["1"]) and insecticide

substance classes (organochlorines ["0"], organophosphates and carbamates ["1"], and pyrethroids ["2"]). The insecticide substance class neonicotinoid was excluded in all linear model analyses due to the low number of concentrations available for complete-case analyses (n = 72). The variable sampling interval and catchment size were log-transformed due to the wide spread of the values (minimum/maximum observations > 1,000) and a very left-skewed distribution (checked visually).

In the linear model building, all independent variables and interactions were added in sequential steps; that is, first, a main effects model was specified, followed by models containing relevant two-way and three-way interactions (Table S6). We employed automated model building to identify the independent variables and respective interactions with the highest explanatory power for the response variable, namely, the logarithmic insecticide concentration to RTL_{SW} ratio. The automated model building started with the null model (no explanatory variable included) and used backward- and forward-entering variables, with the Bayesian Information Criterion (BIC) used as the goodness-of-fit measure, to identify the best-fit linear models. In addition, manual model building based on expert judgment was performed using the t-test to test the significance of individual predictors and interaction terms and the partial F-test to test for significant differences during model simplification. However, the automated model building and manual model building processes resulted in identical best-fit models. Post hoc probing of interactions was performed by testing simple slopes between groups of the different categorical independent variables (Table S12) and differences between regression lines at specific predicted values of the outcome variable using a modified Johnson–Neyman technique (28) (Table S13).

The models were checked for heteroscedasticity, normal distribution of the residuals, and the influence of single observations (the latter using residual leverage plots and Cook's distance). All computations were performed with the open-source software R (version 2.15.2 for Mac OS X 10.6.8).

SI Discussion

Environmental risk assessment procedure and insecticide field concentrations

The regulatory risk assessment procedure for pesticides requires aquatic exposure data that must be predicted using exposure models because the compounds under assessment are usually not yet on the market (15, 29). These exposure predictions are conducted using realistic worst-case assumptions regarding the variables that determine the pesticide concentration in the non-target environment. In parallel, effect data are derived from laboratory and semi-field model ecosystem experiments (micro- or mesocosms) using various organisms. In the case of aquatic risk assessment predictions for surface waters, effect data are generated for different aquatic organisms. To address uncertainties in the effect assessment, safety factors are often used, i.e., the lowest relevant observed toxicity value from a given ecotoxicological test is divided by a factor between 1 and 100 to derive concentrations that are assumed to be ecologically acceptable (here referred to as regulatory threshold levels, RTL). Comparisons of predicted exposure data and measured effect data, including safety factors (RTL), then indicate either an acceptable environmental risk or the need for specific risk mitigation measures (e.g., no-spray field margins close to surface waters) that become part of the registration procedure as legally binding label amendments for the farmer (30, 31). The pesticide risk assessment procedure, which lasts several years and costs approximately US$ 25 million per pesticide compound (32), should ensure that pesticide field concentrations do not exceed the RTL, and registration is granted only if these requirements are met. In essence, RTLs denote the maximum threshold concentrations on whose basis individual pesticides are officially approved by regulatory authorities for usage in agriculture, after considering all aspects of exposure predictions, effect assessment, uncertainty, risk management obligations and cost-benefit evaluations. For insecticides in particular, the procedure for determining RTLs often accepts clear but transient effects on aquatic organisms, e.g., RTLs based on so-called "no observed ecologically adverse effect concentrations" derived from mesocosm studies (15), which, however, are assumed to be ecologically acceptable. Consequently, once the insecticide is registered and in use, real exposure levels in the field must ultimately not exceed the RTL to exclude ecologically unacceptable effects, biodiversity losses, and threats to aquatic ecosystems' structures and functions (33, 34) (Fig. 2*A*, main text). The comparison of insecticide concentrations measured in agriculturally influenced surface waters to RTLs makes it possible therefore to assess the risks whether and to what extent insecticides potentially cause adverse

environmental effects, which must be avoided according to the regulatory legislation (14, 35).

Comparison with other large-scale studies on insecticide surface water exposure

Agricultural land use and associated insecticide use affect large areas worldwide (36). Despite this fact, few large-scale (e.g., continental) studies consider the insecticide exposure of aquatic ecosystems. For example, the US Geological Survey (USGS; findings summarized in ref. 37) summarized pesticide surface water exposure for 83 agricultural streams across the US and reported that 57% of these 83 stream sites investigated exceeded the regulatory threshold or equivalent water-quality benchmark one or more times during 1992-2001; most of these exceedances involved insecticides exceeding the acute exposure thresholds (37). However, there are several differences between this governmental investigation of insecticide surface water exposure and the meta-analysis presented here: (i) the USGS evaluation encompassed only 10 years (1992-2001); thus, recent insecticide exposure data were not available; (ii) modern, recently increasingly used insecticide classes, such as pyrethroids (with the sole exception of cis-permethrin) and neonicotinoids were not considered, and insecticide exposure in bed sediments was evaluated only for organochlorine insecticides; (iii) the USGS analyzed insecticide exposure data collected at 83 agricultural stream sites; in comparison, our meta-analysis covered more than 2,500 different surface water sites (including streams, rivers, lakes, ponds, estuaries, etc.). However, although the results of our meta-analysis generally support the findings of the USGS monitoring program (i.e., the MICs in surface waters exceed regulatory thresholds, even in highly regulated countries such as the US), they differ in terms of the detected exceedance frequencies per site. In detail, our meta-analysis indicates that although the majority of sites were sampled only once, 68.5% ($n > 1,750$) of these sites were exposed to MICs exceeding their RTL; in contrast, one or more threshold exceedance was reported at only 57% of the 83 agricultural stream sites investigated by the USGS, though each of them had been surveyed several times within a 10-year period (37).

In a narrative review, one publication (38) compiled the surface water concentrations of 38 insecticide compounds, as reported in peer-reviewed literature published between 1982 and 2004, for 15 countries worldwide. However, this study lacked a quantitative data analysis, listed only the minimum and maximum field concentrations ($n = 343$) reported in each field study, and qualitatively compared the maxima ($n = 23$ concentrations) of only a few selected insecticide compounds to various water quality guidelines. By evaluating EU governmental monitoring data on a wide variety of different organic chemicals, ref. 39 recently showed that these compounds threaten the integrity of freshwater ecosystems across the EU. However,

only the maximum and mean concentrations were available for risk evaluation by comparison with acute and chronic standard toxicity data. A recent publication (40) synthesized neonicotinoid surface water concentrations from 29 studies. Although global in scale, this review solely focused on neonicotinoids and reported aquatic exposure data for nine countries only. Finally, ref. 41 compared 122 insecticide field concentrations obtained from 22 scientific field studies to the predicted environmental concentrations (PECs) derived from European pesticide registration documents and disclosed potential deficiencies of the European regulatory exposure assessment. However, in addition to the fact that this publication compared MICs with PECs rather than RTLs, the underlying dataset was substantially smaller than those data presented here and was restricted in geographic scope: only six countries were considered.

We are not aware of further large-scale (e.g., continental) studies or reports targeting agricultural insecticide surface water exposure; thus, we conclude that no comprehensive quantitative global synthesis of insecticide surface water exposure exists that is comparable to the meta-analysis presented here.

Evaluation of insecticide monitoring data

In evaluating pesticide surface water monitoring data, the fact that temporal exposure profiles vary greatly among the various groups of pesticides needs to be considered. Insecticide exposure of surface waters is characterized by infrequent (i.e., 4–6 exposure events per year) and short-term (i.e., a few hours) insecticide concentration peaks (4). Thus, levels exceeding the LOQ in most cases occur only for very short periods (i.e., less than 1% of the year) (4, 42), which holds true for compounds belonging to different insecticide classes (4). It follows that for more than 99% of the time, it is neither feasible nor valid to test the hypothesis that MICs do not exceed their respective RTLs because none of the data that are needed to verify or falsify this hypothesis can be generated. Given this fact, the occurrence of a quantifiable insecticide concentration (i.e., an insecticide concentration > LOQ) is essential as an indicator of whether an insecticide entry event into a surface water body has occurred; these data can be used to test the hypothesis that the insecticide concentration in the field does not exceed the respective RTL. However, it is important to note that aquatic organisms in agricultural surface waters are repeatedly exposed to multiple other pesticides (i.e., herbicides and fungicides) during extended periods of the pesticide application season (43).

Therefore, the data to examine whether the registration procedure is sufficiently conservative and whether insecticide surface water concentrations comply with regulatory risk assessment

outcomes can only consist of cases of samples with insecticide concentrations > LOQ. The sheer number of cases (n = 11,300) with MICs > LOQ available for hypothesis testing within our meta-analysis confirms that MICs largely exceed the RTL at the global scale, i.e., that the cornerstone of regulatory insecticide environmental risk assessment and management is jeopardized by actual field conditions worldwide. Within this context, ref. 4 demonstrated that the use of frequency-based exposure data evaluations involving all insecticide monitoring results (including those below the LOQ), which focus on the probability of threshold level exceedances (e.g., ref. 44) are inappropriate and misleading for compounds with transient exposure patterns, such as insecticides. Ref. 4 also demonstrated that insecticide monitoring datasets must be evaluated using a relevance-driven risk assessment approach; that is, only concentrations > LOQ are relevant for insecticide exposure assessment.

However, to provide information on the frequency of occurrence of quantifiable insecticide concentrations in the field (these data are often not or only insufficiently provided by the scientific studies included in our meta-analysis) and thereby show the characteristics underlying specific insecticide exposure patterns using field data, we retrieved and analyzed information on the frequencies and numbers of insecticide concentrations > LOQ obtained from 11 detailed scientific field studies on insecticide surface water exposure (see ref. 4, which provided this information, for details). The evaluation of these monitoring data showed that only 2.6% of the 10,676 field samples collected in these 11 studies contained quantifiable insecticide concentrations. These results are almost identical to the evaluation of large US governmental monitoring datasets derived from the United States Geological Survey (http://waterdata.usgs.gov/nwis) and the US Environmental Protection Agency (http://www.epa.gov/storet/), which showed that insecticide concentrations were quantifiable (i.e., MIC > LOQ) in only 2.8% of the 3,749,848 insecticide surface water measurements recorded at 14,134 sites across the entire US.

Extrapolating the percentages of samples with quantifiable insecticide concentrations derived from the 11 scientific monitoring studies (i.e., 2.6%) to the data examined in our meta-analysis, the 11,300 MICs > LOQ analyzed here refer to a population of n = 434,615 theoretically analyzed samples in the 838 studies considered. However, for the vast majority of samples (n = 423,315; 97.4%), no insecticide concentrations would have been quantified (Table S3).

Overall, the small percentages of samples with quantifiable insecticide residues that we found confirm that insecticide exposure incidences occur extremely rarely in the field (i.e., less than 1% of the year, see above); consequently, the question of whether surface water exposures to

insecticide adhere to RTLs can only be addressed using insecticide concentrations > LOQ.
In essence, the inclusion of values below the LOQ in insecticide monitoring data evaluation underestimate the risk to aquatic life and creates a false sense of certainty and protection (4) because such an approach does not address the extremely high temporal variability of insecticide exposure in the field. In addition, the approach of assessing only peak exposure concentrations used in our meta-analysis is consistent with US EPA and EU procedures used to evaluate potential acute ecological effects (15, 45).

Distribution of insecticide measurements among surface water bodies

Overall, the 11,300 insecticide concentrations were measured in at least 1,434 discernible surface water bodies and at more than 2,500 sites. As approximately 50 studies reported multiple insecticide concentrations that were derived from several different surface waters without relating the measurements to a specific site, the exact number of investigated surface water bodies is even higher than the 1,434 water bodies specified in our dataset. However, to exclude the potential dominance of single surface water systems (i.e., a high number of concentrations measured in only one or a few surface water bodies leading to a geographical sampling bias), we analyzed our data regarding the occurrence of such spatial insecticide measurement clusters. As a result (Fig. S1), more than 50% of all surface water bodies were found to have had three or fewer insecticide measurements, and the 90^{th}, 95^{th}, and 99^{th} percentiles were 19, 30, and 68 measurements per water body, respectively. Only five surface water bodies had more than 100 insecticide measurements, with a maximum of 172 concentrations per surface water body. In essence, we can exclude the possibility that insecticide concentrations derived from a few individual surface water bodies dominated our global insecticide exposure dataset.

Agricultural nonpoint source origin of insecticide concentrations

Technically speaking, the pesticide risk assessment procedures described above and the resulting RTLs are valid only for evaluating agricultural pesticide use (14, 15, 35), which is also the focus of the present meta-analysis. Although we excluded insecticide exposure data that definitely did not result from agricultural nonpoint sources, samples taken in large surface water systems might result from various sources (e.g., urban or industrial use). Therefore, we further classified water-phase concentrations into those resulting with a high certainty from agricultural nonpoint source entries (i.e., rainfall- or irrigation-induced runoff, rainfall- or irrigation-induced drainage, spray drift caused by ground-based or aerial

application, and releases from rice fields) and those that potentially, though not likely, might have resulted from other sources. This classification was based on information provided in the scientific studies; that is, we selected only those insecticide exposure concentrations (i) that the authors explicitly related to agricultural insecticide use (due to land use surrounding the sampling location, the nature of the insecticide compounds identified [e.g., some insecticides are exclusively registered for agricultural use], and the timing of sampling campaigns [e.g., dormant insecticide spraying during winter months in California]) and (ii) for which the authors provided as the definite or very likely route of entry nonpoint sources (e.g., spray drift, runoff) due to observations made during their field campaigns. These criteria enabled us to attribute specific insecticide concentrations to agricultural nonpoint source pollution with a very high degree of reliability.

If the dataset is restricted to only those insecticide concentrations definitely resulting from agricultural nonpoint source inputs (Table S4), an even higher percentage of concentrations exceed their respective RTLs. It follows that an even more stringent selection of published insecticide exposure data would highlight the failure of regulatory environmental risk assessment procedures that are employed for the agricultural use of insecticides even more strongly.

Organic carbon/water partitioning coefficient (K_{OC}) and bioavailability

The bioavailability of pesticides in surface waters generally depends on substance-specific K_{OC} values. While this parameter is less important for other insecticide classes, pyrethroid insecticides are characterized by high hydrophobicity ($K_{OC} = 10^5 – 10^7$) (46) and therefore readily bind to suspended particles, which may reduce their short-term toxicity to water column organisms (47). Analytical measurements of surface water samples without appropriate pre-filtration procedures (e.g., 0.45 μm filtration) reflect both freely dissolved and particle-associated pyrethroid concentrations. Therefore, recent scientific studies have suggested that analytical results based on such “whole water” concentrations are not directly comparable with aquatic acute toxicity effect concentrations measured in laboratory tests using water-only setups (47, 48).

However, any pre-filtering of water samples prior to analysis underestimates total pyrethroid exposure within an aquatic ecosystem due to the loss of analytes adsorbed to particles that are filtered out (45, 49), making an exposure assessment of all relevant constituents impossible. For this reason, some researchers do not recommend pre-filtering in pyrethroid surface water analysis (48, 49). Furthermore, pyrethroid adsorption is estimated to take place within several

hours (50, 51) to a few days for typical streams, which are characterized by less-than-ideal mixing conditions (51). These time spans are of toxicological concern considering that a number of studies indicated that an exposure duration of between 0.5 and 1 h to pyrethroid concentrations as low as 0.001 µg/L in the water phase can cause long-lasting, ecologically relevant effects on some aquatic organisms (52-54). In addition, ref. (55) showed that suspended particle and DOC concentrations in agriculturally influenced surface waters can be too low to have an effect on pyrethroid bioavailability reduction.

In general, the assumption that particle-sorbed pyrethroids in surface water systems are not bioavailable - or are only bioavailable to a limited extent - requires further scientific verification (48). Experimental studies demonstrating the bioavailability of hydrophobic insecticides associated with suspended sediments for bivalves (56-58) or identifying the ecotoxicological importance and bioavailability of field-relevant levels of particle-associated pyrethroids for a multispecies community typical of agricultural streams (59) indicate that toxicological effects are possible even in the presence of suspended particles. Therefore, it remains largely unclear whether and to what extent a separation between particle-free water and whole water with regard to pyrethroids is required.

To address this issue using comprehensive pyrethroid field exposure data, we screened all 919 pyrethroid water-phase measurements included in our meta-analysis for pre-filtration prior to analytical measurements. We found that 126 of the 919 pyrethroid surface water samples (13.7%) were filtered before chemical analyses, and 613 (66.7%) concentrations were reported as whole water concentration. No information regarding sample pre-treatment was available for the remaining 180 (19.6%) pyrethroid measurements in the water phase.

To analyze a potential bioavailability artifact of the strongly lipophilic pyrethroids, we performed a second linear model analysis to predict the logarithmic concentration to RTL_{SW} ratios for pyrethroids, among other variables, as a function of pre-filtration prior to analytical measurement. The following independent variables were considered again using a complete-case approach (27): log sampling interval, log catchment size, sampling date, and the dummy-coded categorical variables for country regulatory classification (HERQ countries [“0”] vs. LERQ countries [“1”]) and pyrethroid sample filtration (yes [“0”] vs. no [“1”]).

The results of the linear model analysis for pyrethroid concentrations showed that surface water samples that were filtered prior to chemical analysis led, though not significant ($p = 0.278$), to an even higher concentration to RTL_{SW} ratio compared to pyrethroids quantified in whole water samples (Table S7). This result clearly demonstrates that the comparison of RTL_{SW} exceedances for the different insecticide substance classes (i.e., significant higher

RTL_{SW} exceedances for highly sorptive pyrethroids compared to organophosphates and organochlorine insecticides) is not biased by potential pyrethroid bioavailability limitations. In consequence, RTL_{SW} exceedance frequencies were higher for pyrethroid surface water samples with pre-filtration procedures (64.5%) than for those that had not been filtered prior to the analytical determination of pyrethroid surface water concentrations (59.7%).

RTL/LOQ ratios

Statistical analysis of the different insecticide generations revealed significantly higher RTL_{SW} exceedance frequencies for pyrethroids than for organophosphates and organochlorines, with the latter two also demonstrating a significant difference (see main text, Fig. 3*A*, and Table S6). In fact, newer insecticide classes such as pyrethroids are characterized by a markedly higher toxicity to aquatic organisms than organophosphates, which in turn exhibit a notably higher acute toxicity in aquatic systems than organochlorines (60). The relationship between insecticide classes and increasing toxicity for aquatic organisms is also expressed in the decreasing RTL_{SW} assessed for the newer insecticide compound classes (Table S8). For example, the pyrethroid median freshwater RTL_{SW} were almost 40 times lower than the RTL_{SW} obtained for organochlorine compounds. However, median LOQs were virtually the same for organochlorines and organophosphates and were only one order of magnitude lower for pyrethroids (Table S8), such that significantly higher RTL_{SW} exceedance frequencies for pyrethroids (compared with the two older insecticide classes) could result from a methodological bias. In particular, lower distances between RTL_{SW} and LOQs of an insecticide class (e.g., pyrethroids) increase the likelihood that the concentrations exceed their RTL_{SW}.

To test the influence of this aspect, we partialled out the effects of RTL_{SW}/LOQ ratios on logarithmic concentration to RTL_{SW} ratios predicted by our main effects model (Table S6). We first regressed the dependent variable (logarithmic concentration to RTL_{SW} ratios) on logarithmic RTL_{SW}/LOQ ratios and obtained the residuals for this model. We then specified a linear model using a complete-case approach (27) that included the independent variables log sampling interval, log catchment size, sampling date, the categorical variables for country regulatory classification (HERQ countries [“0”] vs. LERQ countries [“1”]) and insecticide substance classes (organochlorines [“0”], organophosphates and carbamates [“1”], and pyrethroids [“2”]), with the residuals from the univariate regression model described above as a dependent variable.

The results of this regression analysis confirmed our findings that pyrethroid concentrations

show significantly higher RTL_{SW} exceedances than both organophosphates (B = 0.201331, p < 0.001) and organochlorines (B = 0.296662, p < 0.001), with the latter two also demonstrating a significant difference (B = 0.095332, p = 0.039) (Table S9). It follows that although the statistical consideration of the RTL_{SW}/LOQ ratios decreases the differences in predicted concentration to RTL_{SW} ratios between the insecticide classes, pyrethroids still have significantly higher RTL_{SW} exceedance frequencies compared to organophosphorus and organochlorine insecticides, with the latter two also retaining their statistically significant differences (Tables S6 and S9). In essence we conclude that despite the fact that varying RTL_{SW}/LOQ ratios have an influence on the RTL exceedance rates obtained for the different insecticide substance classes, they were not a major factor in the observed higher RTL_{SW} exceedances for newer insecticide classes.

It is worth noting that a small proportion (i.e., 6.9%) of the MICs were reported in the scientific literature based on analytical methods with LOQs that exceeded their respective RTLs. However, these cases do not contradict our findings, as all MICs detected in the field must not exceed their RTLs to avoid incidences of unacceptable effects on the freshwater biodiversity and to adhere to respective pesticide legislations. To this effect, the use of insecticide field exposure assessments with LOQs larger than the RTL should not lead to the detection of any insecticide concentration, as each individual case of RTL exceedance in the field indicates a failure of the regulatory pesticide risk assessment and a substantial risk for freshwater biodiversity, irrespective of the LOQ employed.

Interaction among substance class, country regulatory classification, and sampling date

The interaction among substance class, country regulatory classification, and sampling date derived from the linear model analysis (Table S6) contributes significantly to the variation in the concentration to RTL_{SW} ratios. To further probe this three-way interaction, we conducted simple slope tests (Table S12) and tested for significant differences for predicted logarithmic concentration to RTL_{SW} ratios for any pairs in the three-way interaction (Table S13) (cf. ref. 28). However, it is important to note here that further explanatory variables not provided in the scientific studies govern insecticide exposure in the field; the non-inclusion of these variables inevitably increases the amount of unexplained variance in our linear model analysis (Table S6).

The results of our three-way interaction analyses showed that for LERQ countries, the predicted concentration to RTL_{SW} ratios for organochlorine and organophosphorus insecticides significantly increased over time, whereas those of pyrethroids significantly

decreased (Fig. S2 and Table S12). For HERQ countries, the ratios of concentration to RTL_{SW} decreased for all three generations of insecticides; however, these declines were significant only for organophosphorus insecticides and pyrethroids. For the year 2010, the predicted concentration to RTL_{SW} ratios were significantly higher for organochlorine and organophosphorus insecticides in LERQ countries than in HERQ countries. Those for pyrethroids were also higher, but the difference was not statistically significant (see Fig. S2 and Table S13 for statistical results of predicted logarithmic concentration to RTL_{SW} ratios for pairs in this three-way interaction). In contrast, the predicted concentration to RTL_{SW} ratios for the year 1980 were higher in HERQ countries than in LERQ countries for organochlorine and organophosphorus insecticides (significant). However, no comparison between HERQ and LERQ countries could be made for this date for pyrethroids given the range of the available monitoring data (the first pyrethroid concentrations were reported in LERQ countries in the year 1993) for this compound class (see, also, Fig. S2, *C* and *D*).

The development and application of legislative and regulatory prescriptions for pesticide use in HERQ countries in recent decades (Table S2) may help to explain the decreasing risks arising from agricultural insecticide applications in those countries over time. In contrast, pesticide use in LERQ countries has increased rapidly in recent decades, but because of prioritizing food production maximization over environmental considerations, these countries only weakly regulate pesticide use and application (61-63). As a result, increasing organochlorine and organophosphorus insecticide concentrations and overall threshold level exceedance rates in surface waters can be observed in these countries. In addition to LERQ countries' weak regulatory frameworks and rule enforcement, farmers' limited knowledge of appropriate pesticide use and environmental awareness also contribute to higher exposure and therefore risks for surface water systems (61, 63). However, in contrast to those for organochlorine and organophosphorus insecticides, pyrethroids' predicted concentration to RTL_{SW} ratios showed a significant decrease in LERQ countries during the last two decades (Fig. S2, *A* to *D*, and Table S12). Although the reasons for this decrease are not completely clear, Fig. S2*D* indicates that only four studies with 27 concentrations (i.e., only 2.9% of all [n = 919] pyrethroid surface water concentrations documented in the scientific literature), which all stemmed from Asia, were available for the period 2005–2011. It follows that the predicted decrease of concentration to RTL_{SW} ratios for the years 1995 to 2010 could be an information bias resulting from a lack of different field investigations on pyrethroid surface water concentrations in LERQ countries, which, however, is not the case for the predicted high concentration to RTL_{SW} ratios for 1995, as ten field studies with 99 concentrations from

Africa, Asia, Europe, and South America were available for the time span 1999–2004 (Fig. S2, *C* and *D*). Overall, the data availability on pyrethroid surface water exposure in LERQ countries must be judged as too weak to definitively conclude that their environmental risk for aquatic ecosystems decreased considerably between 1995 and 2010. It follows that more field investigations are needed to clarify the actual environmental risks of agricultural pyrethroid use in LERQ countries worldwide.

Regarding differences among specific insecticide classes, pyrethroids showed a significantly higher predicted risk for surface waters systems than the other two classes in HERQ countries for 1995 and 2010 (Table S13 and Fig. S2, *A* to *C*). Although the predicted concentration to RTL_{SW} ratios were slightly higher for organophosphorus insecticides for the year 1980, the difference with respect to pyrethroids was not statistically significant, and both were significantly higher than those of organochlorine insecticides. Pyrethroids' predicted risks for aquatic ecosystems were also significantly higher than those for organochlorine and organophosphorus insecticides in LERQ countries for the year 1995. However, no statistically significant difference between concentration to RTL_{SW} ratios of organochlorines and pyrethroids derived from LERQ country data could be observed for 2010, and organophosphorus insecticides exceeded the other two insecticide classes significantly. Organophosphorus insecticide risks for surface waters were predicted to be significantly higher in HERQ countries than those arising from organochlorine insecticides for 1980 and 1995 as well as for 1995 and 2010 when considering LERQ countries (Fig. S2, *A* to *C*, and Table S13).

Overall, the evaluation of real-world monitoring data as presented here does not confirm the assumption that prevails in the scientific literature (64-68) that newer insecticide classes are more environmental friendly than older ones, at least when short-term acute risks for aquatic ecosystems are considered. The probable reason for this observation is the increasing invertebrate toxicity that has accompanied the development of newer insecticide classes in recent decades (60) and that often triggers RTL_{SW} settings for insecticides. In addition, ref. 41 found that the EU regulatory exposure assessment via FOCUS models is significantly less protective in predicting pyrethroid field concentrations than organochlorine and organophosphorus concentrations. This finding may also be true for regulatory pesticide model-based exposure assessments in other countries.

SI Figures

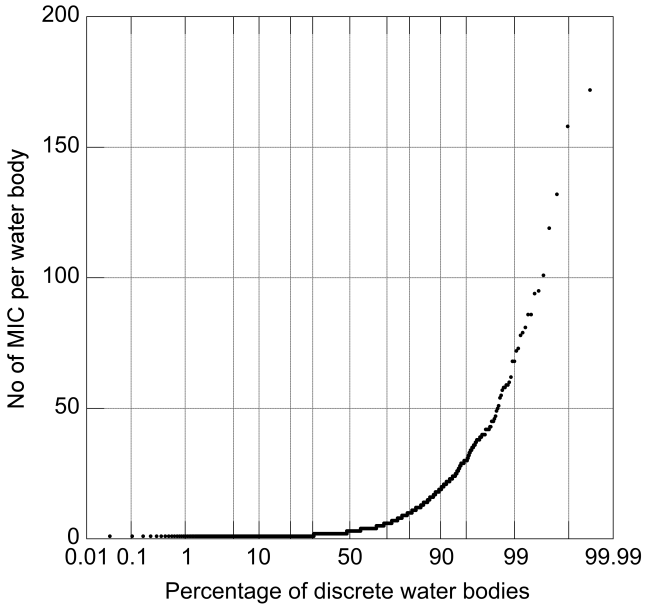

Fig. S1. Number of measured insecticide concentrations (MICs, n = 11,300) reported for individual surface water bodies (n = 1,434). Please note that the actual number of discernible water bodies is higher than 1,434 because approximately 50 studies did not specify the exact location of sites with MICs and multiple water bodies were analyzed for insecticide exposure.

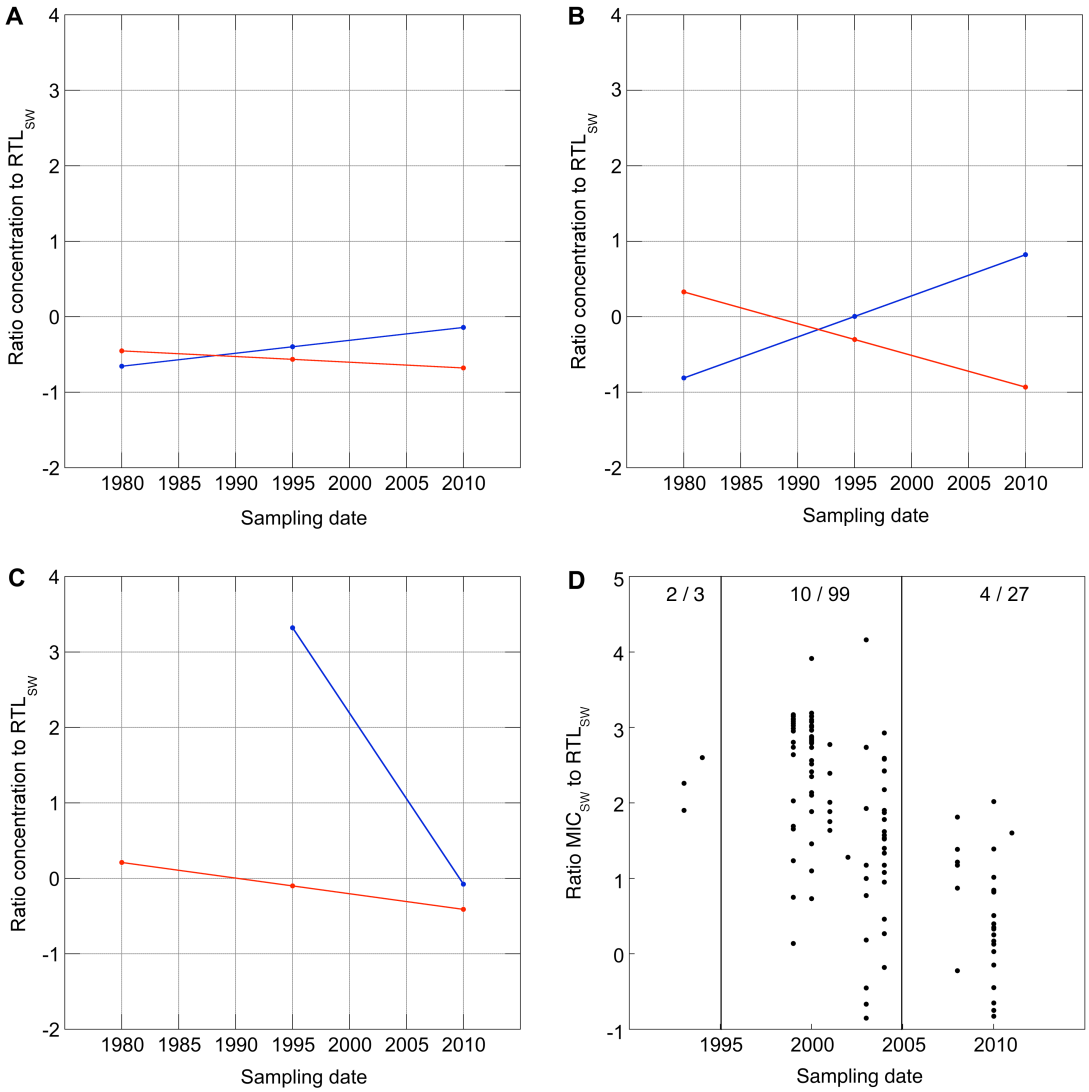

Fig. S2. Three-way interaction among insecticide substance class ([*A*] organochlorine insecticides; [*B*] organophosphate insecticides; [*C*] pyrethroids), country regulatory classification (blue lines: LERQ countries; red lines: HERQ countries), and sampling date versus predicted logarithmic water-phase concentration to regulatory threshold level (RTL_{SW}) ratios. Please note that no predicted concentration to RTL_{SW} ratios were calculated for pyrethroids in LERQ countries for the year 1980 (*C*) because no field study data were available before 1993 (see, also, Table S13). (*D*) Temporal evolution of logarithmic measured aqueous insecticide concentration (MIC_{SW}) to RTL_{SW} ratios (n = 129) derived for pyrethroids from field studies conducted in LERQ countries. Only pyrethroid concentrations available for the linear model analysis are shown. The first figures indicate the numbers of field studies, and the second figures indicate the numbers of concentrations available for specific time periods.

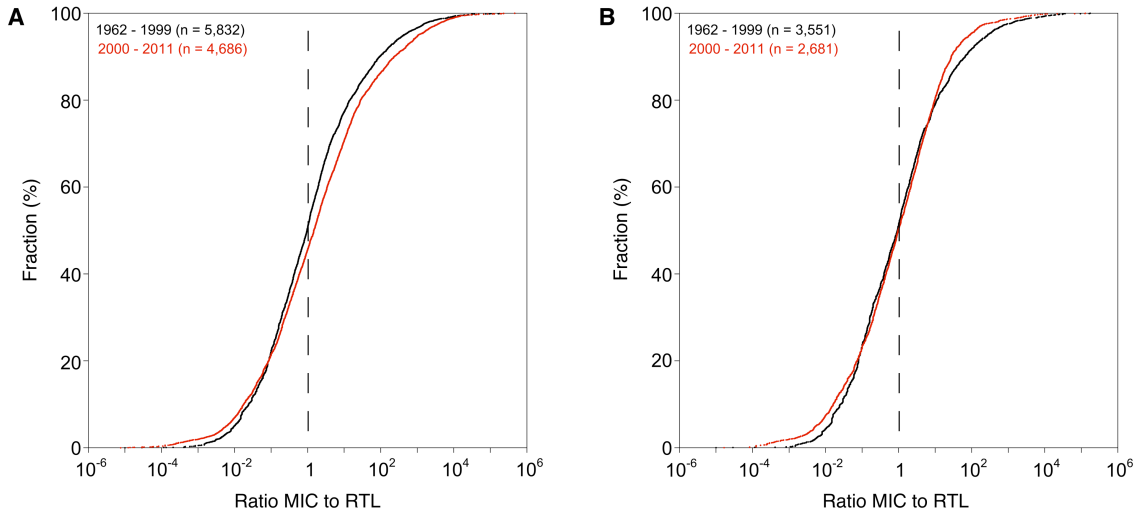

Fig. S3. Distribution curves for reported measured insecticide concentrations (MICs) in water and sediment relative to the respective regulatory threshold levels (RTLs) separated according to whether the values were measured before (i.e., 1962 – 1999; black dots) or after (i.e., 2000 – 2011; red dots) the year 2000. (*A*) Insecticide exposure data for global surface waters; 5,832 concentrations were measured before and 4,686 concentrations were measured after the year 2000. (*B*) Insecticide exposure data for highly regulated countries (Table S10) only; 3,551 concentrations were measured before and 2,681 concentrations were measured after the year 2000.

SI Tables

Table S1. Insecticides included in the meta-analysis and their corresponding regulatory threshold levels for water (RTL_{SW}) and sediments (RTL_{SED}). See *SI Methods* for further details on RTL_{SW} and RTL_{SED} derivation. n.s.: not specified (tau-fluvalinate [three concentrations found in sediments] has no RTL_{SED} or MPC [no maximum permissible concentration or toxicity endpoint available]. Therefore, of the total reported 11,300 concentrations, only 11,297 concentrations were available for all comparisons with threshold levels). - indicates that no freshwater (FW), estuarine water (EST), or sediment concentrations were reported for this insecticide in the literature; sediment refers to sediment and suspended particle concentrations. No US EPA risk assessment documents were available for fenvalerate; thus, toxicity data from the OPP Pesticide Ecotoxicity Database (13) were used for FW and EST RTL_{SW} derivation. MPCs (referred to as RTL_{SED}) for cyfluthrin, esfenvalerate, fenpropathrin, and fenvalerate were derived based on ecotoxicological endpoints published in the scientific literature by applying the modified EPA method according to ref. 19 and ref. 22. Insecticide classes are abbreviated as follows: organochlorine (OC), organophosphate (OP), carbamate (Carb), pyrethroid (Pyr), and neonicotinoid (Neo).

		RTL_{SW} (µg/L)			
Insecticide	**Class**	**North America FW/EST**	**Europe**	**Worldwide FW/EST**	**RTL_{SED} (µg/kg)**
Endosulfan	OC	0.05[69]/0.02[69]	1.3[18]	0.675/0.66	0.026[19]
Azinphos-methyl	OP	0.08[70]/0.105[70]	0.32[71]	0.2/0.2125	0.89[19]
Chlorpyrifos	OP	0.05[72]/0.0175[72]	0.1[73]	0.075/0.05875	1.1[19]
Diazinon	OP	0.105[74]/2.1[75]	2.4[76]	1.2525/2.25	0.95[19]
Malathion	OP	0.005[77]/0.005[77,78]	1.25[79]	0.6275/0.6275	0.9[19]
Parathion-ethyl	OP	0.02[80]/0.0535[80]	0.024[81]	0.022/0.03875	0.13[19]
Parathion-methyl	OP	0.485[82]/0.175[83]	0.073[84]	0.279/0.124	0.96[19]
Carbofuran	Carb	1.115[85]/2.3[85]	0.0205[86]	0.56775/1.16025	0.22[86]
Acrinathrin	Pyr	-/-	0.0087[87]	-/-	-
Bifenthrin	Pyr	0.075[88]/0.002[88]	0.005[89]	0.04/0.0035	4[89]
Cyfluthrin	Pyr	0.0125[90]/0.0012[90]	0.0068[91,92]	0.00965/0.004	0.137[93]
β-cyfluthrin	Pyr	-/-	0.00068[94]	-/-	-
Cypermethrin	Pyr	0.0018[95]/-	0.025[96]	0.0134/-	1.8[95]
α-cypermethrin	Pyr	0.0018[95]/-	0.015[97]	0.0084/-	1.8[95]
ζ-cypermethrin	Pyr	0.0018[95]/-	-	-/-	-
Deltamethrin	Pyr	0.055[98]/0.00085[98]	0.0032[99]	0.0291/0.002025	1.3[19]
Esfenvalerate	Pyr	0.025[100]/0.025[100,101]	0.01[102]	0.0175/0.0175	0.41738[93]
Fenpropathrin	Pyr	0.265[103]/0.0105[103]	0.0053[18]	0.13515/0.0079	0.645[104]
Fenvalerate	Pyr	0.016[105]/0.004[106]	0.0022[18]	0.0091/0.0031	0.88[107]
λ-cyhalothrin	Pyr	0.0035[108]/0.00205[108]	0.0021[109]	0.0028/0.002075	10.5[109]
Permethrin	Pyr	0.0106[110]/0.009[110]	0.025[18]	0.0178/0.017	0.87[19]
Tau-fluvalinate	Pyr	0.175[111]/-	0.022[112]	0.0985/-	n.s.
Tefluthrin	Pyr	-/-	-	-/-	47[113]

Tralomethrin	Pyr	0.0195[114]/-	-	-/-	-
Acetamiprid	Neo	10.5[115]/-	0.5[116, 117]	5.5	-
Imidacloprid	Neo	34.5[118]/-	0.3[119]	17.4/-	-
Thiacloprid	Neo	-/-	1.57[120]	-/-	-
Thiamethoxam	Neo	-/-	2.8[121]	-/-	-

Table S2. List of major international pesticide regulations and guidelines enforced since 1988 in chronological order.

Regulation / guideline
FIFRA Amendments US Federal Law
91/414/EEC EU Pesticide Directive
EPA Risk Assessment "New Paradigm"
EWOFFT (European Workshop on Freshwater Field Test) mesocosm guidance
EPA/ACPA ARAMDG (Aquatic Risk Assessment Mitigation Dialog Group)
Sediment toxicity testing (SETAC guidance document)
"Ganzelmeier/Rautmann" basic spray drift values
FQPA (Food Quality Protection Act)
ECCO (European Community Co-Ordination) aquatic terrestrial guidance
EPA "safer pesticide" program
OPPTS (Office of Prevention, Pesticides and Toxic Substances) study guideline revisions
EMWAT (Endocrine Modulators and Wildlife: Assessment and Testing guideline; EPA, OECD)
ESCORT I (European Standard Characteristics of non-target Arthropod Regulatory Testing) guideline
HARAP (Higher Tier Aquatic Risk Assessment for Pesticides) SETAC guidance document
FOCUS (FOrum for the Coordination of pesticide fate models and their USe) aquatic exposure assessment
ECOFRAM (Ecological Committee on FIFRA Risk Assessment Methods)
CLASSIC (Community Level Aquatic System Studies Interpretation Criteria) SETAC guidance document
ESCORT II (European Standard Characteristics of non-target arthropod Regulatory Testing) guideline
EU DG SANCO Guidance document on Aquatic ecotoxicology revision 4
EUPRA (Probabilistic Risk Assessment for the environmental impact of plant protection products)
EPPO (European and Mediterranean Plant Protection Organisation) guideline revisions
EPA non-target plant Scientific Advisory Panel
1999/45/EEC EU Classification & Labeling Directive
2000/60/EEC EU Water Framework Directive
EU Water Framework Directive amendment priority pollutants
2002/17 EEC EU Environmental Liability Directive
EU Thematic Strategy on Sustainable Use (COM(02)349)
Stockholm Convention on Persistent Organic Pollutants
Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
EPFES (Effects of Plant Protection Products on Functional Endpoints in Soil) guidance document
FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment
ELINK (Linking Aquatic Exposure and Effects in the Registration Procedure of plant protection products)
EU Directive 2009/128/EC Sustainable Use of Pesticides
OECD Strategic Approach in Pesticide Risk Reduction (ENV/JM/MONO(2009)38)
Regulation (EC) 1107/2009 EU Pesticide Directive revision
EFSA Guidance document on tiered risk assessment for plant protection products for aquatic organisms

Table S3. Descriptive statistics (number of concentration measurements) regarding important parameters related to the global insecticide exposure dataset and information on the relation of measured (i.e., quantified) insecticide concentrations (MICs) to the estimated population of analyses conducted.

Parameter[a] (number of MICs with information)	**Minimum**	**25th percentile**	**Median**	**75th percentile**	**Maximum**
MICs per country[b] (n = 11,300)	1	4	31	111	3,854
Sampling date (year; n = 10,521)	1960	1993	1999	2004	2011
Catchment size (km^2; n = 9,290)	0.002	10	200	2,750	3,400,000
Sampling interval (days; n = 8,427)	0.0416[c]	2	15	30	180
Hydrology (n = 10,715)	Lotic surface waters: 8,357 (78%); lentic surface waters: 2,358 (22%)				
Surface water classification (n = 11,300)	Freshwater systems: 9,910 (87.7%); estuarine waters: 1,390 (12.3%)				
Route of entry (n = 11,300)	Nonpoint source[d]: 7,371 (65.2%); runoff: 2,846 (25.2%); rice field effluent: 431 (3.8%); spray drift: 346 (3.1%); aerial application: 179 (1.6%); drainage: 127 (1.1%)				
Relation of MICs to the population of analytical measurements[e]	Total analyses conducted[e]: 434,615 (100%) MIC < LOQ[f]: 423,315 (97.4%) MIC > LOQ[f]: 11,300 (2.6%) MIC > LOQ[f] & RTL[g]: 5,915 (1.4%; 52.4% of cases with MIC > LOQ)				

a: Smaller numbers for some parameters are due to missing information in the studies.

b: Data are available for 73 countries; see Table S10 for details.

c: Event sampling

d: Nonpoint source indicates that the exact route of entry was not further specified in the publications

e: Estimated using information from 11 detailed scientific monitoring studies (see *SI Discussion* "Evaluation of insecticide monitoring data")

f: Limit of quantification

g: Regulatory threshold level

Table S4. Classification of measured insecticide water-phase concentrations (MIC_{SW}; n = 8,166) related to regulatory threshold levels (RTL_{SW}), considering the certainty regarding agricultural nonpoint sources as the origin of exposure.

Classification[a]	**No. of MIC_{SW} values less than RTL_{SW} (%)**	**No. of MIC_{SW} values exceeding RTL_{SW} (%)**
Definitive agricultural nonpoint source origin (n = 2,554) (31.3%)	1,285 (50.3)	1,269 (49.7)
No definitive agricultural nonpoint source origin[b] (n = 5,612) (68.7%)	3,550 (63.3)	2,062 (36.7)

a: In addition to information on the route of entry and the origin of the MIC_{SW} provided in the studies, the classification used was based on the surrounding land use of the sampling locations, the insecticide compounds identified (e.g., some are exclusively registered for agricultural use), and the timing of the sampling campaigns (e.g., dormant insecticide spraying during the winter months in California).

b: The classification "No definitive agricultural nonpoint source origin" does not mean that MIC_{SW} originated from non-agricultural or point sources because this classification was often applied because limited information was provided in the studies.

Table S5. Market introduction (23, 122), development of insecticide market shares (123), and mode of action (8) for major insecticide classes.

Insecticide class	**Introduction to the market**	**Insecticide market share (%) 1990 / 2008**	**Mode of action**
Organochlorines	1940	- / -	GABA-gated chloride channel antagonists
Organophosphates/Carbamates[a]	1950/1962	59 / 24.4	Acetylcholinesterase inhibitors
Pyrethroids	1973	18 / 15.5	Sodium channel modulators
Neonicotinoids	1991	0 / 23.7	Nicotinic acetylcholine receptor agonists

a: Named "organophosphates" in the main text.

Table S6. The results of linear model analyses (main effects model and full model including two- and three-way interactions) for predicting logarithmic insecticide water-phase concentration to RTL_{SW} ratios (n = 5,746). Substance class (SC) (reference category: organochlorine insecticides) and country regulatory classification (CRC) (reference category: high environmental regulatory quality) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables. The same main effects analysis was also carried out using the insecticide substance class organophosphates/carbamates as the reference category to calculate the significance level of pyrethroids vs. organophosphates/carbamates (B = 0.435925; t-value = 8.170; $p < 0.001$). The insecticide substance class neonicotinoid was excluded due to the small number of cases (n = 72) available for analysis.

Step	Multiple R^2	Predictors within final models	Estimate	t-value
Main effects model	0.2331	Intercept	28.3543***	7.159
		Catchment size	-0.2049***	-19.355
		Sampling interval	-0.3669***	-24.701
		Sampling date	-0.014***	-7.166
		SC (OP)[a]	0.4327***	10.870
		SC (Pyr)[a]	0.8687***	14.590
		CRC (LERQ)[a]	0.6349***	17.899
Model with two-way and three-way interactions[b]	0.312 (ΔR^2: 0.0789***)	Intercept	15.22	1.373
		Catchment size	-0.2189***	-21.390
		Sampling interval	-0.3594***	-25.354
		Sampling date	-0.0075	-1.353
		SC (OP)[a]	69.19***	5.608
		SC (Pyr)[a]	26.84	1.668
		CRC (LERQ)[a]	-48.95**	-2.738
		Sampling date x CRC (LERQ)[a]	0.02462**	2.749
		SC (OP)[a] x CRC (LERQ)[a]	-143.2***	-7.009
		SC (Pyr)[a] x CRC (LERQ)[a]	462.9***	8.936
		Sampling date x SC (OP)[a]	-0.03455***	-5.584
		Sampling date x SC (Pyr)[a]	-0.01322	-1.641
		Sampling date x SC (OP)[a] x CRC (LERQ)[a]	0.07185***	7.024
		Sampling date x SC (Pyr)[a] x CRC (LERQ)[a]	-0.2304***	-8.902

a: OP: organophosphates/carbamates; Pyr: pyrethroids; LERQ: low environmental regulatory quality countries

b: See, also, Fig. S2 for a graphical presentation of the three-way interaction.

Significance codes: *** p <0.001; ** p < 0.01; * p < 0.05

Table S7. The results of linear model analyses for predicting logarithmic concentration to RTL_{SW} ratios (n = 650) for pyrethroid surface water concentrations as a function of sample filtration. Country regulatory classification (reference category: high environmental regulatory quality) and pyrethroid sample filtration (reference category: yes) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables.

	Estimate	**t-value**	**p-value**
Intercept	101.329221	8.390	<0.001
Catchment size	-0.180251	-5.095	<0.001
Sampling interval	-0.261243	-9.290	<0.001
Sampling date	-0.050284	-8.342	<0.001
CRC (LERQ)[a]	0.997281	6.473	<0.001
Pyrethroid sample filtration[b] (no)	-0.147252	-1.086	0.278

a: Low environmental regulatory quality countries

Multiple R^2: 0.3012; adjusted R^2: 0.2958

Table S8. Central tendencies (mean and median) of organochlorines (n = 515), organophosphates (n = 1,762), and pyrethroids (n = 546) limit of quantification (LOQ) (derived from studies reporting respective measured insecticide concentrations), mean, and median of freshwater (FW) regulatory threshold levels (RTL_{SW}) (expressed as the average of European and North American FW RTL_{SW}, as listed in Table S1) of the different insecticide classes and the mean and median of specific RTL_{SW}/LOQ ratios for each insecticide concentration.

	Organochlorines	**Organophosphates**	**Pyrethroids**
LOQ (µg/L) (mean / median)	0.045 / 0.01	0.039 / 0.01	0.041 / 0.001
FW RTL_{SW} (µg/L) (mean / median)	0.675 / 0.675	0.432 / 0.279	0.035 / 0.0175
RTL_{SW}/LOQ-ratio (mean / median)	658.1 / 45.5	952.5 / 12.5	36.4 / 6.3

Table S9. The results of linear model analyses (n = 2,367) for predicting the residuals of the linear model "log concentration to RTL_{SW} ratio = 0.83789 – 0.87558 x log RTL_{SW}/LOQ-ratio". Substance class (reference category: organochlorine insecticides) and country regulatory classification (reference category: high environmental regulatory quality) were entered as dummy-coded variables, and catchment size and sampling interval were entered as log-transformed variables. The same regression model was also analyzed using the insecticide substance class organophosphates/carbamates as the reference category to calculate the significance level of pyrethroids vs. organophosphates/carbamates (*B* = 0.201331; t-value = 5.101; p < 0.001).

	Estimate	**t-value**	**p-value**
Intercept	15.518538	3.946	<0.001
Catchment size	-0.050470	-5.307	<0.001
Sampling interval	-0.129792	-10.359	<0.001
Sampling date	-0.007756	-3.934	<0.001
Substance class (OP)[a]	0.095332	2.069	0.0386
Substance class (Pyr)[a]	0.296662	5.168	<0.001
CRC (LERQ)[a]	0.137455	3.673	<0.001

a: OP: organophosphates/carbamates; Pyr: pyrethroids; LERQ: low environmental regulatory quality countries

Multiple R^2: 0.07274; adjusted R^2: 0.07038

Table S10. Classification of countries (n = 73) according to their environmental regulatory quality and number of measured insecticide concentrations (MICs) per country. See *SI Methods* for the detailed classification procedure. HERQ: High Environmental Regulatory Quality, LERQ: Low Environmental Regulatory Quality; ERRI: Environmental Regulatory Regime Index (24); RQ percentile rank: Regulatory Quality percentile rank (25), subdivided as follows: I: Regulatory Quality Percentile Rank 0-25; II: Regulatory Quality Percentile Rank 25-50; III: Regulatory Quality Percentile Rank 50-75; IV: Regulatory Quality Percentile Rank 75-100. GNI per capita: Gross National Income (GNI) per capita (26) classified as follows: 1: Low-income economies GNI per capita: $1,025 or less; 2: Lower-middle-income economies GNI per capita: $1,026-$4,035; 3: Upper-middle-income economies GNI per capita: $4,036-$12,475; 4: High-income economies GNI per capita: $12,476 or more. n.s.: not specified.

Country classification[a]		**Classification category**		
HERQ	**LERQ**	**ERRI score**	**RQ percentile rank**	**GNI per capita**
Australia (531)		pos. (> 1)	IV	4
Belgium (26)		pos. (> 1)	IV	4
Bahrain (4)		n.s.	IV	4
Canada (632)		pos. (> 1)	IV	4
Cyprus (3)		n.s.	IV	4
Denmark (7)		pos. (> 1)	IV	4
France (46)		pos. (> 1)	IV	4
Germany (138)		pos. (> 1)	IV	4
Hungary (3)		pos. (< 1)	IV	4
Israel (1)		pos. (< 1)	IV	4
Italy (152)		pos. (< 1)	IV	4
Japan (477)		pos. (> 1)	IV	4
Netherlands (60)		pos. (> 1)	IV	4
Norway (3)		pos. (> 1)	IV	4
Poland (33)		pos. (< 1)	IV	4
Singapore (6)		pos. (> 1)	IV	4
Spain (415)		pos. (< 1)	IV	4
Sweden (17)		pos. (> 1)	IV	4
Switzerland (6)		pos. (> 1)	IV	4
Taiwan (41)		n.s.	IV	4
United Kingdom (79)		pos. (> 1)	IV	4
United States (3854)		pos. (> 1)	IV	4
	Albania (5)	n.s.	III	2
	Argentina (258)	neg.	II	3
	Bangladesh (20)	neg.	I	1
	Belize (2)	n.s.	II	2
	Benin (13)	n.s.	II	1
	Brazil (192)	neg.	III	3
	Bulgaria (1)	neg.	III	3

Country classification[a]		Classification category		
HERQ	**LERQ**	**ERRI score**	**RQ percentile rank**	**GNI per capita**
	Chile (29)	pos. (< 1)	IV	3
	China (411)	neg.	II	3
	Costa Rica (45)	neg.	III	3
	Cote d`Ivoire (12)	n.s.	I	2
	Egypt (111)	neg.	II	2
	El Salvador (2)	neg.	III	2
	Fiji Islands (1)	n.s.	II	2
	Gambia (4)	n.s.	II	1
	Ghana (51)	n.s.	III	2
	Greece (487)	neg.	III	4
	Honduras (17)	neg.	II	2
	India (551)	neg.	II	2
	Indonesia (60)	neg.	II	2
	Iran (368)	n.s.	I	3
	Jamaica (410)	neg.	III	3
	Jordan (2)	pos. (< 1)	III	3
	Kenya (164)	n.s.	II	1
	Korea (10)	neg.	IV	4
	Macedonia (12)	n.s.	III	3
	Malaysia (57)	neg.	III	3
	Mexico (251)	neg.	III	3
	Moldova (4)	n.s.	III	2
	Nicaragua (70)	neg.	II	2
	Nigeria (69)	neg.	II	2
	Oman (4)	n.s.	III	4
	Pakistan (31)	n.s.	II	2
	Panama (1)	neg.	III	3
	Philippines (101)	neg.	II	2
	Portugal (94)	neg.	III	4
	Qatar (3)	n.s.	III	4
	Romania (5)	neg.	IV	3
	Serbia (1)	n.s.	III	3
	South Africa (360)	neg.	III	3
	Sri Lanka (37)	neg.	III	2
	Tanzania (12)	n.s.	II	1
	Thailand (69)	neg.	III	3
	Togo (4)	n.s.	I	1
	Tunisia (4)	n.s.	II	3
	Turkey (250)	n.s.	III	3

Country classification[a]		Classification category		
HERQ	**LERQ**	**ERRI score**	**RQ percentile rank**	**GNI per capita**
	Uganda (18)	n.s.	III	1
	United Arab Emirates (2)	n.s.	III	4
	Venezuela (41)	neg.	I	3
	Vietnam (35)	neg.	II	2
	Zambia (5)	n.s.	II	2

a: Numbers in brackets denote MICs per country.

Table S11. Descriptive statistics for potential covariates of aqueous-phase measured insecticide concentrations (MIC_{SW}) separated by countries' environmental regulatory quality. Note that the cumulative statistical sample sizes for watershed catchment sizes (n = 6,780), sampling intervals (n = 6,445), and sampling dates (n = 7,633) are smaller than the total number of MIC_{SW} present in surface water (n = 8,166) due to missing data in the studies evaluated. HERQ: High Environmental Regulatory Quality, LERQ: Low Environmental Regulatory Quality; see Table S10 for the classification of countries according to their environmental regulatory quality.

Covariate	Mean	Median	Range
Catchment size			
HERQ (n = 4,341)	9,998 km^2	152.5 km^2	0.002 – 2,900,000 km^2
LERQ (n = 2,439)	60,213 km^2	400 km^2	0.1 – 3,400,000 km^2
Sampling Interval			
HERQ (n = 4,167)	25.4 d	10 d	Event – 180 d
LERQ (n = 2,278)	44.8 d	30 d	Event – 180 d
Sampling date			
HERQ (n = 4,775)	-	1997	1960 – 2011
LERQ (n = 2,858)	-	1999	1970 – 2011

Table S12. Test of simple slopes (28) for the three-way interaction of country regulatory classification x substance class x sampling date (see, also, Fig. S2) specified using the full model for predicting logarithmic concentration to RTL_{SW} ratios (see Table S6). Substance classes (SC) are abbreviated as follows: organochlorine (OC), organophosphate (OP), pyrethroid (Pyr). Country regulatory classifications (CRC) are abbreviated as follows: HERQ (high environmental regulatory quality), LERQ (low environmental regulatory quality).

SC / CRC	Simple slope	t-value	p-value
OC / HERQ	-0.007521	-1.353	0.17625
OC / LERQ	0.0171	2.43	0.01512
OP / HERQ	-0.04207	-15.711	< 0.001
OP / LERQ	0.0544	12.991	< 0.001
Pyr / HERQ	-0.02074	-3.538	< 0.001
Pyr / LERQ	-0.22649	-9.622	< 0.001

Table S13. The results of the modified Johnson–Neyman technique (28) to test for significant differences for predicted logarithmic concentration to RTL_{SW} ratios for any pairs of the three-way interaction country regulatory classification x substance class x sampling date (see, also, Fig. S2). Substance classes are abbreviated as follows: organochlorine (OC), organophosphate (OP), pyrethroid (Pyr). Country regulatory classifications are abbreviated as follows: HERQ (high environmental regulatory quality), LERQ (low environmental regulatory quality).

Pair tested for significant difference (first item denotes the reference category)	Estimate	t-value	p-value
HERQ vs LERQ: 1980, OC	-0.207742	-1.277	0.20148
HERQ vs LERQ: 1980, OP	-1.105435	-11.465	<0.001
HERQ vs LERQ: 1980, Pyr	n/a[a]	n/a[a]	n/a[a]
HERQ vs LERQ: 1995, OC	0.161536	2.322	0.020274
HERQ vs LERQ: 1995, OP	0.341623	7.952	<0.001
HERQ vs LERQ: 1995, Pyr	3.476451	16.358	<0.001
HERQ vs LERQ: 2010, OC	0.530814	3.818	<0.001
HERQ vs LERQ: 2010, OP	1.788681	24.325	<0.001
HERQ vs LERQ: 2010, Pyr	0.390167	1.858	0.063156
OC vs OP: 1980, HERQ	0.780945	7.675	<0.001
OC vs Pyr: 1980, HERQ	0.665452	4.073	<0.001
OP vs Pyr: 1980, HERQ	-0.115493	-0.797	0.425671
OC vs OP: 1980, LERQ	-0.116748	-0.734	0.4627
OC vs Pyr: 1980, LERQ	n/a[a]	n/a[a]	n/a[a]
OP vs Pyr: 1980, LERQ	n/a[a]	n/a[a]	n/a[a]
OC vs OP: 1995, HERQ	0.262673	4.973	<0.001
OC vs Pyr: 1995, HERQ	0.467186	5.87	<0.001
OP vs Pyr: 1995, HERQ	0.204513	3.15	0.001639
OC vs OP: 1995, LERQ	0.442760	7.275	<0.001
OC vs Pyr: 1995, LERQ	3.782101	18.064	<0.001
OP vs Pyr: 1995, LERQ	3.339341	16.133	<0.001
OC vs OP: 2010, HERQ	-0.2556	-2.291	0.022025
OC vs Pyr: 2010, HERQ	0.268921	2.185	0.028955
OP vs Pyr: 2010, HERQ	0.52452	6.62	<0.001
OC vs OP: 2010, LERQ	1.002267	8.997	<0.001
OC vs Pyr: 2010, LERQ	0.128273	0.221507	0.562548
OP vs Pyr: 2010, LERQ	-0.873994	-4.196	<0.001

a: Data not available due to a lack of field study data for pyrethroids in LERQ countries before 1993 (see, also, Fig. S2).

SI References

1. Cooper H, Hedges LV (2009) Research synthesis as a scientific process. *The Handbook of Research Synthesis and Meta-Analysis*, eds Cooper H, Hedges LV, Valentine JC (Russel Sage Foundation, New York, ed. 2), pp 3-16.
2. Pilkington K, Boshnakova A, Clarke M, Richardson JSJ (2005) "No language restrictions" in database searches: what does this really mean? *J Altern Complement Med* 11(1):205-207.
3. White HD (2009) Scientific communication and literature retrieval. *The Handbook of Research Synthesis and Meta-Analysis*, eds Cooper H, Hedges LV, Valentine JC (Russel Sage Foundation, New York, ed. 2), pp 51-71.
4. Stehle S, Knäbel A, Schulz R (2013) Probabilistic risk assessment of insecticide concentrations in agricultural surface waters: a critical appraisal. *Environ Monit Assess* 185(8):6295–6310.
5. Cooper H (2010) *Research Synthesis and Meta-Analysis* (Sage Publications, Thousand Oaks, ed. 4).
6. Lubick N (2010) Endosulfan's exit: U.S. EPA pesticide review leads to a ban. *Science* 328(5985):1466.
7. Gianessi L, Reigner N (2006) Pesticide Use in U.S. Crop Production: 2002 - Insecticides & other Pesticides (Crop Life Foundation, Washington, DC).
8. Yu SJ (2008) *The Toxicology and Biochemistry of Insecticides* (CRC Press, Boca Raton, FL).
9. Moran KD (2003) Insecticide Market Trends and Potential Water Quality Implications (TDC Environmental, LLC Rep., San Mateo, CA).
10. Stokstad E (2013) Pesticides under fire for risks to pollinators. *Science* 340(6133):674-676.
11. U.S. Environmental Protection Agency (2014) Pesticide Chemical Search. Available at http://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1. Accessed November 20, 2012.
12. U.S. Environmental Protection Agency (2014) Technical Overview of Ecological Risk Assessment – Risk Characterization. Available at www.epa.gov/oppefed1/ecorisk_ders/toera_risk.htm. Accessed March 12, 2012.
13. U.S. Environmental Protection Agency (2014) OPP Pesticide Ecotoxicity Database. Available at www.ipmcenters.org/Ecotox/index.cfm. Accessed November 23, 2012.

14. European Commission (2009) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Off J Eur Union* L309/1:1-50.
15. European Food Safety Authority (2013) Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. *EFSA J* 11(7):3290 (186 pp.).
16. European Food Safety Authority (2014) Pesticides Publications. Available at http://www.efsa.europa.eu/en/pesticides/pesticidesscdocs.htm. Accessed November 28, 2012.
17. DG SANCO (2014) EU Pesticide Database. Available at http://ec.europa.eu/sanco_pesticides/public/index.cfm?event. Accessed November 14, 2012.
18. German Federal Office of Consumer Protection and Food Safety (BVL; BBA) (2001) Database of Pesticide Risk Assessment Endpoints.
19. Crommentuijn T, Sijm D, de Bruijn J, van Leeuwen K, van de Plassche E (2000) Maximum permissible and negligible concentrations for some organic substances and pesticides. *J Environ Manag* 58(4):297-312.
20. European Commission (2013) Directive 2013/39/EU of the European parliament and the council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. *Off J Eur Union* L226:1-17.
21. Swiss Centre for Applied Ecotoxicology (2014) Proposals for Acute and Chronic Quality Criteria. Available at http://www.oekotoxzentrum.ch/expertenservice/qualitaetskriterien/vorschlaege/index_EN. Accessed February 12, 2015.
22. Akerblom N, Arbjörk C, Hedlund M, Goedkoop W (2008) Deltamethrin toxicity to the midge *Chironomus riparius* Meigen - effects of exposure scenario and sediment quality. *Ecotoxicol Environ Saf* 70(1):53-60.
23. Denholm I, Devine GJ, Williamson MS (2002) Insecticide resistance on the move. *Science* 297(5590):2222-2223.
24. Esty DC, Porter ME (2005) National environmental performance: an empirical analysis of policy results and determinants. *Environ Dev Econ* 10(4):391-434.
25. Kaufmann D, Kraay A, Mastruzzi M (2010) The Worldwide Governance Indicators: Methodology and Analytical Issues (World Bank Policy Research Working Paper

5430).

26. The World Bank (2014) Country and Lending Groups. Available at http://data.worldbank.org/about/country-and-lending-groups. Accessed February 05, 2013.
27. Pigott TD (2009) Handling missing data. *The Handbook of Research Synthesis and Meta-Analysis*, eds Cooper H, Hedges LV, Valentine JC (Russel Sage Foundation, New York, ed. 2), pp 399-416.
28. Aiken LS, West SG (1991) *Multiple Regression: Testing and Interpreting Interactions* (Sage Publications, Thousand Oaks).
29. U.S. Environmental Protection Agency (2014) Technical Overview of Ecological Risk Assessment – Analysis Phase: Exposure Characterization. Available at www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_exp.htm. Accessed February 07, 2013.
30. De Snoo GR (2003) Variations in agricultural practice and environmental care. *Pesticides: Problems, Improvements, Alternatives*, eds Den Hond F, Groenewegen P, van Straalen NM (Blackwell, Oxford, UK), pp 100-112.
31. Touart LW, Maciorowski AF (1997) Information needs for pesticide registration in the United States. *Ecol Appl* 7(4):1086-1093.
32. European Crop Protection Association (2012) Registering Plant Protection Products in the EU (ECPA, Brussels).
33. Beketov MA, Kefford BJ, Schäfer RB, Liess M (2013) Pesticides reduce regional bio-diversity of stream invertebrates. *Proc Natl Acad Sci USA* 110(27):11039–11043.
34. Schäfer RB, et al. (2012) Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environ Sci Technol* 46(9):5134–5142.
35. FIFRA (1947) Federal Insecticide, Fungicide and Rodenticide Act, U.S. Federal Law amended in 1972 and 1988.
36. Foley JA, et al. (2011) Solutions for a cultivated planet. *Nature* 478(7369):337-342.
37. Gilliom RJ (2007) Pesticides in U.S. streams and groundwater. *Environ Sci Technol* 41(10):3408-3414.
38. Schulz R (2004) Field studies on exposure, effects, and risk mitigation of aquatic nonpoint-source insecticide pollution: a review. *J Environ Qual* 33(2):419-448.
39. Malaj E, et al. (2014) Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. *Proc Nat Acad Sci USA* 111(26):9549-9554.

40. Morrissey CA, et al. (2015) Neonicotinoid contamination of global surface waters and associated risk to aquatic invertebrates: a review. *Environ Int* 74:291-303.
41. Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS surface water models fail to predict insecticide concentrations in the field. *Environ Sci Technol* 46(15):8397-8404.
42. Crawford CG (2004) Sampling strategies for estimating acute and chronic exposures of pesticides in streams. *J Am Water Resour As* 40(2):485–502.
43. Moschet C, et al. (2014) How a complete pesticide screening changes the assessment of surface water quality. *Environ Sci Technol* 48(10):5423-5432.
44. Hall LW, Jr, Anderson RD (2003) Parametric and probabilistic analysis of historical chlorpyrifos surface water monitoring data from the San Joaquin River watershed: 1991-2001. *Water Air Soil Pollut* 150(1-4):275-298.
45. Gilliom RJ, et al. (2006) Pesticides in the Nation's Streams and Ground Water, 1992-2001 (U.S. Geological Survey (USGS) Circular 1291, Reston, Virginia).
46. Laskowski DA (2002) Physical and chemical properties of pyrethroids. *Rev Environ Contamin Toxicol* 174:49-170.
47. Yang W, Spurlock F, Liu W, Gan J (2006) Inhibition of aquatic toxicity of pyrethroid insecticides by suspended sediment. *Environ Toxicol Chem* 25(7):1913-1919.
48. Spurlock F, Bacey J, Starner K, Gill S (2005) A probabilistic screening model for evaluating pyrethroid surface water monitoring data. *Environ Monit Assess* 109(1-3):161-179.
49. Heines R, Halpin P (2008) Analysis of pyrethroid pesticides in sediment and waters by EPA method 8270 Gas Chromatography/Mass Spectrometer (GC/MS) narrow-range scan selected ion monitoring. *Synthetic Pyrethroids, Occurrence and Behavior in Aquatic Environments*, eds Gan J, Spurlock F, Hendley P, Weston D (American Chemical Society, Washington, DC), pp 114-129.
50. Shamim M, Hoffmann M, Melendez J, Ruhman M (2008) Ecological risk characterization for the synthetic pyrethroids. *Synthetic Pyrethroids, Occurrence and Behavior in Aquatic Environments*, eds Gan J, Spurlock F, Hendley P, Weston D (American Chemical Society, Washington, DC), pp 257-309.
51. Werner I, Moran K (2008) Effects of pyrethroid insecticides on aquatic organisms. *Synthetic Pyrethroids, Occurrence and Behavior in Aquatic Environments*, eds Gan J, Spurlock F, Hendley P, Weston D (American Chemical Society, Washington, DC), pp 310-334.

52. Schulz R, Liess M (2001) Toxicity of aqueous-phase and suspended particle-associated fenvalerate: chronic effects after pulse-dosed exposure of *Limnephilus lunatus* (Trichoptera). *Environ Toxicol Chem* 20(1):185-190.
53. Lauridsen RB, Friberg N (2005) Stream macroinvertebrate drift response to pulsed exposure of the synthetic pyrethroid lambda-cyhalothrin. *Environ Toxicol* 20(5):513-521.
54. Heckmann L-H, Friberg N, Ravn HW (2005) Relationship between biochemical biomarkers and pre-copulatory behaviour and mortality in *Gammarus pulex* following pulse-exposure to lambda-cyhalothrin. *Pest Manage Sci* 61(7):627-635.
55. Weston DP, Lydy MJ (2010) Urban and agricultural sources of pyrethroid insecticides to the Sacramento-San Joaquin Delta of California. *Environ Sci Technol* 44(5):1833-1840.
56. Bejarano AC, Widenfalk A, Decho AW, Chandler T (2005) Bioavailability of the organophosphorous insecticide chlorpyrifos to the suspension-feeding bivalve, *Mercenaria mercenaria*, following exposure to dissolved and particulate matter. *Environ Toxicol Chem* 22(9):2100-2105.
57. Hermsen W, Sims I, Crane M (1994) The bioavailability and toxicity to *Mytilus edulis* L. of two organochlorine pesticides adsorbed to suspended solids. *Mar Environ Res* 38(1):61-69.
58. Neff JM (1984) Bioaccumulation of organic micropollutants from sediments and suspended particulates by aquatic animals. *Fresenius Z Anal Chem* 319(2):132-136.
59. Schulz R, Liess M (2001) Acute and chronic effects of particle-associated fenvalerate on stream macroinvertebrates: a runoff simulation study using outdoor microcosms. *Arch Environ Contamin Toxicol* 40(4):481-488.
60. Spurlock F, Lee M (2008) Synthetic pyrethroid use patterns, properties, and environmental effects. *Synthetic Pyrethroids, Occurrence and Behavior in Aquatic Environments*, eds Gan J, Spurlock F, Hendley P, Weston D (American Chemical Society, Washington, DC), pp 3-25.
61. Schreinemachers P, Tipraqsa P (2012) Agricultural pesticides and land use intensification in high, middle and low income countries. *Food Policy* 37(6):616-626.
62. Carvalho FP (2006) Agriculture, pesticides, food security and food safety. *Environ Sci Policy* 9(7):685-692.
63. Ecobichon DJ (2001) Pesticide use in developing countries. *Toxicology* 160(1-3):27-33.

64. Lamberth C, Jeanmart S, Luksch T, Plant A (2013) Current challenges and trends in the discovery of agrochemicals. *Science* 341(6147):742-746.
65. Liu X, et al. (2012) Almond organophosphate and pyrethroid use in the San Joaquin Valley and their associated environmental risk. *J Soils Sediments* 12(7):1066-1078.
66. Elliot M (1989) The pyrethroids: early discovery, recent advances and the future. *Pestic Sci* 27(4):337-351.
67. Clark T, Hamer M (2000) Pesticides in perspective. Ecological risk assessment for agricultural pesticides. *J Environ Monit* 2(6):104N-109N.
68. Long RF, et al. (2002) Insecticide choice for alfalfa may protect water quality. *Calif Agr* 56(5):163-169.
69. U.S. Environmental Protection Agency (2009) Risks of Endosulfan Use to the Federally Threatened California Red-legged Frog (*Rana aurora draytonii*), Bay Checkerspot Butterfly (*Euphydryas editha bayensis*), Valley Elderberry Longhorn Beetle (*Desmocerus californicus dimorphus*), and California Tiger Salamander (*Ambystoma californiense*) and the Federally Endangered San Francisco Garter Snake (*Thamnophis sirtalis tetrataenia*), San Joaquin Kit Fox (*Vulpes macrotis mutica*), and Salt Marsh Harvest Mouse (*Reithrodontomys raviventris*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).
70. U.S. Environmental Protection Agency (2005) Azinphos Methyl Insecticide: Ecological Risk Assessment for the Use of Azinphos Methyl on Caneberries, Cranberries, Peaches, Potatoes, and Southern Pine Seeds (Group 2 Uses) (U.S. EPA, Office of Prevention, Pesticides and Toxic Substances, Washington, DC).
71. European Commission (2001) Azinphos-Methyl – Monograph Prepared by the Rapporteur Member State Germany in the Framework of Directive 91/414/EEC. Addendum 7, Volume 3, Annex B.9: Ecotoxicology.
72. U.S. Environmental Protection Agency (2006) Reregistration Eligibility Decision for Chlorpyrifos (U.S. EPA, Office of Pesticide Programs, Washington, DC).
73. European Commission (2005) Review Report for the Active Substance Chlorpyrifos (SANCO/3059/99 – rev. 1.5.).
74. U.S. Environmental Protection Agency (2007) Risks of Diazinon Use to the Federally Listed California Red Legged Frog (*Rana aurora draytonii*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).
75. U.S. Environmental Protection Agency (2006) Reregistration Eligibility Decision for Diazinon (U.S. EPA, Office of Pesticide Programs, Washington, DC).

76. European Food Safety Authority (2006) Conclusion Regarding the Peer Review of the Pesticide Risk Assessment of the Active Substance Diazinon (EFSA Scientific Report 85, 1-73).
77. U.S. Environmental Protection Agency (2007) Risks of Malathion Use to the Federally Listed California Red Legged Frog (*Rana aurora draytonii*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).
78. U.S. Environmental Protection Agency (2009) Reregistration Eligibility Decision for Malathion (U.S. EPA, Office of Prevention, Pesticides and Toxic Substances, Washington, DC).
79. European Food Safety Authority (2009) Conclusion on Pesticide Peer Review – Peer Review of the Pesticide Risk Assessment of the Active Substance Malathion (EFSA Scientific Report 333, 1-118).
80. U.S. Environmental Protection Agency (1998) EFED Environmental Risk Assessment for the Ethyl Parathion Reregistration Eligibility Decision (U.S. EPA, Office of Prevention, Pesticides and Toxic Substances, Washington, DC).
81. European Commission (2000) Full Report on Parathion (Report of the ECCO Peer Review Programme).
82. U.S. Environmental Protection Agency (2008) Risks of Methyl Parathion Use to the Federally Listed California Red Legged Frog (*Rana aurora draytonii*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).
83. U.S. Environmental Protection Agency (2006) Reregistration Eligibility Decision for Methyl Parathion (U.S. EPA, Office of Pesticide Programs, Washington, DC).
84. European Commission (2002) Full Report on Parathion-Methyl (Report of the ECCO Peer Review Programme).
85. U.S. Environmental Protection Agency (2006) Reregistration Eligibility Decision for Carbofuran (U.S. EPA, Office of Pesticide Programs, Washington, DC).
86. European Food Safety Authority (2009) Conclusion Regarding the Peer Review of the Pesticide Risk Assessment of the Active Substance Carbofuran (EFSA Scientific Report 310, 1-132).
87. European Food Safety Authority (2010) Conclusion on the Peer Review of the Pesticide Risk Assessment of the Active Substance Acrinathrin. *EFSA J* 8(12):1872 (72 pp.) (2010).
88. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Revised Problem Formulation in Support of Registration Review for

Bifenthrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).

89. European Food Safety Authority (2011) Conclusion on the peer review of the pesticide risk assessment of the active substance bifenthrin. *EFSA J* 9(5):2159 (101 pp.).

90. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review for Cyfluthrin and Beta-Cyfluthrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).

91. European Commission (2002) Review Report for the Active Substance Cyfluthrin (6843/VI/97-final).

92. European Commission (2002) Cyfluthrin – Monograph Prepared by the Rapporteur Member State Germany in the Framework of Directive 91/414/EEC. Addendum 2 to the Monograph of Cyfluthrin of 30 September 1996, Annex B.9: Ecotoxicology.

93. Amweg EL, Weston DP, Ureda NM (2005) Use and toxicity of pyrethroid pesticides in the Central Valley, California. *Environ Toxicol Chem* 24(4):966-972.

94. European Commission (2002) Review Report for the Active Substance Beta-Cyfluthrin (6841/VI/97-final, EC).

95. U.S. Environmental Protection Agency (2006) Reregistration Eligibility Decision for Cypermethrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).

96. European Commission (2005) Review Report for the Active Substance Cypermethrin (SANCO/4333/2000 final).

97. European Commission (2004) Review Report for the Active Substance Alpha-Cypermethrin (SANCO/4335/2000 final).

98. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review for Deltamethrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).

99. European Commission (2002) Review Report for the Active Substance Deltamethrin (6504/VI/99-final).

100. U.S. Environmental Protection Agency (2008) Risks of Esfenvalerate Use to Federally Threatened California Red-Legged Frog (*Rana aurora draytonii*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).

101. U.S. Environmental Protection Agency (2009) Problem Formulation for the Environmental Fate, Ecological Risk, and Endangered Species Assessments in Support of Registration Review for Esfenvalerate (U.S. EPA, Office of Pesticide Programs, Washington, DC).

102. European Commission (2005) Review Report for the Active Substance Esfenvalerate (6846/VI/97-final).
103. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review for Fenpropathrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).
104. Xu Y, Spurlock F, Wang Z, Gan J (2007) Comparison of five methods for measuring sediment toxicity of hydrophobic contaminants. *Environ Sci Technol* 41(24):8394-8399.
105. U.S. Environmental Protection Agency (2014) OPP Pesticide Ecotoxicity Database - Ecotox Results Details for Search on Fenvalerate, EPA Identification: 40098001. Available at http://www.ipmcenters.org/Ecotox/Details.cfm?RecordID=535. Accessed November 14, 2012.
106. U.S. Environmental Protection Agency (2014) OPP Pesticide Ecotoxicity Database - Ecotox Results Details for Search on Fenvalerate, EPA identification: 40228401. Available at http://www.ipmcenters.org/Ecotox/Details.cfm?RecordID=531. Accessed November 14, 2012.
107. Clark JR, Patrick JM, Moore JC, Lores EM (1987) Waterborne and sediment-source toxicities of six organic chemicals to grass shrimp (*Palaemonetes pugio*) and amphioxus (*Branchiostoma caribaeum*). *Arch Environ Contamin Toxicol* 16(4):401-407.
108. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review of Lambda-cyhalothrin and Gamma-cyhalothrin (U.S. EPA, Office of Pesticide Programs, Washington).
109. European Commission (2001) Review Report for the Active Substance Lambda-cyhalothrin (7572/VI/97-final).
110. U.S. Environmental Protection Agency (2008) Risks of Permethrin Use to the Federally Threatened California Red-legged Frog (*Rana aurora draytonii*) and Bay Checkerspot Butterfly (*Euphydryas editha bayensis*), and the Federally Endangered California Clapper Rail (*Rallus longirostris obsoletus*), Salt Marsh Harvest Mouse (*Reithrodontomys raviventris*), and San Francisco Garter Snake (*Thamnophis sirtalis tetrataenia*) (U.S. EPA, Office of Pesticide Programs, Washington, DC).
111. U.S. Environmental Protection Agency (2010) Problem Formulation for the Ecological Risk and Drinking Water Exposure Assessments in Support of the

Registration Review of Tau-Fluvalinate (U.S. EPA, Office of Pesticide Programs, Washington, DC).

112. European Food Safety Authority (2010) Conclusion on the peer review of the pesticide risk assessment of the active substance tau-fluvalinate. *EFSA J* 8(7):1645 (75 pp.).

113. European Food Safety Authority (2010) Conclusion on the peer review of the pesticide risk assessment of the active substance tefluthrin. *EFSA J* 8(12):1709 (65 pp.).

114. U.S. Environmental Protection Agency (2010) Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review of Tralomethrin (U.S. EPA, Office of Pesticide Programs, Washington, DC).

115. U.S. Environmental Protection Agency (2011) Ecological Risk Assessment for the Proposed National (Section 3) Registration of Acetamiprid for Use on Various Agricultural Crops and as a Bait Near Animal Areas and Enclosed Dumpsters to Control Flies, Eye Gnats, and Flesh Flies (U.S. EPA, Office of Pesticide Programs, Washington, DC).

116. European Commission (2004) Review Report for the Active Substance Acetamiprid (SANCO/1392/2001-final).

117. European Commission (2002) Acetamiprid - Monograph Prepared by the Rapporteur Member State Greece in the Framework of Directive 91/414/EEC. Addendum to the Monograph, Volume 3, Annex B.9: Ecotoxicology.

118. U.S. Environmental Protection Agency (2008) Problem Formulation for the Imidacloprid Environmental Fate and Ecological Risk Assessment (U.S. EPA, Office of Pesticide Programs, Washington, DC).

119. European Food Safety Authority (2008) Conclusion on the Peer Review of the Pesticide Risk Assessment of the Active Substance Imidacloprid (EFSA Scientific Report 148, 1-120).

120. European Commission (2003) Thiacloprid - Draft Assessment Report Prepared by the Rapporteur Member State United Kingdom in the Framework of Directive 91/414/EEC. Addendum II to the Draft Assessment Report, Annex B9: Ecotoxicology.

121. European Commission (2006) Review Report for the Active Substance Thiamethoxam (SANCO/10390/2002 – rev. final).

122. Elbert A, Haas M, Springer B, Thielert W, Nauen R (2008) Applied aspects of neonicotinoid uses in crop protection. *Pest Manage Sci* 64(11):1099-1105.

123. Jeschke P, Nauen R, Schindler M, Elbert A (2011) Overview of the status and global strategy for neonicotinoids. J *Agric Food Chem* 59(7):2829-2908.

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RESEARCH ARTICLE

Pesticide authorization in the EU—environment unprotected?

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Abstract Pesticides constitute an integral part of high-intensity European agriculture. Prior to their authorization, a highly elaborated environmental risk assessment is mandatory according to EU pesticide legislation, i.e., Regulation (EC) No. 1107/2009. However, no field data-based evaluation of the risk assessment outcome, i.e., the regulatory acceptable concentrations (RACs), and therefore of the overall protectiveness of EU pesticide regulations exists. We conducted here a comprehensive meta-analysis using peer-reviewed literature on agricultural insecticide concentrations in EU surface waters and evaluated associated risks using the RACs derived from official European pesticide registration documents. As a result, 44.7 % of the 1566 cases of measured insecticide concentrations (MICs) in EU surface waters exceeded their respective RACs. It follows that current EU pesticide regulations do not protect the aquatic environment and that insecticides threaten aquatic biodiversity. RAC exceedances were significantly higher for insecticides authorized using conservative tier-I RACs and for more recently developed insecticide classes, i.e., pyrethroids. In addition, we identified higher risks, e.g., for smaller surface waters that are specifically considered in the regulatory risk assessment schemes. We illustrate the shortcomings of the EU regulatory risk assessment using two case studies that contextualize the respective risk assessment outcomes to field exposure. Overall, our meta-analysis challenges the field relevance and protectiveness of the regulatory environmental risk assessment conducted for pesticide authorization in the EU and indicates that critical revisions of related pesticide regulations and effective mitigation measures are urgently needed to substantially reduce the environmental risks arising from agricultural insecticide use.

Keywords Pesticide · Surface water · Europe · Risk assessment · Regulation (EC) No. 1107/2009 · Regulatory acceptable concentration · Meta-analysis

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Introduction

Agricultural areas cover 40 % (174.1 million hectares) of the total land area of the EU-28, and two thirds (65.8 %) of these farmlands are used for the cultivation of arable and permanent crops (Eurostat 2013). In 2013, pesticides with an approximate input value of 11 billion Euros were applied to European arable lands (European Commission 2014). The widespread and intentional release of these highly biologically active substances poses threats to non-target aquatic and terrestrial ecosystems across the EU. Surface waters are especially at risk as systems that are likely to receive agricultural non-point source inputs due to their often close proximities to arable lands (Stehle and Schulz 2015; Davies et al. 2008; Schulz 2004). We focus here on insecticides, as this particularly toxic group of pesticides exhibits a high toxicity potential for aquatic organisms that are crucial for ecosystem structure and functions (Schulz 2004; Schäfer et al. 2012; US EPA 2014).

Stehle and Schulz (2015) showed that insecticides threaten aquatic biodiversity on a global scale, but did they not specify results, e.g., for the highly regulated EU. Although large-scale

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investigations of insecticide exposure of EU surface waters are lacking (Stehle and Schulz 2015), a recent study (Malaj et al. 2014) using governmental monitoring data and standard toxicity data derived from a single species laboratory test showed that, out of various organic pollutants, insecticides particularly jeopardize the integrity of EU freshwater ecosystems. In addition, several additional small-scale field studies conducted in the EU reported that pesticide exposure produced adverse effects on the aquatic ecosystem structure and function (e.g., Bereswill et al. 2013; Schäfer et al. 2012; Beketov et al. 2013; Schulz 2004). However, no scientific study exists that has evaluated pesticide, or specifically insecticide, field concentrations in EU agricultural surface waters using the regulatory acceptable concentrations (RACs) defined by the environmental risk assessment conducted for official EU authorization. The present study thus particularly addresses for the first time the essential question of whether the fundamental assumption of this pre-authorization EU pesticide risk assessment, i.e., that RACs are not exceeded in the field, is indeed met.

The new EU Regulation (EC) No. 1107/2009 (European Commission 2009a), which replaced Directive 91/414/EEC (European Commission 1991), together with the recently updated guidance document on tiered risk assessment for plant protection products (EFSA 2013, taking effect 01. January 2015), form the basis of the environmental regulatory risk assessment, which is mandatory for the authorization of active substances in the EU. Generally, the EU regulatory risk assessment is based on a single active ingredient toxicity assessment concept, and it follows a tiered approach, in which higher tiers are less conservative but more complex and are meant to be more realistic than lower tiers (EFSA 2013). Tier I of the aquatic effect assessment consists of acute and chronic laboratory toxicity tests using standard test organisms and the application of large assessment factors (AFs, i.e., 100 for acute and 10 for chronic toxicity tests) for RAC derivation (see EFSA (2013) for details). In cases in which there is an unacceptable risk indicated in this first tier, higher tier studies, such as species sensitivity distributions and aquatic micro-/mesocosm tests, are performed to derive an RAC, which is considered more realistic and less conservative (EFSA 2013). In particular, micro-/mesocosm studies are often conducted for the refined risk assessment of insecticides (Table 1). The AFs applied to these higher-tier studies are substantially lower than tier-I AFs and are set on a case-by-case basis (see EFSA (2013) for details). RAC comparisons with the predicted environmental concentrations (PECs) derived from exposure modeling (see FOCUS (2001) and EFSA (2013) for details) thus indicate either an acceptable risk for aquatic ecosystems or the need for a specific application prescription (e.g., no-spray buffer zones close to surface waters) that becomes part of the registration procedure as legally binding label amendments for the farmer. Overall, the EU Regulation (EC) No. 1107/2009 claims that a high level of environmental protection is required (e.g., in article 1 and 4.3). In detail, this directive states that "no unacceptable effects on the environment" shall result from pesticide use and particularly refers in this context to biodiversity (European Commission 2009a). In addition to these general protection goals, Nienstedt et al. (2012) and EFSA (2010) defined specific protection goals for main groups of aquatic organisms (algae, aquatic plants, aquatic invertebrates, aquatic vertebrates, aquatic microbes) covering ecosystem services potentially affected by pesticides. In general, to maintain ecosystem services and thus to adhere to these specific protection goals, aquatic taxa need to be protected at the population level (see Nienstedt et al. (2012) and EFSA (2010) for details).

Therefore, after a pesticide is authorized and in use, field concentrations exceeding their RACs must not occur in order not to compromise pre-authorization risk assessment outcome and to adhere to the general and specific protection goals outlined in EU pesticide legislation (EFSA 2010, 2013; European Commission 2009a; Nienstedt et al. 2012). Based on a meta-analysis of field studies conducted by Beketov et al. (2013), Stehle and Schulz (2015) argued that aquatic biodiversity is reduced by 29 % at agricultural stream sites with insecticide concentrations only slightly (i.e., a factor of 1.12) above regulatory threshold levels relative to uncontaminated sites. It follows that insecticide concentrations exceeding their RAC in the field in fact lead to unacceptable effects on aquatic biodiversity. Consequently, the extent of RAC exceedances in EU surface waters reveals two important details: (i) the actual protectiveness and effectiveness of pre-authorization regulatory risk assessment schemes and thus EU pesticide legislations and (ii) the significance of insecticide exposure as a threat to aquatic biodiversity in EU surface waters. However, despite extensive decades-long pesticide application in European agricultural areas, this information has never been analyzed on a European scale. Such an analysis is urgently needed considering that a recent study (Knäbel et al. 2012) revealed substantial failures in the European regulatory pesticide exposure assessment due to insecticide surface water concentrations. However, this study did not provide any information on the relationship between insecticide surface water concentrations and the RACs.

Therefore, the present study had the following three objectives:

i. To evaluate the overall protectiveness of the official EU regulatory pesticide risk assessment conducted for pesticide authorization using the agriculturally related insecticide exposure of EU surface waters and RACs;
ii. To contextualize the different risk assessment tiers and the associated protection levels with the insecticide risks in the field and to validate the field relevance of the EU regulatory risk assessment by considering, e.g., different

Table 1 The insecticides included in the meta-analysis, their final regulatory acceptable concentrations for water (RAC_{SW}) and sediments (RAC_{SED}), their respective tiers (higher tiers denote microcosm/mesocosm studies) of the RAC_{SW} setting and their approval status under Regulation (EC) No. 1107/2009 (DG SANCO 2014)

Insecticide	Class	Status under Reg. (EC) No. 1107/2009	RAC_{SW} (μg/L)	EU risk assessment tier of final RAC_{SW} setting (tier-I RAC_{SW}[a] in μg/L)	RAC_{SED} (μg/kg)
Endosulfan	OC	Not approved	1.3[b]	Higher tier (0.02)	0.026[c]
Azinphos-methyl	OP	Not approved	0.32[d]	Higher tier (0.011)	–
Chlorpyrifos	OP	Approved	0.1[d]	Higher tier (0.001)	1.1[c]
Diazinon	OP	Not approved	2.4[d]	Higher tier (0.0041)	0.95[c]
Malathion	OP	Approved	1.25[d]	Higher tier (0.0072)	0.9[c]
Parathion-ethyl	OP	Not approved	0.024[d]	Tier I	0.13[c]
Parathion-methyl	OP	Not approved	0.073[d]	Tier I	0.96[c]
Carbofuran	Carb	Not approved	0.0205[d]	Tier I	–
Acrinathrin	Pyr	Approved	0.0087[d]	Higher tier (0.00022)	–
Bifenthrin	Pyr	Approved	0.005[d]	Higher tier (0.001)	–
Cyfluthrin	Pyr	Approved	0.0068[d]	Tier I	–
β-cyfluthrin	Pyr	Approved	0.00068[d]	Tier I	–
Cypermethrin	Pyr	Approved	0.025[d]	Higher tier (0.003)	1.8[e]
α-cypermethrin	Pyr	Approved	0.015[d]	Higher tier (0.003)	1.8[e]
Deltamethrin	Pyr	Approved	0.0032[d]	Higher tier (0.0026)	1.3[c]
Esfenvalerate	Pyr	Approved	0.01[d]	Higher tier (0.001)	0.41738[f]
Fenvalerate	Pyr	Not approved	0.0022[b]	Tier I	0.88[f]
λ-cyhalothrin	Pyr	Approved	0.0021[d]	Tier I	10.5[d]
Permethrin	Pyr	Not approved	0.025[b]	Tier I	0.87[c]
Acetamiprid	Neo	Approved	0.5[d]	Tier I	–
Imidacloprid	Neo	Approved	0.3[d]	Higher tier (0.552)	–
Thiacloprid	Neo	Approved	1.57[d]	Higher tier (252)	–
Thiamethoxam	Neo	Approved	2.8[d]	Tier I	–

See Stehle and Schulz (2015) for further details on RAC_{SW} and RAC_{SED} derivation. "–" denotes that no sediment concentrations were reported for this insecticide in the literature; sediment refers to sediment and suspended particle concentrations

OC organochlorine, *OP* organophosphate, *Carb* carbamate, *Pyr* pyrethroid, *Neo* neonicotinoid

[a] RAC_{SW} set at the tier I level of the regulatory risk assessment for insecticides, which, however, did not pass at tier 1, meaning that a higher tier RAC_{SW} was used for final authorization

[b] BBA (2001)

[c] Crommentuijn et al. (2000)

[d] EFSA (2014); DG SANCO (2014)

[e] US EPA (2012)

[f] RAC_{SED} derived by the application of the modified EPA method according to Crommentuijn et al. (2000) and Akerblom et al. (2008)

types of water bodies and the pesticide mixture toxicity; and

iii. To relate the ecotoxicological significance of insecticide surface water exposure to those of other pesticide groups, to analyze the aquatic risks for different insecticide classes, specifically those of EU Water Framework Directive (WFD) priority substances.

The present study thus denotes an important extension of the work of Stehle and Schulz (2015) as it is the first to report insecticide RAC exceedance frequencies particularly for EU surface waters and, among others, as it subsequently contextualizes insecticide field exposure to the pre-authorization regulatory risk assessment schemes and EU pesticide legislations.

Materials and methods

Dataset on the insecticide exposure of EU surface waters

We extracted all scientific studies (n=165, published between 1972 and 2012) reporting measured insecticide concentrations (MICs, i.e., the concentrations actually detected and

quantified) resulting from the agricultural non-point source pollution of surface waters for the 28 EU member states from the global insecticide exposure dataset provided in Stehle and Schulz (2015; see this publication for detailed information on the entire literature review process, selection criteria and information retrieval). The dataset evaluated here thus represents an exhaustive compilation of Europe-wide insecticide surface water concentrations. In addition to the insecticide concentrations in the water (μg/L), sediment or suspended particles (μg/kg), the scientific studies provided information on the sampling location (including the distinction between freshwater and estuarine waters and the hydrology of surface water bodies), the catchment size, the sampling interval, the sampling date, the limit of quantification (LOQ), and the quantity and concentrations of additional pesticides present in a given sample. Further on, we classified the certainty that the MIC resulted from an agricultural non-point source entry.

In total, our analysis comprised MICs of 23 insecticide compounds, and 15 of these 23 insecticides are currently authorized for agricultural uses in the EU under the new pesticide Regulation (EC) No. 1107/2009 (Table 1); the other eight compounds that are currently not authorized had, however, formerly been authorized for agricultural uses in the EU. We classified these compounds for further analyses into four (organochlorines, organophosphates and carbamates (named "organophosphates"), pyrethroids, neonicotinoids) generations of insecticide classes (see Table 1) based on their ecotoxicological mode of action (Yu 2008) and the time period of their market introduction (Denholm et al. 2002).

Compilation of European RACs

The derivation and application of the RACs were as follows (see Stehle and Schulz (2015) for further details): The RAC_{SW} (Table 1) were used to evaluate the measured insecticide concentrations in the water phase (MIC_{SW}). The RAC_{SW} were derived from official European pesticide registration documents (EFSA 2014; DG SANCO 2014) and denote the final acute tier-I or higher-tier ecotoxicity endpoints, including the AF determined within the regulatory aquatic risk assessment of their respective insecticide compounds. As no official European pesticide registration documents were available for the insecticides endosulfan, fenvalerate, and permethrin, we used the toxicity endpoints and associated AFs provided by the German Federal Office of Consumer Protection and Food Safety (BVL) for their respective RAC_{SW} (BBA 2001). Further details, EU risk assessment tiers of the final RAC_{SW} setting, and references for RACs are specified in Table 1.

RAC_{SED} (Table 1) are not determined by default for all pesticide compounds within the official EU regulatory risk assessment procedure (EFSA 2013; DG SANCO 2002); this threshold level was thus only available from EU risk assessment documents for the insecticide lambda-cyhalothrin. To overcome this limitation, we applied the RAC_{SED} derived from the regulatory US EPA pesticide ecological risk assessment (US EPA 2012; available for cypermethrin and cypermethrin-alpha) or, in cases in which no official EU or US RAC_{SED} was available, maximum permissible concentrations (referred to here also as RAC_{SED}; Crommentuijn et al. 2000) to insecticide sediment concentrations (MIC_{SED}).

An evaluation of the EU regulatory risk assessment using MICs

We evaluated the protectiveness and field relevance of the pre-authorization EU pesticide regulatory risk assessment and underlying EU pesticide legislations and guidance documents in the following contexts:

First, we assessed the overall protectiveness of the regulatory EU pesticide risk assessment and the ecological significance of insecticide exposure by comparing all MICs to the respective EU-level RACs for the approval of active substances.

Second, we evaluated the insecticide exposure of the water bodies specifically considered in the EU pesticide regulatory risk assessment, i.e., the small edge-of-field freshwater bodies in close proximity to agricultural fields (European Commission 2009a; EFSA 2013; FOCUS 2001). We therefore restricted the evaluation of our dataset to MICs reported for water bodies with catchment sizes of up to 1 km^2 (i.e., the water body size used in the regulatory FOCUS exposure assessment (FOCUS 2001; EFSA 2013)) and to MICs reported for water bodies with catchment sizes of up to 10 km^2 in order to be less restrictive about the specific focus of the EU regulatory risk assessment and to include surface waters that are still typical for agricultural landscapes (Davies et al. 2008) but are not particularly addressed under the EU WFD. We further distinguished between different types of surface waters, i.e., we evaluated the MICs separately for freshwater and estuarine water bodies. As the regulatory pesticide risk assessment and the resulting RACs are valid only for MICs caused by agricultural non-point source pollution (European Commission 2009a; EFSA 2013), we further restricted our dataset to the MICs definitively attributable to this source using information, e.g., on land use, insecticide application schemes, and the routes of entry provided in the scientific studies (see Stehle and Schulz (2015) for detailed classification criteria). This strict classification procedure enabled us to attribute a specific insecticide concentration to agricultural non-point source pollution with high confidence and to subsequently analyze those exposure incidences separately. It is important to note that all these restricted analyses led to even worse outcomes, i.e., even higher RAC

exceedance rates; therefore, the evaluation of the EU pesticide risk assessment using the entire dataset indicates less risk than is actually present.

Third, from the official EU pesticide registration documents, we determined whether the final RAC_{SW} used for the authorization of a given active substance was derived from the first tier of the regulatory risk assessment, or, in cases in which tier I was not passed, by conducting higher-tier effect assessment studies. In the latter case, we also extracted the associated tier-I RAC_{SW} from the respective registration documents (Table 1). Given this information, we evaluated the MIC_{SW} separately for (i) the compounds finally regulated by tier-I risk assessment and (ii) the compounds regulated using higher-tier RACs. In addition, we applied in an additional assessment respective tier-I RAC_{SW} to all MIC_{SW}, i.e., also to the insecticides that were in fact authorized using higher-tier risk assessments.

Finally, we separately evaluated the RAC exceedance frequencies for the different insecticide substance classes (i.e., organochlorines, organophosphates, pyrethroids, neonicotinoids) and for the different pesticide groups (i.e., herbicides, fungicides, insecticides). Regarding the latter, we evaluated the differences in pesticide water-phase concentration levels, tier-I RAC_{SW} values, as determined by the official EU pesticide risk assessment of a given pesticide compound, and the respective concentration to tier-I RAC_{SW} ratios for fungicides, herbicides, and insecticides using all the samples analyzed for multiple pesticide exposure. In detail, we extracted from samples containing pesticide mixtures in addition to insecticide concentrations, the concentrations of all further pesticide compounds detected.

It is worth mentioning that the pesticide registration in the EU is based on a two-stage registration system, with an initial assessment of active substances at the EU level (which is considered in this study) and the subsequent registration of plant protection products containing approved active substances by member states. However, member states can only authorize the use of plant protection products after an active substance has passed the EU regulatory risk assessment and has been added to the list of approved active substances eligible for agricultural uses in the EU.

Water Framework Directive: an assessment of priority substances

The EU WFD 2000/60/EEC (European Commission 2000) uses a retrospective risk assessment approach by comparing chemical monitoring data with environmental quality standards (EQSs) for EU-wide priority substances. We assessed the MIC_{SW} of the three compounds listed as priority substances by the WFD (i.e., endosulfan, chlorpyrifos, and cypermethrin (including isomers)) (European Commission 2013), as detected in the water bodies considered in this directive (i.e., catchment sizes > 10 km^2), by using their respective maximum acceptable concentration EQS values (MAC-EQSs) for inland surface waters. The MAC-EQSs, which should not be exceeded by a single concentration in the aquatic ecosystem of concern, are as follows: 0.01 μg/L for endosulfan, 0.1 μg/L for chlorpyrifos, and 0.0006 μg/L for cypermethrin (including isomers) (European Commission 2013).

An evaluation of pesticide mixture toxicity

To evaluate the ecotoxicological significance of mixture toxicity for EU surface waters, we compared all water-phase pesticide concentrations quantified in a given sample containing multiple pesticides (n=516 out of the total of 1140 samples analyzed) to the respective tier-I threshold levels (i.e., ecotoxicity values including AFs) for the three taxonomic groups (i.e., fishes, invertebrates, primary producers) considered in the EU regulatory risk assessment. We calculated tier-I threshold levels by dividing the lowest acute LC_{50} or EC_{50} values (compiled from PPDB (2013) and official EU pesticide registration documents (EFSA 2014)) for fish, *Daphnia*, green alga, an additional arthropod species (for substances with an insecticidal mode of action), and macrophytes (for substances with a herbicidal mode of action) by their respective AFs (i.e., 100 in the case of fish, *Daphnia*, and arthropods and 10 in the case of primary producers; EFSA 2013).

The mixture toxicity was calculated separately for each respective taxonomic group by summing up the concentration to tier-I threshold level ratios for all the pesticides detected in a surface water sample to obtain the risk quotient of the mixture (RQ_{mix}) for a given taxonomic group:

$$\mathrm{RQmix} = \sum_{i=1}^{n} \frac{\mathrm{MPCi}}{\mathrm{TLi}}$$

where MPCi is the measured pesticide concentration of the compound *i* quantified in a given sample; TLi is the acute tier-I threshold level for a given taxonomic group of the pesticide *i*; and with $RQ_{mix}<1$ indicating an acceptable risk for a specific taxonomic group.

We used this approach as its modified version (which uses modeled exposure data instead of MPC), and the underlying principle of concentration addition (Kortenkamp et al. 2009) is proposed by the EU Commission for the regulatory risk assessment of pesticide mixture toxicities for individual taxonomic groups (EFSA 2013). Moreover, this approach is generally considered as broadly applicable for pesticide mixture toxicity evaluations (Deneer 2000; Cedergreen et al. 2008).

Linear model analysis

We conducted a hierarchical linear model analysis to quantify the influence of different drivers on the outcome variable logarithmic MIC_{SW} to RAC_{SW} ratio. The following independent variables were entered in the analysis using a complete-case approach (Pigott 2009): (i) the log sampling interval, (ii) the log catchment size, (iii) the sampling date, and the dummy-coded categorical variables for (iv) EU risk assessment tiers of the RAC_{SW} setting (tier I ("0") vs. higher tier ("1")), (v) status under Regulation (EC) No. 1107/2009 (approved ("0") vs. not approved ("1")), and (vi) insecticide substance classes (organochlorines ("0"), organophosphates and carbamates ("1"), pyrethroids ("2")). We excluded the neonicotinoid substance class as only a total of 33 EU surface water concentrations were documented in the peer-reviewed literature, and this number was further reduced to only six MIC_{SW} available for complete-case linear model analysis.

Automatic and manual model building were used to identify independent variables and potential interactions with the highest explanatory power for the response variable logarithmic MIC_{SW} to RAC_{SW} ratio and best-fit models (see Stehle and Schulz (2015) for further details). Model checking included heteroskedasticity, the normal distribution of residuals and the influence of single observations using residual-leverage plots and Cook's distance. All computations were done with the open source software R (version 2.15.2 for Mac OS X 10.6.8).

Results

The insecticide exposure of EU surface waters: an evaluation of the regulatory risk assessment

Overall, 44.7 % (n=700 cases) of the 1566 MICs reported for EU surface waters exceeded their respective RACs. In particular, 37.1 % of the 1352 MIC_{SW} exceeded their RAC_{SW} up to a factor of 125,750, and 93 % of the 214 MIC_{SED} exceeded their RAC_{SED} up to a factor of 31,154 (Fig. 1). Information on the MICs for the 23 insecticide compounds was available for 385 sites located in 16 of the 28 EU member states (Fig. S1 in Supplementary Material), with most MICs originating from southern EU countries: Greece (n=487), Spain (n=415), and Italy (n=152). Additional summary statistics for the EU dataset are displayed in Table 2.

The temporal analyses of the insecticide exposure data (Fig. S2; Fig. S3; Table S1) indicates that risks did not decrease over time; this is in accordance with the results of the linear model analysis (Table 3), which predicted significant increases in MIC_{SW} to RAC_{SW} ratios over time when considering the influences of covariates. In total, 546 (38 %) of all

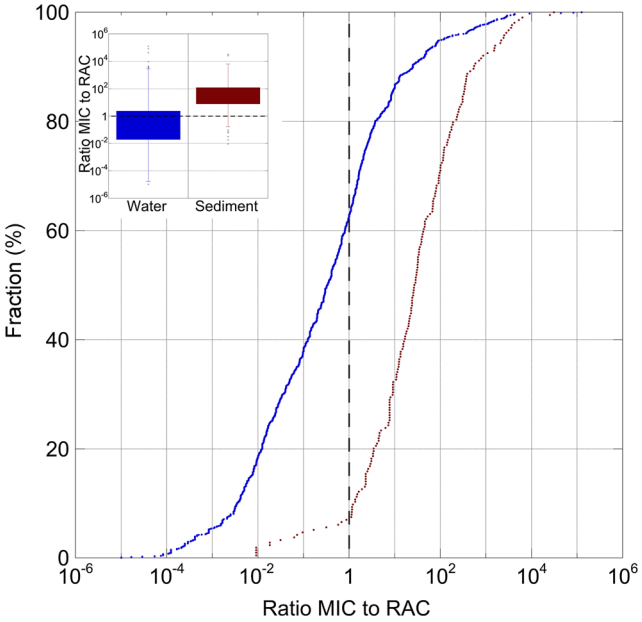

Fig. 1 Distribution curves for MICs relative to their respective RACs. *Blue* represents the MIC_{SW} relative to substance-specific RAC_{SW} (n=1352) and *brown* represents MIC_{SED} relative to substance-specific RAC_{SED} (n=214). The *inlet* shows the overall variation of the MIC to RAC ratios for water and sediment concentrations

MICs were detected after the year 2000, with 40.5 % of these exposure incidences exceeded the respective RAC (Table S1).

Approximately 90 % of all MICs (n=126) exceeded their RACs in small edge-of-field surface waters with catchment sizes of up to 1 km^2, as well as >75 % of all MICs (n=273) in the case of water bodies with catchment sizes of up to 10 km^2 (Table S2). The linear model analysis, which predicted significantly higher MIC_{SW} to RAC_{SW} ratios for smaller surface waters (Table 3), supports these results. In addition, RAC exceedance frequencies for freshwater systems (45.4 %, n=1430) were higher compared with those derived for estuarine surface waters (37.5 %, n=136) (Table S2). The restriction to exposure incidences (n=581), which could be linked with high confidence to agricultural non-point source entries, resulted in RAC exceedance frequencies of 60.9 % (Table S3).

The risk assessment of the three WFD priority substances (i.e., chlorpyrifos, endosulfan, cypermethrin (including isomers)) included in our meta-analysis showed that 57.5 % of their MIC_{SW} (n=146) exceeded their respective MAC-EQS values. All cypermethrin concentrations (n=29), as well as 73.3 % of the endosulfan (n=60) and 19.3 % of the chlorpyrifos concentrations (n=57), exceeded their respective MAC-EQS values.

The risk assessment tiers of RAC_{SW} determination and aquatic risks in the field

Ten of the 23 insecticide compounds considered here gained authorization for agricultural uses in the EU by passing tier I

Table 2 Summary statistics (the number of measured insecticide concentrations (MICs)) for important parameters of the EU insecticide exposure dataset

Parameter[a]	Minimum	25th percentile	Median	75th percentile	Maximum
Sampling date (n=1447)	1969	1989	1996	2004	2010
Catchment size (km^2, n=1320)	0.02	15	800	3315	180,000
Sampling interval[b] (days, n=1192/1054)	0.0416/0.0416	14/12	30/30	60/60	180/180
RAC exceedances per country (%, n=1566)		Belgium (n=26) 3.9 Bulgaria (n=1) 100 Cyprus (n=3) 66.7 Denmark (n=7) 100 France (n=46) 76.1 Germany (n=138) 83.3 Greece (n=487) 35.2 Hungary (n=3) 0 Italy (n=152) 54.6 Netherlands (n=60) 33.3 Poland (n=33) 27.3 Portugal (n=94) 21.3 Romania (n=5) 0 Spain (n=415) 33.5 Sweden (n=17) 94.1 UK (n=79) 78.5			
Hydrology (n=1419)		Lotic surface waters: 1211 (85.3 %); lentic surface waters: 208 (14.7 %)			
Type of surface water (n=1566)		Freshwater systems: 1430 (91.3 %); estuarine waters: 136 (8.7 %)			
Source (n=1566)		Non-point source[c]: 1222 (78 %); rainfall-induced runoff: 159 (10.2 %); rice field effluents: 81 (5.2 %); spray drift: 41 (2.6 %); aerial application: 27 (1.7 %); irrigation-induced runoff: 18 (1.1 %); drainage: 18 (1.1 %)			
Insecticide classes (n=1566)		Organochlorine insecticide: 143; organophosphorus insecticides: 1224; pyrethroids: 143; neonicotinoids: 33			

[a] There are fewer MICs for some parameters due to missing information in studies

[b] The first value is for all (water and sediment) MICs, and the second value is for MIC_{SW} only

[c] The non-point source denotes that the exact diffuse pollution source was not specified

of the regulatory environmental risk assessment for aquatic organisms, whereas 13 compounds were approved using higher risk assessment tiers (i.e., RAC_{SW} derivation using microcosms or mesocosms) (Table 1). The tier-I RAC_{SW} levels of the 10 insecticides (median 0.02225 μg/L) are noticeably lower than the RAC_{SW} levels of the 13 compounds (median 0.1 μg/L) derived through higher-tier risk assessment (Fig. 2). However, the median toxicity towards tier-I standard test organisms is approximately one order of magnitude higher (i.e., lower RAC_{SW} values) for the latter 13 compounds. Furthermore, the higher-tier RAC_{SW} of these 13 compounds are approximately 1.5 orders of magnitude higher than their associated tier-I RAC_{SW} levels (median: 0.003 μg/L; Fig. 2).

The MIC_{SW} of the 10 compounds that were approved using tier-I RAC_{SW} led to significantly (Table 3) higher RAC_{SW} exceedances (64.9 %; n=576) compared with those of the 13 insecticides that were approved using higher-tier RAC_{SW} (16.4 %; n=776; Table 4). However, if we only consider the tier-I RAC_{SW} for all 23 insecticide compounds in the assessment of MIC_{SW}, 71.4 % (n=1352) of the MIC_{SW} exceeded the RAC_{SW} (Table 4).

The risk assessment for different insecticide substance classes and pesticide groups

The MIC_{SW} of pyrethroids (n=108) led to the highest percentage of RAC_{SW} exceedances (70.4 %; see also Table 3 for a comparison of insecticide classes in the linear model analysis), followed by the MIC_{SW} of organophosphorus insecticides (37.5 %; n=1100) and neonicotinoids (24.2 %; n=33); in contrast, only 3.6 % of the MIC_{SW} (n=111) reported for the organochlorine insecticide endosulfan exceeded the RAC_{SW} (Fig. S4). Insecticide sediment exposure led to >90 % RAC_{SED} exceedance frequencies for all substance classes (organochlorine insecticides (n=32) 100 %; organophosphorus insecticides (n=124): 90.3 %; pyrethroids (n=58) 94.8 % RAC_{SED} exceedance frequencies), except for neonicotinoids, for which no MIC_{SED} was reported in the scientific literature.

We detected higher absolute field concentrations for fungicides (median 0.96 μg/L) compared with those of herbicides (median 0.063 μg/L) and insecticides (median 0.034 μg/L) (Fig. 3a) in the samples containing multiple pesticides (n=516). However, the risk assessment for these pesticide groups showed higher tier-I RAC_{SW} exceedance frequencies for

Table 3 The results of linear model analyses predicting logarithmic MIC_{SW} to RAC_{SW} ratios (R^2=0.612; adjusted R^2=0.609; p<0.001; n=942)

	Estimate	*t* value	*p* value
Intercept	−22.270	−2.992	0.00285
Catchment size	−0.262	−9.076	<0.001
Sampling interval	−0.274	−6.566	<0.001
Sampling date	0.012	3.160	0.00163
SC (OP)	0.108	0.474	0.6355
SC (Pyr)	1.349	5.267	<0.001
RA tier (higher tier)	−2.017	−28.142	<0.001

The substance class (SC) (reference category: organochlorine insecticides) and risk assessment tier of RAC_{SW} derivation (RA tier) (reference category: tier I) were entered as dummy-coded variables, and the catchment size and sampling interval were entered as log-transformed variables. The same main effects analysis was also performed using the organophosphates/carbamates insecticide substance class as the reference category for calculating the significance level of pyrethroids vs. organophosphates/carbamates (B=1.241; t value=9.646; p<0.001). The insecticide substance class neonicotinoid was excluded due to the small number of cases (n=6) available for statistical analysis. The categorical variable authorization status under Regulation (EC) No. 1107/2009 did not show significant explanatory power for the outcome variable

OP organophosphates/carbamates, *Pyr* pyrethroids

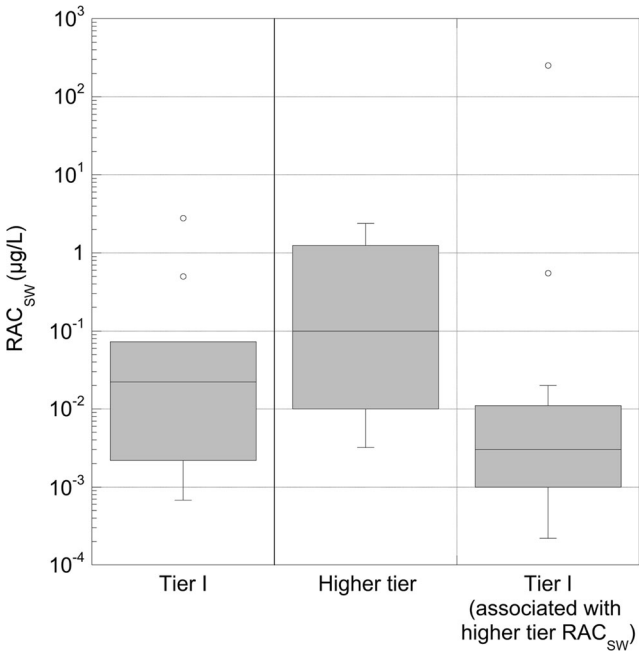

Fig. 2 A comparison of the RAC_{SW} levels derived from the different tiers of the official EU pesticide risk assessment (n (insecticides) tier-I risk assessment: 10, median RAC_{SW}=0.02225 µg/L; n (insecticides) higher-tier risk assessment: 13, median RAC_{SW}=0.1 µg/L). The tier-I RAC_{SW} associated with higher-tier RAC_{SW} (n (insecticides): 13, median RAC_{SW}=0.003 µg/L) denote RAC_{SW} derived from the first tier risk assessment for insecticides, which were finally approved using higher-tier studies (microcosms/mesocosms, see Table 1)

insecticides (53.1 %) compared with those of fungicides (31 %) and herbicides (3.8 %); in addition, the insecticide median concentration to tier-I RAC_{SW} ratio (1.25) is approximately one and two orders of magnitude higher compared with those of fungicides (0.13) and herbicides (0.019) (Fig. 3c).

Risk assessment for pesticide mixtures in EU surface waters

Overall, 135 different pesticides (66 insecticides; 42 herbicides; 27 fungicides) were detected in the 608 samples analyzed in total (i.e., water and sediment samples) for pesticide mixture occurrence in EU surface waters. Mixtures of pesticides occurred in 90 % (n=462 cases) of the insecticide water-phase samples with information on additional pesticides (n=516 out of the total of 1140 samples analyzed); these samples contained up to 13 pesticide compounds (Table S4). The results for sediment samples were comparable, i.e., 87 % of all samples with information on additional compounds (n=92) contained up to 11 pesticides.

The RQ_{mix} of the water-phase samples containing multiple pesticides (n=462) indicated the highest risks for invertebrates, as 82.7 % of these samples showed RQ_{mix} exceedances for this taxonomic group of up to a factor of 1,840,805 (Fig. 4). In relation to fish, 39.6 % of the samples had a RQ_{mix} >1 up to a factor of 18,377, whereas only 8.2 % of the water-phase samples led to a RQ_{mix} >1 for algae/macrophytes, with 829 as the highest RQ_{mix}.

Discussion

The insecticide exposure of EU surface waters: the protectiveness of EU pesticide legislation

Our meta-analysis shows that approximately 45 % of all MICs at >215 sites (i.e., >55 % of all (n=385) sites with MIC data) across the EU exceeded their respective RACs (Fig. 1; Fig. S1). It follows that insecticides are an important threat to European freshwater biodiversity, as insecticide levels > RACs lead to severe biodiversity reductions (Stehle and Schulz 2015). This conclusion is in line with smaller-scale field studies reporting pesticide-induced adverse effects on ecosystem function and aquatic biodiversity in small agricultural surface waters (e.g., Schäfer et al. 2012; Berenzen et al. 2005; Bereswill et al. 2013) and a study conducted on organic pollutants in larger EU surface waters (Malaj et al. 2014). However, for the first time, the present meta-analysis uses empirical evidence based on scientific data and official RACs to illustrate the extent of the risk for European aquatic ecosystems. In terms of regulatory implications, the risk assessment findings presented here question the fulfillment of

Table 4 An evaluation of MIC_{SW} as a function of the regulatory risk assessment tiers of the RAC_{SW} setting

	No. (%) of MIC_{SW} below RAC_{SW}	No. (%) of MIC_{SW} above RAC_{SW}
An evaluation of MIC_{SW} based on the final RAC_{SW} used for the authorization of compounds		
Insecticides with a tier-I RAC_{SW} (n=10; 576 MIC_{SW})	202 (35.1)	374 (64.9)
Insecticides with a higher-tier RAC_{SW} (n=13; 776 MIC_{SW})	649 (83.6)	127 (16.4)
An evaluation of MIC_{SW} based on tier-I RAC_{SW} for the 23 insecticide compounds		
Insecticides authorized by a higher-tier RAC_{SW} (n=13; 776 MIC_{SW})	184 (23.7)	592 (76.3)
All MIC_{SW} (n=23; 1352 MIC_{SW})	386 (28.6)	966 (71.4)

the general protection goals outlined in Regulation (EC) No. 1107/2009 and of the specific protection goals defined by Nienstedt et al. (2012) and the EFSA PPR Panel (EFSA 2010) based on the ecosystem service concept for the regulatory risk assessment of pesticides in the EU. Regarding the latter, Nienstedt et al. (2012) argued that the protection of ecosystem services for the fulfillment of the specific protection goals requires the protection of biodiversity in agricultural landscapes; our data, however, indicate clear biodiversity impairments (see also Stehle and Schulz 2015) in agricultural surface waters due to insecticide exposure. Importantly, not only the endpoints of the regulatory effect assessment (i.e., RAC) are exceeded in the field but also those of the regulatory exposure assessment (i.e., PEC; Knäbel et al. 2012; Knäbel et al. 2014); it must therefore be concluded that the current pre-authorization regulatory risk assessment schemes including associated risk mitigation obligations (i.e., pesticide application prescriptions) and underlying EU pesticide regulations, do not protect the aquatic environment. In addition, the insecticide field exposure data presented here do not provide a final conclusion on the reasons for RAC exceedances in the field, i.e., the failure of the prospective regulatory exposure and risk assessment or of farmers' adherence to regulatory risk mitigation obligations such as no-spray buffers; however, Knäbel et al. (2012) suggest both factors' contributions to insecticide risks for EU surface waters.

In addition to its overall protectiveness, our data also challenge the field relevance and focus of the EU pesticide regulatory risk assessment. Interestingly, we found the highest RAC exceedances for the MICs detected in small edge-of-field water bodies (Table S2) and for those definitively resulting from agricultural non-point source entries (Table S3). Although this finding can be explained (Schulz 2004; Stehle et al. 2013), one would nevertheless expect lower risks in surface waters and for exposure sources that are the specific focus of the aquatic regulatory risk assessment. On the contrary, surface waters not specifically targeted by regulatory risk assessment schemes, such as estuarine ecosystems (EFSA 2013), are also heavily affected by insecticide pollution; 37.5 % of the MICs exceeded their RACs, even though estuaries often are not located in close proximity to agricultural areas and non-contaminated seawater dilutes insecticide exposure (Steen et al. 1999).

There are additional issues that alert us to severe problems. First, approximately 90 % of the MIC_{SW} assessed here were measured using single or fixed-interval sampling strategies, which considerably underestimate actual insecticide exposure levels (Stehle et al. 2013; see also the result of the linear model

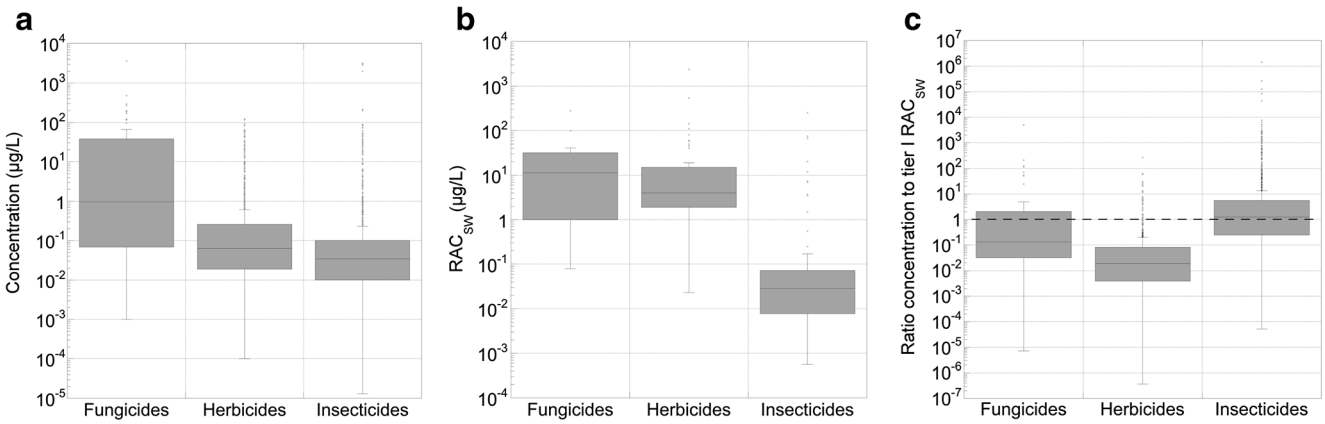

Fig. 3 Boxplots of the water-phase concentrations detected in EU surface waters (**a**), the regulatory acceptable concentrations (RAC_{SW}) derived from tier I of the European pesticide risk assessment (**b**) and related field concentration to tier-I RAC_{SW} ratios (**c**, *dashed line* indicates the RAC_{SW}) for the different pesticide groups. The comparison is based on fungicide (n=87; 23 compounds), herbicide (n=852; 36 compounds), and insecticide (n=1408; 59 compounds) water-phase concentrations detected in the 516 samples analyzed for the occurrence of multiple pesticide exposure

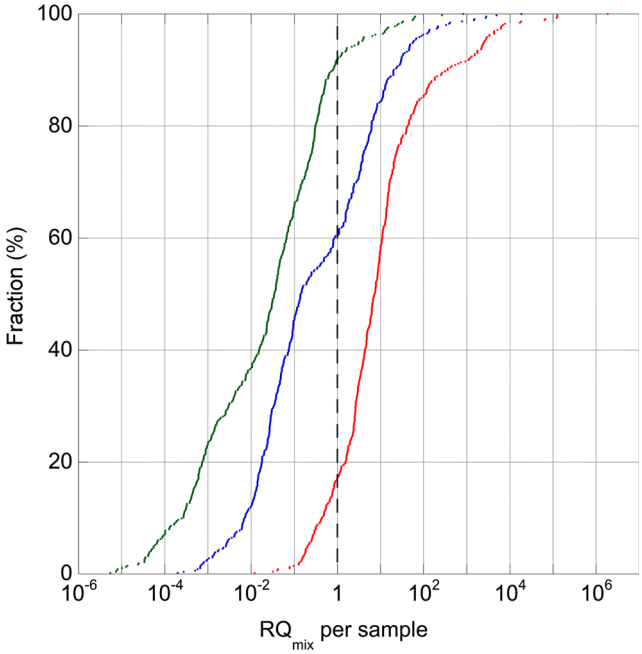

Fig. 4 Pesticide mixture toxicities detected in the water phase of EU surface water samples (n=462), expressed as risk quotients (RQ_{mix}) for algae/macrophytes (*green*), fishes (*blue*), and invertebrates (*red*). A RQ_{mix} >1 indicates a risk for the respective taxonomic group

analysis (Table 3), which indicates higher RAC_{SW} exceedances for shorter sampling intervals). Second, no scientific knowledge on insecticide surface water exposure exists for large parts (i.e., approximately 80 %) of European high-intensity agricultural areas (Fig. S1), which indicates that future monitoring studies are needed to further quantify risks across the EU; this research is of even more importance because climate change is expected to lead to increasing insecticide application in EU agriculture (Kattwinkel et al. 2011). Third, our meta-analysis shows that pesticides occur as mixtures in 90 % of the samples analyzed for multiple compounds (Table S4), with nearly 40 % of these samples containing more than 5 and up to 13 pesticides per sample. Importantly, most of the studies analyzed surface water samples for selected pesticide compounds only; thereby most likely they potentially missed compounds that were additionally present (see also Moschet et al. (2014) on this topic). However, these findings on pesticide mixture occurrences in the field challenge the protectiveness of the RAC, which is defined for single active ingredients only (EFSA 2013) and thus not covering potential combined or even synergistic effects (e.g., Denton et al. 2003; Belden and Lydy 2006). Fourth, only a marginal difference in RAC exceedances exists between the 15 insecticide compounds currently authorized in the EU and the eight compounds that are no longer approved (Table S5). This finding is supported by our linear model analysis, which could not detect a significant explanatory power for the differentiation of authorized and non-authorized compounds (Table 3). We therefore conclude that the cancelation of the authorization of obsolete active ingredients under Directive 91/414/EEC and Regulation (EC) No. 1107/2009 did not reduce insecticides' acute risks for surface waters; this claim, again, challenges the overall effectiveness of EU pesticide legislations. Within this context, we identified even higher MIC_{SW} to RAC_{SW} ratios after the enforcement of the Directive 91/414/EEC in 1993 (Fig. S2; Fig. S3) and, as opposed to the global MIC data presented by Stehle and Schulz (2015), for more recent sampling dates independent of the influence of covariates, such as the increased detection of more toxic pyrethroids in recent years (Table 3). Moreover, 40.5 % of all MICs detected since the year 2000 exceeded respective RACs (Table S1), which challenges the general perception of decreasing environmental risks (see, e.g., Lamberth et al. 2013; Devine and Furlong 2007) due to the market introduction of newer insecticide compounds and the enforcement of more stringent environmental regulations. However, other reasons not concerning aquatic organisms (e.g., high mammalian and avian toxicities of organophosphates) presumably led to the withdrawal of hazardous pesticide compounds under Directive 91/414/EEC, so that the overall environmental risks might nonetheless be reduced over time (Cross and Edward-Jones 2011).

Overall, our data and those of Knäbel et al. (2012, 2014) indicate that a critical reconsideration of the entire EU pesticide regulatory risk assessment approach including enforcement of mandatory risk mitigation obligations is imperatively needed; these findings must be seriously considered in future revisions of EU pesticide regulations. In addition, effective risk mitigation measures (e.g., Reichenberger et al. 2007; Stehle et al. 2011) have to be implemented and enforced, inter alia within National Action Plans, as requested by EU Directive 2009/128/EC (Sustainable Use Directive for Plant Protection Products (European Commission 2009b)). EU agricultural policies and subsidies should also be critically reconsidered, as they currently foster agricultural intensification and agrochemical use (Pe`er et al. 2014).

In relation to the WFD, the scientific exposure data presented here confirm recent findings based on governmental data (Malaj et al. 2014), which showed that insecticide pollution is a significant stressor in large EU surface waters. This confirmation, however, is a crucial finding, as the characterization of the chemical status of a large proportion of water bodies is still deficient due to lacking (European Environment Agency 2012) and often inappropriate (Stehle et al. 2013) governmental monitoring. Furthermore, our meta-analysis identified substantially higher RAC_{SW} exceedance frequencies (32.6 %; n=763) in large EU surface waters for the 20 non-priority substances included in our meta-analysis compared with those of the three priority substances (15.8 %; n=146). This finding challenges the WFD priority substance selection criteria (see also Von der Ohe et al. (2011) and Schäfer et al. (2011)) that currently disregard the high ecotoxicity potential of modern insecticides. Real-world exposure data and

actual ecological risks in the field should trigger the future identification and prioritization of WFD priority substances.

The protectiveness of the regulatory risk assessment tiers

The MIC_{SW} of the compounds authorized using a higher-tier risk assessment show considerably lower RAC_{SW} exceedances (Table 4). This finding is in line with the general principles underlying the pre-authorization regulatory risk assessment, i.e., the outcomes of higher risk assessment tiers are less conservative compared with those of lower tiers (EFSA 2013), which consequentially leads to less frequent exceedances of these higher-tier RACs in the field. Most importantly, tier-I RACs are derived based on the ecological threshold option (ETO), which accepts only negligible effects, whereas the derivation of higher-tier RACs based on micro-/mesocosm studies generally accepts (temporary) clear population level effects (i.e., RACs derived based on the ecological recovery option, ERO-RACs; see EFSA (2013) for details). However, it is thought-provoking that such liberal higher-tier RACs drive the final regulatory risk assessment specifically of extremely toxic insecticide compounds. These insecticides have a substantially higher intrinsic ecotoxicity potential towards aquatic (standard test) organisms compared with those of the compounds authorized using tier-I RAC_{SW} (Fig. 2; Table S6). It follows that the most toxic insecticides are authorized using least conservative RACs, i.e., those based on ERO. Considering this high toxicity potential and that these liberal higher-tier RACs are set with hardly any margin of safety, they should never be exceeded in the field to prevent unacceptable adverse effects. Our data (Table 4), however, clearly disprove this assumption.

There are two more critical issues that have to be considered in this context. First, higher-tier RAC_{SW} are considerably less conservative compared with tier-I RAC_{SW} levels (Fig. 2) due to the substantial reduction of AFs (up to two orders of magnitude); however, this reduction in conservatisms is not justified by actually lower ecotoxicity potentials (Table S6). Although this AF reduction is often reasoned by the higher complexities and ecological realism of the higher-tier microcosm/mesocosms studies (EFSA 2013), the inherent limitations of these artificial model ecosystem studies (see, for example, Crane and Giddings (2004) and references therein) jeopardize the protectiveness of higher-tier RAC_{SW} for real-world situations in the field, especially in cases in which an AF of one was employed (Table S6); these limitations and the resulting uncertainties are therefore not covered by the regulatory pesticide risk assessment. In addition, the occurrence of pesticide mixtures, consecutive exposure events, and confounding factors (e.g., hydraulic stress, exposure to nutrients) in the field further challenge the protectiveness of higher-tier RAC_{SW} set with low AFs. However, according to EFSA (2013), an AF of one is not used anymore since commencement of this guideline. Nevertheless, higher-tier RAC_{SW} should, in consistency with tier-I RACs, generally be derived using the ETO and thus without already allowing for clear population level effects (sensu ERO-RACs).

Second, recent field studies (Schäfer et al. 2012; Beketov et al. 2013; Peters et al. 2013) reported pesticide-induced adverse effects at concentrations even well below (i.e., 1/10 to 1/100) conservative tier-I RAC_{SW}. In addition, based on statistical analyses, Luttik et al. (2011) argued that the AFs of 100 used for tier-I RAC_{SW} derivation may not adequately cover interspecies sensitivity variation. These findings provide evidence that even the conservative RAC_{SW} are potentially not protective in the field. An even worse protection level may thus be expected for the even less conservative higher-tier ERO-RAC_{SW}, although they have been established under conditions that are considered more realistic.

Overall, we conclude that in addition to cases with RAC exceedances, the occurrence of unacceptable adverse effects in the field can potentially not be excluded for the 35 % of MIC_{SW} that comply with conservative tier-I ERO-RAC_{SW} and are even more likely for the 83.6 % of MIC_{SW} that comply with higher-tier ERO-RAC_{SW} (Table 4). Our findings on the lack of the protectiveness of higher-tier RACs for insecticide compounds are in line with a recent study on aquatic ecosystems and fungicides (Zubrod et al. 2015), which also claimed that the higher-tier regulatory EU risk assessment does not provide an adequate level of protection. EFSA (2013) acknowledges these regulatory risk assessment shortcomings by admitting that the RAC_{SW} may not be protective for all cases occurring in the field; the effects not covered by the prospective risk assessment, the combined effects between pesticides and environmental stressors, the exposure to multiple pesticides, and the repeated exposure due to serial pesticide application are potential reasons for these uncertainties. As a consequence, EFSA (2013) postulates further strengthening the link between the RACs and real-world field situations, e.g., by conducting appropriate field studies that clearly link pesticide exposure to related effects. We believe our study addresses one aspect of this issue. However, further targeted studies are urgently needed.

Risk assessment for pesticide groups and insecticide classes: a proposal for a new hazard-based cut-off criterion

The comparison of pesticide risks shows that insecticides particularly threaten EU surface waters (Fig. 3c). This finding is explained by the substantially higher ecotoxicity potential of insecticides. The median insecticide tier-I RAC_{SW} (0.029 μg/L) is more than two orders of magnitude lower compared with those of herbicides (4 μg/L) and fungicides (11.3 μg/L; Fig. 3b). This high ecotoxicity potential of insecticides overcompensates the absolutely higher field

concentrations of fungicides and herbicides (Fig. 3a), which result from higher application rates and physicochemical properties (e.g., large DT_{50} values, high water solubilities), which foster surface water exposure (Stehle et al. 2011, 2013). Our findings support those of Stehle et al. (2011), who also reported lower concentrations and higher ecotoxicological risks for insecticides compared with those of herbicides and fungicides at the inlet and outlet of vegetated treatment systems. The high ecotoxicity of insecticides, particularly for aquatic invertebrates (Devine and Furlong 2007), together with the overall high sensitivity of this group of organisms to pesticide exposure (US EPA 2014), is also a major reason that aquatic invertebrates are at risk to the largest extent when exposed to multiple pesticides (Fig. 4).

Overall, our results provide strong evidence that regulatory risk assessment and risk management for insecticides particularly needs reconsideration; targeted and more protective risk assessment concepts, stricter decision criteria, and mandatory risk mitigation obligations should be defined specifically for the authorization procedures of insecticides. However, it is important to note that field data-based meta-analyses are also needed for herbicides and fungicides to thoroughly evaluate the protectiveness and field relevance of the EU regulatory risk assessment for these pesticide groups. For example, the standard test organisms currently used in the aquatic effect assessment of pesticides are potentially unsuitable for adequately assessing fungicide effects in the field (Zubrod et al. 2015; Maltby et al. 2009).

Excluding neonicotinoids, for which a valid conclusion is hindered due to insufficient data, the development and authorization of newer insecticide classes led to an increase in acute environmental risks for surface waters (Fig. S4; Table 3), with the pyrethroids outpacing the other insecticide classes due to their extremely high toxicities for non-target organisms (Spurlock and Lee 2008) and their fast mode of action (Schulz and Liess 2000; Forbes and Cold 2005; Solomon et al. 2001). Pyrethroids' acute toxicities for fishes and invertebrates are several orders higher than those of other pesticides (Table S7), which substantially increases the ecotoxicological risks for aquatic ecosystems. Balderacchi and Trevisan (2010) showed that authorized pesticides are generally less toxic, less hydrophilic, and more rapidly degraded than non-authorized pesticide compounds; this finding, however, does not account for pyrethroids (Table S7). We therefore propose considering a new hazard-based cut-off criterion, very Toxic, fast Mode of Action (vTfMoA), in the regulatory risk assessment of pesticides. This criterion could complement the hazard-based cut-off criteria introduced by the new Regulation (EC) No. 1107/2009, which aim to enhance human and environmental health protection (Table S8). However, the exact classification schemes for the vTfMoA criterion still have to be defined, e.g., by using acute toxicity thresholds and time-to-event analyses (Newman and McCloskey 1996). The implementation of the vTfMoA criterion could substantially reduce the environmental risks caused by extremely toxic and rapidly acting pesticides, such as pyrethroids, which, despite their high acute risk potentials and related RAC exceedances, are still predominantly authorized in the EU (Table 1). However, another fact to consider here is that the introduction of additional hazard-based cut-off criteria potentially decreases the anticipated number of active ingredients to be (re-)authorized and therefore available for crop protection in Europe (ECPA 2006); this fact should not be ignored considering the increasing resistance of target pests (Denholm et al. 2002).

Until now, only very limited field data are available for neonicotinoids (Fig. S4), which, in addition to their entirely different mode of action, selectivity, plant systemicity, persistence, and resulting delayed effects (Jeschke and Nauen 2008; Tennekes and Sanchez-Bayo 2011; Sanchez-Bayo 2014), hinders a thorough assessment of their acute risks for EU surface waters. However, numerous recent studies reporting the substantial ecological effects of neonicotinoids in aquatic and terrestrial ecosystems (e.g., van Dijk et al. 2013; Hallmann et al. 2014; Chagnon et al. 2015; Goulson 2013) strongly indicate that further research is needed on the ecological consequences of neonicotinoid use. In this context, it is important to note that insecticide use patterns in the EU have changed substantially over the past few decades, with the discontinuation of many organochlorine and organophosphate insecticides and recent increases in pyrethroid and neonicotinoid use (together, with an insecticide market share of approximately 40 % in 2008; Jeschke et al. 2010). Future monitoring studies should therefore particularly focus on contemporary insecticide classes and newly introduced insecticide compounds; the sampling strategy must be suitable for the compounds of concern (Stehle et al. 2013) and must be conducted by independent organizations.

Case studies: EU regulatory risk assessments for bifenthrin and imidacloprid

This study uses the EU authorizations of the insecticides bifenthrin (EFSA 2011) and imidacloprid (EFSA 2008) to illustrate the lack of field relevance and margins of safety in the current EU regulatory risk assessment schemes. The predicted aquatic exposure concentration of bifenthrin was calculated to be 0.0049 μg/L, using FOCUS step-4 PEC_{SW} (incorporating 20 m no-spray buffer and 80 % runoff reduction) and thus making use of essentially all exposure mitigating assumptions that the FOCUS model provides. The effect assessment for aquatic organisms for this compound defined based on a higher-tier mesocosms study with a no observed ecologically adverse effect concentration (NOEAEC) of 0.015 μg/L and an AF set to 3, a RAC_{SW} of 0.005 μg/L. Overall, the final higher-tier regulatory risk assessment for bifenthin indicated an acceptable aquatic risk, as the final RAC_{SW} of 0.005 μg/L is

higher than the final PEC_{SW} of 0.0049 μg/L. In essence, the active substance bifenthrin was authorized in the EU using the highest and therefore least conservative tiers in both the exposure and effect assessment, with a difference of 0.0001 μg/L (or 0.1 ng/L) between the PEC_{SW} and the higher-tier RAC_{SW}. Although this procedure appears formally correct according to legal requirements, it immediately becomes evident that, from a scientific point of view, it cannot be ensured that this small margin of safety is protective considering multifaceted field conditions. It must be concluded that the field relevance, as well as the margin of safety, of such an aquatic risk assessment is considerably questionable. Within this context, it is worth noting that all bifenthrin concentrations detected in EU surface waters (n=8) exceeded both the PEC_{SW} and the RAC_{SW}, which suggests that unacceptable effects occur in the field and further challenges the protectiveness of the current regulatory risk assessment approach for real-world situations.

The case study for the neonicotinoid insecticide imidacloprid reveals further regulatory risk assessment uncertainties. The EU authorization of this compound was based on FOCUS step-4 PEC_{SW} (incorporating 95 % spray drift reduction and 90 % runoff reduction) ranging between 0.152 and 0.429 μg/L subject to crop and FOCUS scenarios (see EFSA (2008) for details). The higher-tier RAC_{SW} of 0.3 μg/L was based on a mesocosm study with a NOEC of 0.6 μg/L and an AF of 2. It follows that the risk assessment already forecasts surface water concentrations potentially to exceed the RAC_{SW} under certain conditions. EFSA (2008) thus admits: "Overall it is concluded that a high risk for aquatic organisms is indicated for the representative uses in orchards and tomatoes requiring substantial risk mitigation measures to reduce spray drift and runoff. "Imidacloprid surface water concentrations (n=21) were reported for six countries across the EU, with concentrations reaching up to >200 μg/L (Mohr et al. 2012; Starner and Goh 2012) and 28.6 % of all MIC_{SW} exceeding the RAC_{SW}; these findings, again, challenge the overall protectiveness of the pre-authorization regulatory risk assessment in the EU.

Conclusion and recommendations for risk assessment amendments

For the first time, we evaluated the protectiveness and field relevance of the regulatory EU pesticide risk assessment on a continental scale. As a result, our meta-analysis shows that MICs frequently exceed the RACs set for the authorization of active substances at the EU level. This finding reveals the critical failures of the EU pesticide regulations and the substantial and widespread ecological risks for the aquatic biodiversity. Moreover, even compliance, especially with higher-tier RACs, may not provide sufficient protection for aquatic ecosystems. The lack of consideration of pesticide mixtures and significantly increasing risks due to the market introduction of newer insecticide compounds poses further challenges to the overall protectiveness of EU pesticide legislation; the latter are also important for the future selection of WFD priority substances. Overall, we conclude that the European pre-authorization regulatory risk assessment for insecticides (and pesticides in general) must be substantially improved in terms of field relevance and environmental protectiveness. We therefore propose the following five risk assessment amendments:

(i) The conservatism of the regulatory exposure assessment must be increased, e.g., by only considering step 1 PECs or by applying safety factors to step 3 and 4 PECs (see also Knäbel et al. (2012) and Knäbel et al. (2014) for further information); in addition, the scope of the exposure assessment must be extended to larger surface waters and estuarine systems. Alternatively, the entire FOCUS exposure assessment approach must be completely revised and the protectiveness of the revised approach must be validated independently using field data.

(ii) The uncertainties of the overall pre-authorization risk assessment must be substantially reduced, and its protectiveness must be increased; in particular, a critical reconsideration of the ecotoxicity endpoints (including magnitude and duration of effects considered acceptable for ERO-RACs) and AF used in higher-tier risk assessment for the RAC derivation and authorization of highly toxic compounds must thoroughly be addressed. In addition, mixture toxicity must be considered in the prospective regulatory risk assessment, and the implementation of additional hazard-based cut-off criteria, e.g., for extremely toxic compounds, should be considered. Incidences of unacceptable adverse effects at concentrations below the RACs in the field should be excluded with high confidence.

(iii) The overall link between the regulatory risk assessment and the actual situation in the field must be considerably strengthened, and findings from field studies on pesticide exposure and effects must be used for a retrospective validation of the current EU regulatory risk assessment, particularly for its future development. The fundamental rationale of the risk assessment, i.e., to protect aquatic biocenoses in the field, not in the computer or any sort of artificial test system, must be the driver for all future risk assessment revisions.

(iv) Effective risk management measures (e.g., large non-cropped buffer zones) should be mandatory for all pesticide approvals.

(v) An obligatory validation of the risk assessment through targeted chemical and biological post-authorization monitoring programs must be implemented for compounds of concern to ensure that their application does not lead to unacceptable effects in the field.

In addition to these risk assessment amendments, farmers' knowledge about appropriate pesticide use and environmental awareness must also substantially be improved through obligatory professional training, and adherence to risk mitigation obligations (i.e., application prescriptions) should be monitored. Above all, the reliance of EU agriculture on pesticides should be critically reconsidered and replaced by more environmental friendly alternatives, such as truly integrated pest management and organic farming, wherever possible.

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References

Akerblom N, Arbjörk C, Hedlund M, Goedkoop W (2008) Deltamethrin toxicity to the midge *Chironomus riparius* Meigen—effects of exposure scenario and sediment quality. Ecotoxicol Environ Saf 70: 53–60

Balderacchi M, Trevisan M (2010) Comments on pesticide risk assessment by the revision of Directive EU 91/414. Environ Sci Pollut Res 17:523–528

BBA (2001) German Federal Office of Consumer Protection and Food Safety (BVL) database of pesticide risk assessment endpoints

Beketov MA, Kefford BJ, Schäfer RB, Liess M (2013) Pesticides reduce regional biodiversity of stream invertebrates. PNAS 110:11039–11043

Belden JB, Lydy MJ (2006) Joint toxicity of chlorpyrifos and esfenvalerate to fathead minnows and midge larvae. Environ Toxicol Chem 25:623–629

Berenzen N, Kumke T, Schulz HK, Schulz R (2005) Macroinvertebrate community structure in agricultural streams: impact of runoff-related pesticide contamination. Ecotoxicol Environ Saf 60:37–46

Bereswill R, Streloke M, Schulz R (2013) Current-use pesticides in stream water and suspended particles following runoff: exposure, effects, and mitigation requirements. Environ Toxicol Chem 32: 1254–1263

Cedergreen N, Christensen AM, Kamper A, Kudsk P, Mathiassen SK, Streibig JC, Sørensen H (2008) Review of independent action compared to concentration addition as reference models for mixtures of compounds with different molecular target sites. Environ Toxicol Chem 27:1621–1632

Chagnon M, Kreutzweise D, Mitchell EAD, Morrissey CA, Noome DA, van der Sluijs JP (2015) Risks of large-scale use of systemic insecticides to ecosystem functioning and services. Environ Sci Pollut Res 22:119–134

Crane M, Giddings JM (2004) Risk around the world—"ecologically acceptable concentrations" when assessing the environmental risks of pesticides under European Directive 91/414/EEC. Hum Ecol Risk Assess 10:733–747

Crommentuijn T, Sijm D, de Bruijn J, van Leeuwen K, Van de Plassche E (2000) Maximum permissible and negligible concentrations for some organic substances and pesticides. J Environ Manag 58:297–312

Cross P, Edward-Jones G (2011) Variation in pesticide hazard from arable crop production in Great Britain from 1992 to 2008: an extended time-series analysis. Crop Prot 30:1579–1585

Davies BR, Biggs J, Williams PJ, Lee JT, Thompson S (2008) A comparison of the catchment sizes of rivers, streams, ponds, ditches and lakes: implications for protecting aquatic biodiversity in an agricultural landscape. Hydrobiologia 597:7–17

Deneer JW (2000) Toxicity of mixtures of pesticides in aquatic systems. Pest Manag Sci 56:516–520

Denholm I, Devine GJ, Williamson MS (2002) Insecticide resistance on the move. Science 297:2222–2223

Denton DL, Wheelock CE, Murray SA, Deanovic LA, Hammock BD, Hinton DE (2003) Joint acute toxicity of esfenvalerate and diazinon to larval fathead minnows (*Pimephales promelas*). Environ Toxicol Chem 22:336–341

Devine GJ, Furlong MJ (2007) Insecticide use: contexts and ecological consequences. Agricul Human Val 24:281–306

DG SANCO (2002) Guidance document on aquatic ecotoxicology in the context of the Directive 91/414/EEC. European Commission Health & Consumer Protection Directorate-General, Sanco/3268/2001 rev.4 (final)

DG SANCO (2014) EU pesticides database. http://ec.europa.eu/sanco_pesticides/public/index.cfm2011. Accessed 08 March 2014

ECPA (2006) Proposal for a regulation concerning the placing on the market of plant protection products—impact of the criteria for 'non-approval' and 'candidates for substitution'. ECPA evaluation, PP/06/EJ/15809, Brussels

EFSA (2008) Conclusion regarding the peer review of the pesticide risk assessment of the active substance imidacloprid. EFSA Sci Report 148:1–120

EFSA (2010) Scientific opinion on the development of specific protection goal options for environmental risk assessment of pesticides, in particular in relation to the revision of the guidance documents on aquatic and terrestrial ecotoxicology (SANCO/3268/2001 and SANCO/10329/2002). EFSA J 8:1821 **(55 pp)**

EFSA (2011) Conclusion on the peer review of the pesticide risk assessment of the active substance bifenthrin. EFSA J 9:2159 **(101 pp)**

EFSA (2013) Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA J 11:3290 **(186 pp)**

EFSA (2014) Pesticides publications. http://www.efsa.europa.eu/en/pesticides/pesticidesscdocs.htm. Accessed 12 March 2014

European Commission (1991) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. Off J Eur Union L230:1–32

European Commission (2000) Directive 2000/60/EC of the European parliament and of the council of 23 October 2000 establishing a framework for community action in the field of water policy. Off J Eur Comm L327:1–72

European Commission (2009a) Regulation (EC) No 1107/2009 of the European parliament and the council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. Off J Eur Union L309:1–50

European Commission (2009b) Directive 2009/128/EC of the European parliament and the council of 21 October 2009 establishing a framework for community action to achieve sustainable use of pesticides. Off J Eur Union L309:71–86

European Commission (2013) Directive 2013/39/EU of the European parliament and the council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. Off J Eur Union L226:1–17

European Commission (2014) Member states factsheets—European Union. DG Agriculture and Rural Development, Agricultural Policy Analysis and Perspectives Unit

European Environment Agency (2012) European waters—assessment of status and pressures. EEA Report No 8/2012, Office for Publications of the European Union, Luxembourg

Eurostat (2013) Agriculture, forestry and fishery statistics 2013 edition. European Union, Luxembourg

FOCUS (2001) FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2

Forbes VE, Cold A (2005) Effects of the pyrethroid esfenvalerate on life-cycle traits and population dynamics of *Chironomus riparius*—importance of exposure scenario. Environ Toxicol Chem 24:78–86

Goulson D (2013) An overview of the environmental risks posed by neonicotinoid insecticides. J Appl Ecol 50:977–987

Hallmann CA, Foppen RPB, van Turnhout CAM, de Kroon H, Jongejans E (2014) Declines in insectivorous birds are associated with high neonicotinoid concentrations. Nature 511:341–343

Jeschke P, Nauen R (2008) Neonicotinoids—from zero to hero in insecticide chemistry. Pest Manag Sci 64:1084–1098

Jeschke P, Nauen R, Schindler M, Elbert A (2010) Overview of the status and global strategy for neonicotinoids. J Agric Food Chem 59:2897–2908

Kattwinkel M, Kühne J-V, Foit K, Liess N (2011) Climate change, agricultural insecticide exposure, and risk for freshwater communities. Ecol Appl 21:2068–2081

Knäbel A, Stehle S, Schäfer RB, Schulz R (2012) Regulatory FOCUS surface water models fail to predict insecticide concentrations in the field. Environ Sci Technol 46:8397–8404

Knäbel A, Meyer K, Rapp J, Schulz R (2014) Fungicide field concentrations exceed FOCUS surface water predictions: urgent need of model improvement. Environ Sci Technol 48:455–463

Kortenkamp A, Backhaus T, Faust M (2009) State of the art on mixture toxicity. Final report, study contract number 070307/2007/485103/ETU/D.1, European Commission, Brussels

Lamberth C, Jeanmart S, Luksch T, Plant A (2013) Current challenges and trends in the discovery of agrochemicals. Science 341:742–746

Luttik R, Hart A, Roelofs W, Craig P, Mineau P (2011) Variation in the level of protection afforded to birds and crustaceans exposed to different pesticides under standard risk assessment procedures. Integr Environ Assess Manag 7:459–465

Malaj E, von der Ohe PC, Grote M, Kühne R, Mondy CP, Usseglio-Polatera P, Brack W, Schäfer RB (2014) Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. PNAS 111:9549–9554

Maltby L, Brock TCM, Van den Brink PJ (2009) Fungicide risk assessment for aquatic ecosystems: importance of interspecific variation, toxic mode of action, and exposure regime. Environ Sci Technol 43:7556–7563

Mohr S, Berghahn R, Schmiediche R, Hübner V, Loth S, Feibicke M, Mailahn W, Wogram J (2012) Macroinvertebrate community response to repeated short-term pulses of the insecticide imidacloprid. Aqua Toxicol 110–111:25–36

Moschet C, Wittmer I, Simovic J, Junghans M, Piazzoli A, Singer H, Stamm C, Leu C, Hollender J (2014) How a complete pesticide screening changes the assessment of surface water quality. Environ Sci Technol 48:5423–5432

Newman MC, McCloskey JT (1996) Time-to-event analyses of ecotoxicity data. Ecotoxicology 5:187–196

Nienstedt KM, Brock TCM, Van Wensem J, Montforts M, Hart A et al (2012) Development of a framework based on an ecosystem services approach for deriving specific protection goals for environmental risk assessment of pesticides. Sci Total Environ 415:31–38

Pe`er G, Dicks LV, Visconti P, Arlettaz R, Baldi A et al (2014) EU agricultural reform fails on biodiversity. Science 344:1090–1092

Peters K, Bundschuh M, Schäfer RB (2013) Review on the effects of toxicants on freshwater ecosystem functions. Environ Poll 180:324–329

Pigott TD (2009) Handling missing data. In: Cooper H, Hedges LV, Valentine JC (eds) The handbook of research synthesis and meta-analysis, 2nd edn. Russel Sage Foundation, New York, pp 399–416

PPDB (2013) The Pesticide Properties Database (PPDB) developed by the Agriculture & Environment Research Unit (AERU), University of Hertfordshire, funded by UK national sources and the EU-funded Footprint project (FP6-SSP-022704). http://sitem.herts.ac.uk/aeru/ppdb/en/index.htm. Accessed 15 December 2013

Reichenberger S, Bach M, Skitschak A, Frede H-G (2007) Mitigation strategies to reduce pesticide inputs into ground- and surface water and their effectiveness; a review. Sci Total Environ 384:1–35

Sanchez-Bayo F (2014) The trouble with neonicotinoids. Science 346:806–807

Schäfer RB, von der Ohe PC, Kühne R, Schüürmann G, Liess M (2011) Occurrence and toxicity of 331 organic pollutants in large rivers of north Germany over a decade (1994 to 2004). Environ Sci Technol 45:6167–6174

Schäfer RB, von der Ohe PC, Rasmussen J, Kefford BJ, Beketov MA, Schulz R, Liess M (2012) Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. Environ Sci Technol 46:5134–5142

Schulz R (2004) Field studies on exposure, effects and risk mitigation of aquatic nonpoint-source insecticide pollution—a review. J Environ Qual 33:419–448

Schulz R, Liess M (2000) Toxicity of fenvalerate to caddis fly larvae: chronic effects of 1- vs 10-h pulse-exposure with constant doses. Chemosphere 41:1511–1517

Solomon KR, Giddings JM, Maund SJ (2001) Probabilistic risk assessment of cotton pyrethroids: I. Distributional analysis of laboratory aquatic toxicity data. Environ Toxicol Chem 20:652–659

Spurlock F, Lee M (2008) Synthetic pyrethroid use patterns, properties, and environmental effects. In: Gan J, Spurlock F, Hendley P, Weston D (eds) Synthetic pyrethroids: occurrence and behavior in aquatic environments. American Chemical Society, Washington, DC, pp 3–25

Starner K, Goh KS (2012) Detections of the neonicotinoid insecticide imidacloprid in surface waters of three agricultural regions of California, USA, 2010–2011. Bull Environ Contamin Toxicol 88:316–321

Steen RJCA, Leonards PEG, Brinkman UAT, Barcelo D, Tronczynski J, Albanis TA, Cofino WP (1999) Ecological risk assessment of agrochemicals in European estuaries. Environ Toxicol Chem 18:1574–1581

Stehle S, Schulz R (2015) Agricultural insecticides threaten surface waters at the global scale. PNAS 112:5750–5755

Stehle S, Elsaesser D, Gregoire C, Imfeld G, Niehaus E, Passeport E, Payraudeau S, Schäfer RB, Tournebize J, Schulz R (2011) Pesticide risk mitigation by vegetated treatment systems: a meta-analysis. J Environ Qual 40:1068–1080

Stehle S, Knäbel A, Schulz R (2013) Probabilistic risk assessment of insecticide concentrations in agricultural surface waters: a critical appraisal. Environ Monit Assess 185:6295–6310

Tennekes HA, Sanchez-Bayo F (2011) Time-dependent toxicity of neonicotinoids and other toxicants: implications for a new approach to risk assessment. J Environ Anal Toxicol S4:001. doi:10.4172/2161-0525.S4-001

US EPA (2012) Pesticide reregistration status. http://www.epa.gov/pesticides/reregistration/status.htm. Accessed 12 December 2012

US EPA (2014) ECOTOXicology database system. Version 4.0. http://www.epa.gov/ecotox/. Accessed 03 February 2013

Van Dijk TC, van Staalduinen MA, van der Sluijs JP (2013) Macro-invertebrate decline in surface water polluted with imidacloprid. PLoS One 8, e62374 **(10 pp)**

Von der Ohe PC, Dublio V, Slobodnik J, De Deckere E, Kühne R et al (2011) A new risk assessment approach for the prioritization of 500 classical and emerging organic microcontaminants as potential river basin specific pollutants under the European Water Framework Directive. Sci Total Environ 409:2064–2077

Yu SJ (2008) The toxicology and biochemistry of insecticides. CRC Press, Boca Raton

Zubrod JP, Englert D, Feckler A, Koksharova N et al (2015) Does the current fungicide risk assessment provide sufficient protection for key drivers in aquatic ecosystem functioning? Environ Sci Technol 49:1173–1183

Supporting Information for

Pesticide authorization in the EU - environment unprotected?

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Supporting Tables

Table S1. A temporal overview of RAC exceedance and compliance for MICs detected in EU surface waters per decade.

Decade	No. (%) of MICs below RAC	No. (%) MICs above RAC
1960-1969		
MIC_{SW} (n = 4)	4 (100)	0 (0)
MIC_{SED}	-	-
MIC (water and sediment) (n = 4)	4 (100)	0 (0)
1970-1979		
MIC_{SW} (n = 49)	26 (53)	23 (47)
MIC_{SED} (n = 3)	0 (0)	3 (100)
MIC (water and sediment) (n = 52)	26 (50)	26 (50)
1980-1989		
MIC_{SW} (n = 314)	224 (71.3)	90 (28.7)
MIC_{SED} (n = 16)	0 (0)	16 (100)
MIC (water and sediment) (n = 330)	224 (67.9)	106 (32.1)
1990-1999		
MIC_{SW} (n = 385)	230 (59.7)	155 (40.3)
MIC_{SED} (n = 130)	7 (5.4)	123 (94.6)
MIC (water and sediment) (n = 515)	237 (46)	278 (54)
2000-2010		
MIC_{SW} (n = 511)	317 (62)	194 (38)
MIC_{SED} (n = 35)	8 (22.9)	27 (77.1)
MIC (water and sediment) (n = 546)	325 (59.5)	221 (40.5)

Table S2. An evaluation of RAC exceedance and compliance for MICs detected in surface water bodies specifically targeted by EU pesticide regulations (EFSA 2013; FOCUS 2001; see main text for details) and for different surface water types.

	No. (%) of MICs below RAC	**No. (%) MICs above RAC**
Catchment sizes		
MIC_{SW}		
Water bodies with catchment sizes of up to 1 km^2 (n = 105)	14 (13.3)	91 (86.7)
Water bodies with catchment sizes of up to 10 km^2 (n = 229)	61 (26.6)	168 (73.4)
MIC_{SED}		
Water bodies with catchment sizes of up to 1 km^2 (n = 21)	0 (0)	21 (100)
Water bodies with catchment sizes of up to 10 km^2 (n = 44)	1 (2.3)	43 (97.7)
MICs (water + sediment)		
Water bodies with catchment sizes of up to 1 km^2 (n = 126)	14 (11.1)	112 (88.9)
Water bodies with catchment sizes of up to 10 km^2 (n = 273)	62 (22.7)	211 (77.3)
Type of surface water		
MIC_{SW}		
Freshwater systems (n = 1,257)	766 (60.9)	491 (39.1)
Estuarine systems (n = 95)	85 (89.5)	10 (10.5)
MIC_{SED}		
Freshwater systems (n = 173)	15 (8.7)	158 (91.3)
Estuarine systems (n = 41)	0 (0)	41 (100)
MICs (water + sediment)		
Freshwater systems (n = 1,430)	781 (54.6)	649 (45.4)
Estuarine systems (n = 136)	85 (62.5)	51 (37.5)

Table S3. The classification of RAC_{SW} and RAC_{SED} exceedance and compliance separated by the certainty that a MIC resulted from an agricultural non-point source (nps) entry.

Classification[a]	No. (%) of MICs below RAC	No. (%) of MICs above RAC
MIC_{SW}		
A definitive agricultural nps origin (n = 512) (37.9%)	225 (43.9)	287 (56.1)
Not a definitive agricultural nps origin[b] (n = 840) (62.1%)	626 (74.5)	214 (25.5)
MIC_{SED}		
A definitive agricultural nps origin (n = 69) (32.2%)	2 (2.9)	67 (97.1)
Not a definitive agricultural nps origin[b] (n = 145) (67.8%)	13 (9)	132 (91)
MICs (water + sediment)		
A definitive agricultural origin (n = 581) (37.1%)	227 (39.1)	354 (60.9)
Not a definitive agricultural nps origin[b] (n = 985) (62.9%)	639 (64.9)	346 (35.1)

a: In addition to the information on the origin of MICs provided in the studies, the classification was also on based on the land use of sampling locations, the insecticide compounds detected (e.g., some are exclusively registered for agricultural use), and the timing of sampling campaigns.

b: The classification "Not a definitive agricultural origin" does not necessarily mean that the MICs originated from non-agricultural sources (e.g., urban), as this classification often had to be applied due to the limited information provided in the studies.

Table S4. The occurrence of pesticide mixtures detected in water-phase samples of EU surface waters.

Samples analyzed for other pesticides and possible sample-related attribution: n = 516, including the following:	
Samples without (although sought) other pesticides: n = 54 (10.5%)	
Samples with at least one additional pesticide compound: n = 462 (89.5%), including the following:	
No. of pesticides per sample	**No. of samples**
2-5	291 (63%)
6-10	152 (32.9%)
11-13	19 (4.1%)
Samples not analyzed for other pesticides or no possible sample-related attribution[a]: n = 624, including the following:	
Samples not analyzed for other pesticides: n = 72	
Sample analyzed for other pesticides but for no possible sample-related attribution [a]: n = 547	
No information if sample was analyzed for other pesticides: n = 5	

a: Concentrations could not be allocated to specific samples due to missing information in the studies.

Table S5. An evaluation of MICs as a function of insecticides' authorization status under Reg. (EC) No. 1107/2009 (DG SANCO 2014).

	No. (%) of MICs below RAC	No. (%) MICs above RAC
MIC_{SW}		
Approved in the EU (n = 345)	223 (64.6)	122 (35.4)
Not approved in the EU (n = 1,007)	628 (62.4)	379 (37.6)
MIC_{SED}		
Approved in the EU (n = 46)	7 (15.2)	39 (84.8)
Not approved in the EU (n = 168)	8 (4.8)	160 (95.2)
MICs (water + sediment)		
Approved in the EU (n = 391)	230 (58.8)	161 (41.2)
Not approved in the EU (n = 1,175)	636 (54.1)	539 (45.9)

Table S6. A comparison of toxicity values and assessment factors (AFs) separated by the different regulatory risk assessment (RA) tiers used for the final RAC_{SW} derivation of insecticides.

Substance	RA tier	Toxicity value (µg/L)	AF	RAC_{SW} (µg/L)
Parathion-ethyl	Tier I	2.4	100	0.024
Parathion-methyl	Tier I	7.3	100	0.073
Carbofuran	Tier I	2.05	100	0.0205
Cyfluthrin	Tier I	0.68	100	0.0068
β-cyfluthrin	Tier I	0.068	100	0.00068
Fenvalerate	Tier I	0.22	100	0.0022
λ-cyhalothrin	Tier I	0.21	100	0.0021
Permethrin	Tier I	2.5	100	0.025
Acetamiprid	Tier I	5	10	0.5
Thiamethoxam	Tier I	14	5	2.8
Mean		3.443	81.5	0.345
Median		2.225	100	0.02225
Endosulfan	Higher tier	1.3	1	1.3
Azinphos-methyl	Higher tier	0.32	1	0.32
Chlorpyrifos	Higher tier	0.1	1	0.1
Diazinon	Higher tier	2.4	1	2.4
Malathion	Higher tier	5	4	1.25
Acrinathrin	Higher tier	0.026	3	0.0087
Bifenthrin	Higher tier	0.015	3	0.005
Cypermethrin	Higher tier	0.05	2	0.025
α-cypermethrin	Higher tier	0.015	1	0.015
Deltamethrin	Higher tier	0.0032	1	0.0032
Esfenvalerate	Higher tier	0.01	1	0.01
Imidacloprid	Higher tier	0.6	2	0.3
Thiacloprid	Higher tier	1.57	1	1.57
Mean		0.878	1.69	0.562
Median		0.1	1	0.1
Ratio between tier I and higher tier:				
Mean		**3.92**	**48.22**	**0.614**
Median		**22.25**	**100**	**0.2225**

Table S7. Quartile and median values of acute aquatic toxicity endpoints and environmental fate properties of all pesticides and pyrethroids (listed in the EU Pesticide Database (DG SANCO 2014)) and of the pesticides and pyrethroids listed on Annex I of the Regulation (EC) No. 1107/2009. The data for all pesticides are taken from Balderacchi and Trevisan (2010).

Parameter	**Pesticides**						**Pyrethroids**[a]					
	Annex I 25th percentile	Annex I median	Annex I 75th percentile	All 25th percentile	All median	All 75th percentile	Annex I 25th percentile	Annex I median	Annex I 75th percentile	All 25th percentile	All median	All 75th percentile
Fish acute LC_{50} (mg/L)	0.6	3.7	100	0.4	3.3	40	0.000155	0.00047	0.00275	0.00031	0.0025	0.0109
Daphnia acute EC_{50} (mg/L)	0.2	3.6	60.4	0.1	2.7	30.9	0.000125	0.0003	0.00073	0.0001175	0.000545	0.0073
Soil DT_{50} typical (d)	6	15	37	7	23	58	13	35	46.5	11.5	31	43
K_{OC} (ml/g)	76	380	2,000	100	502	3,015	53,060	121,786	156,625	9,500	100,000	156,250
Water solubility (mg/L)	3.5	63.8	2,638	1.5	30	945	0.00105	0.0045	0.01425	0.0012	0.009	0.2

a: Pyrethroids listed on Annex I of the Regulation (EC) No. 1107/2009: n = 13; all pyrethroids: n = 29, 14 not approved, 2 pending, 13 approved.

Table S8. The hazard-based cut-off criteria for human and environmental health, according to the new EU Regulation (EC) No. 1107/2009.

Human Health	**Environmental Health**
Carcinogen C1A & C1B	PBT (Persistent, Bioaccumulative, Toxic)
Mutagen M1A & M1B	POP (Persistent Organic Pollutant)
Toxic for reproduction R1A & R1B	vPvB (very Persistent, very Bioaccumulative)
Endocrine disruptor	Endocrine disruptor

Supporting Figures

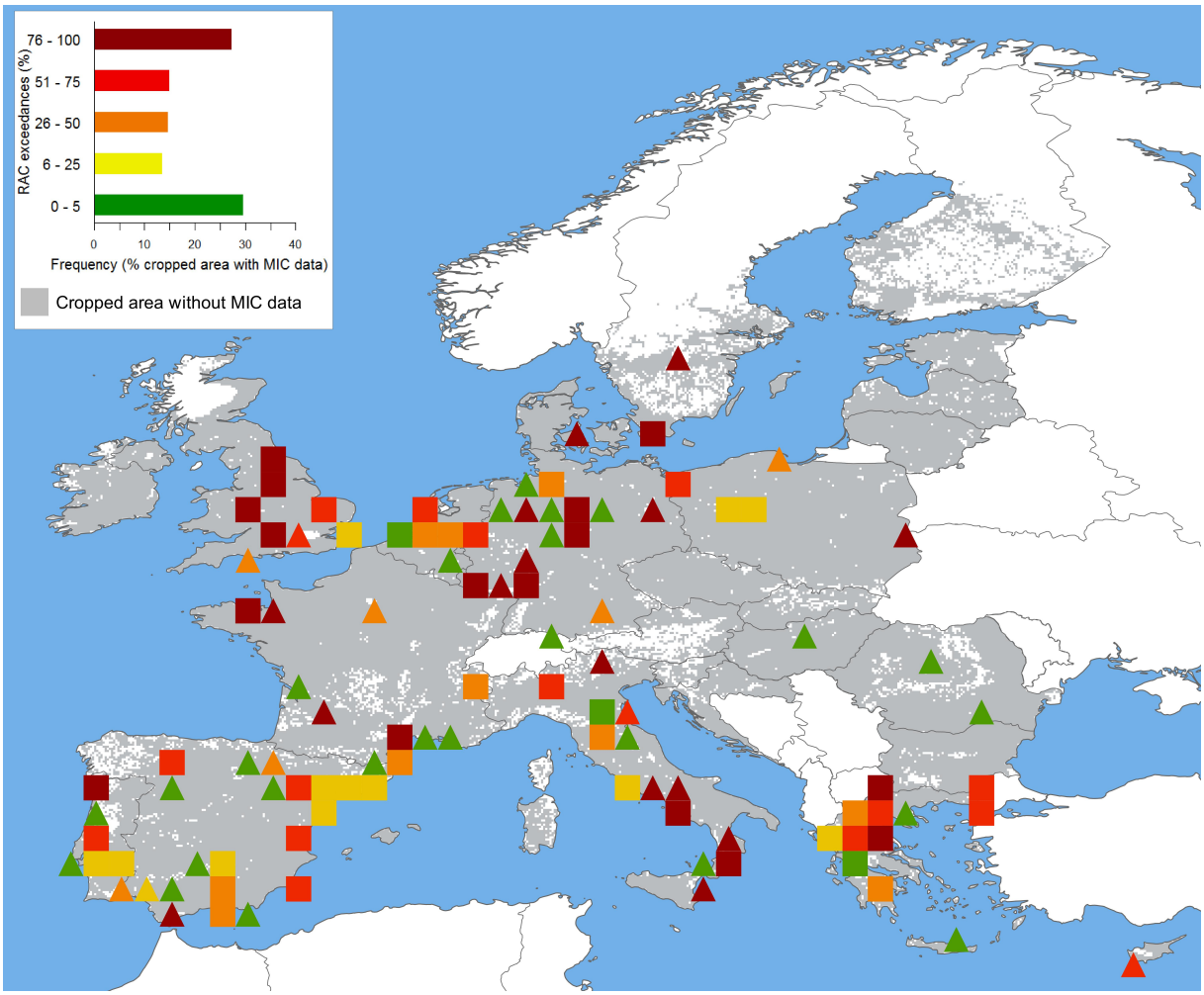

Fig. S1 The cropped areas in the EU (grey) and the distribution of regulatory acceptable concentration (RAC) exceedance rates for the reported measured insecticide concentrations (MICs, n = 1,471), aggregated in 1° grid cells. Information on insecticide surface water exposure was available for 16 EU member states and 0.2273 x 10^6 km^2 (19.84%, calculated on the basis of 1° grid cells) of the 1.1457 x 10^6 km^2 of European croplands. Rectangles represent subclassified cropped areas with five or more MICs, and triangles display grid cells with fewer than 5 MICs. Please note that 95 MICs could not be allocated to a specific grid cell due to the provision of imprecise location information in the studies. The horizontal bars in the legend illustrate the relative distributions of the respective insecticide RAC exceedance classes among the European cropped area with information on insecticide exposure. Modified after Stehle and Schulz (2015).

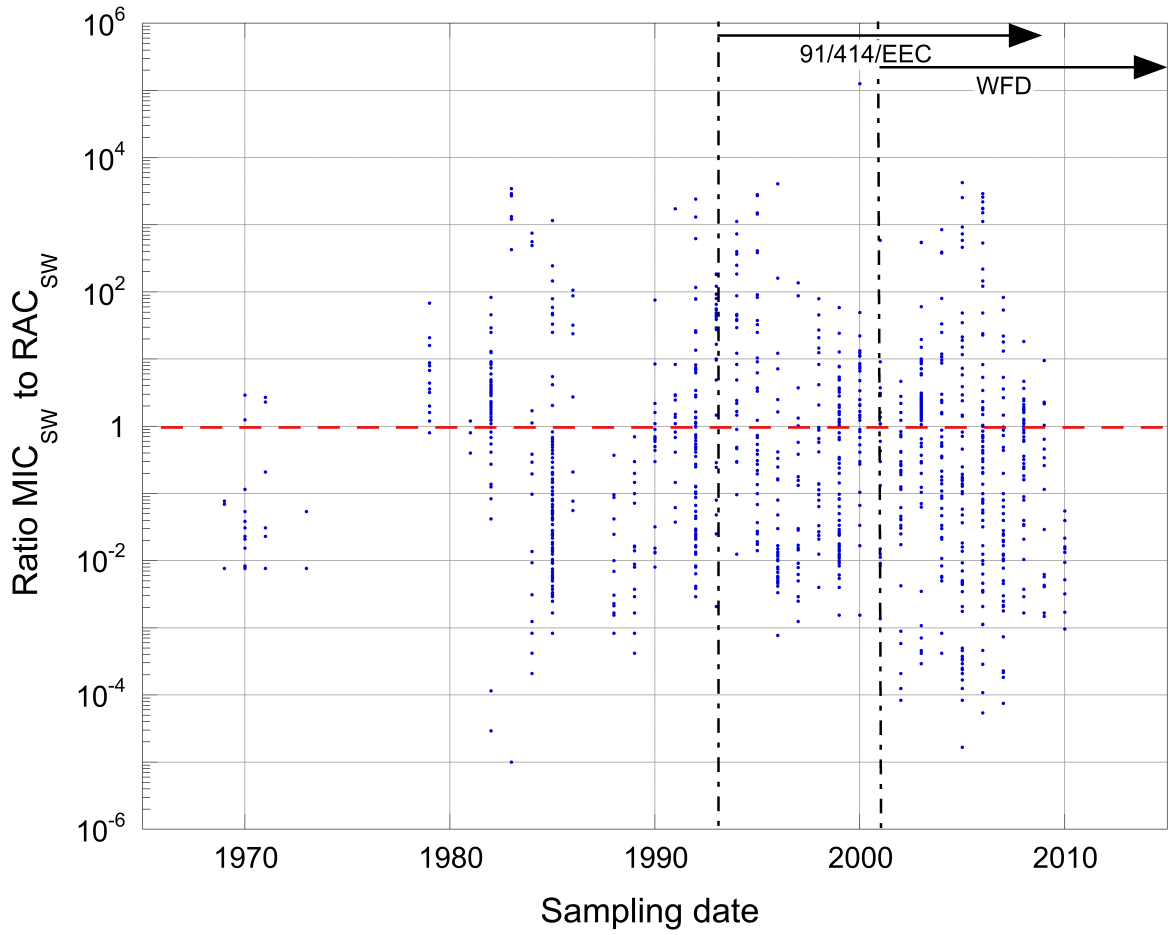

Fig. S2 Temporal evolution of MIC_{SW} to RAC_{SW} ratios (n = 1,263) and enforcement dates of major pesticide- and surface water-related EU legislations.

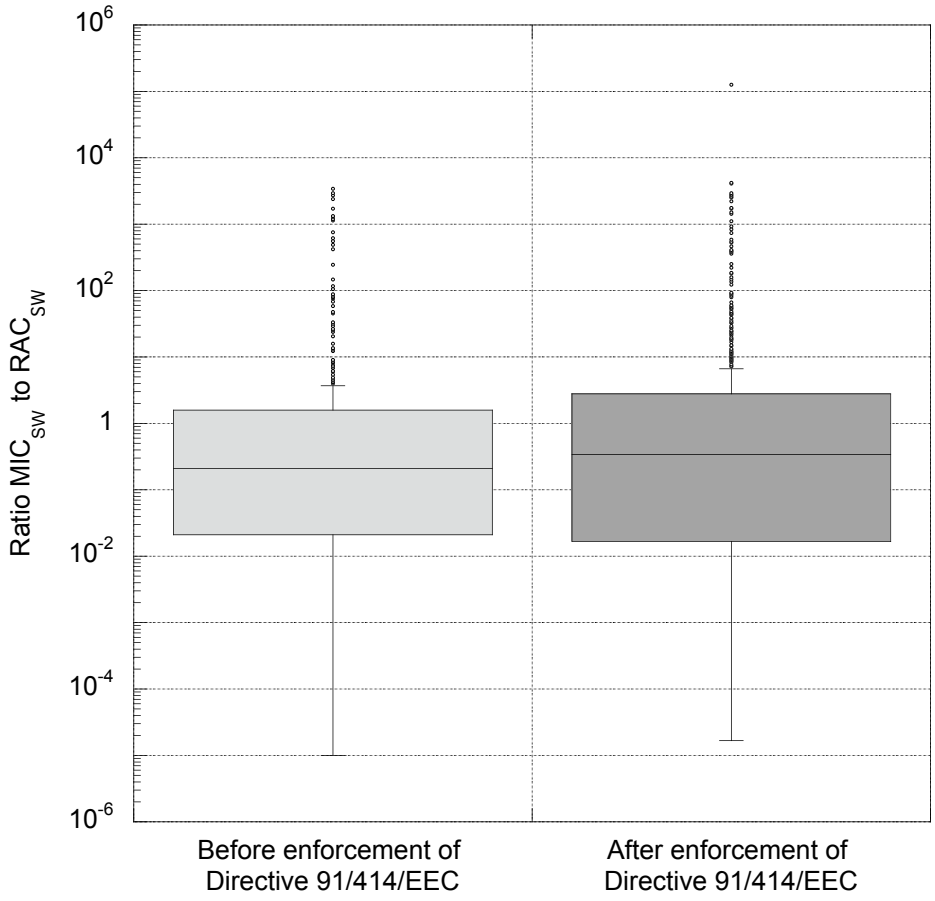

Fig. S3 Boxplots of MIC_{SW} to RAC_{SW} ratios reported for EU surface waters before (light grey) and after (dark grey) the enforcement of the EU pesticide Directive 91/414/EEC (1993; before enforcement: n = 476; mean: 48.83; median: 0.2083; after enforcement: n = 787; mean: 226.74; median: 0.3425)

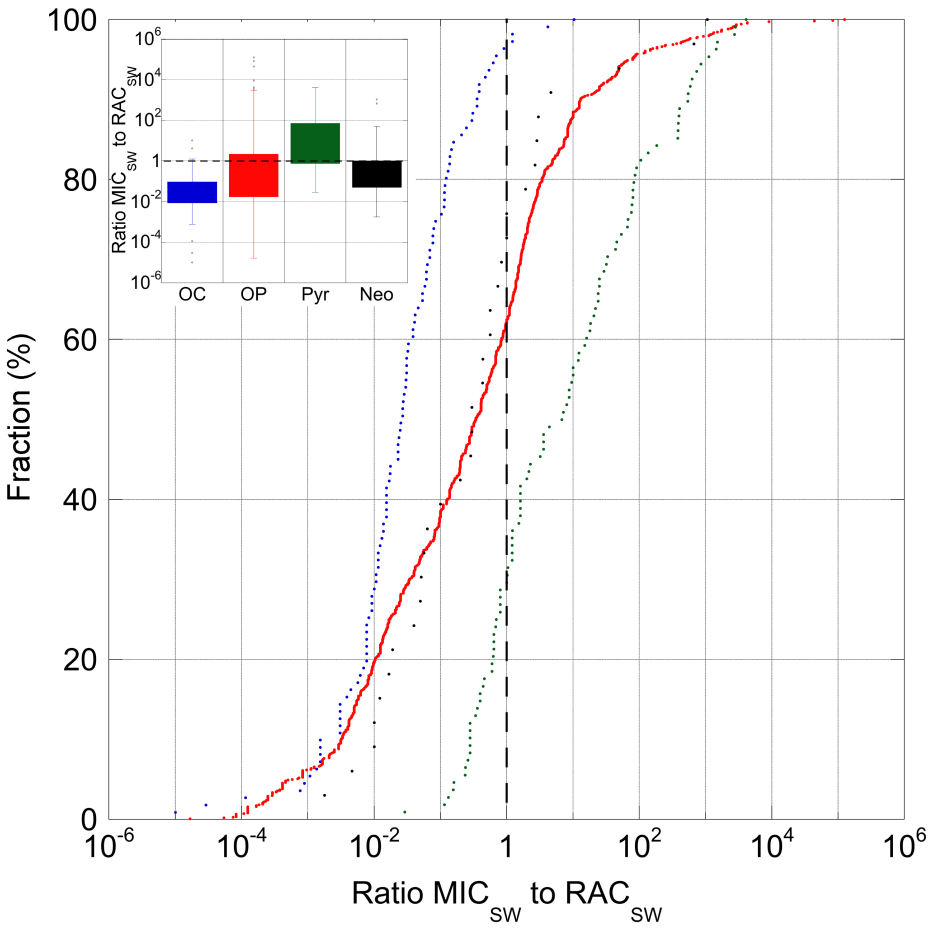

Fig. S4 Distribution curves for the MIC_{SW} of the different insecticide classes relative to substance-specific RAC_{SW}. Blue represents data obtained for organochlorine insecticides (OC; n = 111); red represents data for organophosphate insecticides (OP; n = 1,100); green represents data for pyrethroid insecticides (Pyr; n = 108); and black represents data for neonicotinoide insecticides (Neo; n = 33). The vertical dashed lines indicate the RAC_{SW}. The inlet shows the overall variation of the MIC_{SW} to RAC_{SW} ratios for the different insecticide classes

References

Balderacchi M, Trevisan M (2010) Comments on pesticide risk assessment by the revision of directive EU 91/414. Environ Sci Pollut Res 17:523-528

DG SANCO (2014) EU pesticides database. http://ec.europa.eu/sanco_pesticides/public/index.cfm2011. Accessed 08 March 2014

EFSA (2013) Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA J 11:3290 (186 pp)

FOCUS (2001) FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev.2

Stehle S, Schulz R (2015) Agricultural insecticides threaten surface waters at the global scale. PNAS 112:5750–5755

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Regulatory FOCUS Surface Water Models Fail to Predict Insecticide Concentrations in the Field

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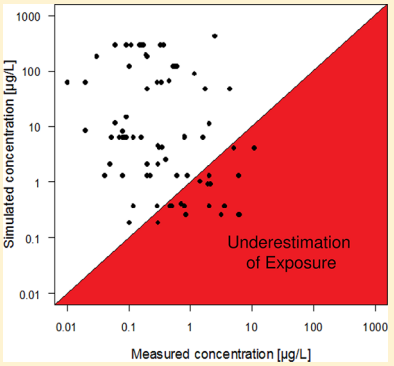
Supporting Information

ABSTRACT: The FOrum for the Co-ordination of pesticide fate models and their USe (FOCUS) exposure models are used to predict the frequency and magnitude of pesticide surface water concentrations within the European regulatory risk assessment. The predictions are based on realistic worst-case assumptions that result in predicted environmental concentrations (PEC). Here, we compared for the first time a larger data set of 122 measured field concentrations (MFC) of agricultural insecticides extracted from 22 field studies to respective PECs by using FOCUS steps 1−4. While FOCUS step 1 and 2 PECs generally overpredicted the MFCs, 23% of step 3 and 31% of step 4 standard PECs were exceeded by surface water MFCs, which questions the protectiveness of the FOCUS exposure assessment. Using realistic input parameters, step 3 simulations underpredicted MFCs in surface water and sediment by 43% and 78%, respectively, which indicate that a higher degree of realism even reduces the protectiveness of model results. The ratios between PEC and MFC in surface water were significantly lower for pyrethroids than for organophosphorus or organochlorine insecticides, which suggests that the FOCUS predictions are less protective for hydrophobic insecticides. In conclusion, the FOCUS modeling approach is not protective for insecticide concentrations in the field.



INTRODUCTION

The application of pesticides to agricultural areas can result in transport to adjacent nontarget environments. In particular, surface water systems are likely to receive agricultural pesticide input.[1] When insecticides enter aquatic environments, they may pose a substantial threat to the ecological integrity of surface water systems, as they are highly toxic to a wide range of aquatic organisms such as invertebrates and many fish species.[2,3] In the European Union (E.U.), the registration procedure (i.e., E.U. Directive 1107/2009)[4] for the authorization of new pesticides consists of an effect assessment, which is based on a variety of toxicity tests, and an exposure assessment, which relies on modeling, as usually no field data are available.[5] The FOrum for the Co-ordination of pesticide fate models and their USe (FOCUS) modeling approach[6] is used in the European Union to determine the predicted environmental concentration (PEC) in surface water and sediment and is intended to reflect the exposure levels of specific pesticide compounds under (realistic) worst-case conditions.

FOCUS step 1 is based on very simple assumptions and scenarios and accounts for extreme worst-case pesticide loading[6] without considering specific additional characteristics such as pesticide application time, crop type, or climate. Within step 2, sequential application patterns and pesticide degradation are taken into account in concert with regional or site-specific parameters such as crop interception and runoff. A static ditch with a water depth of 30 cm and a sediment layer of 5 cm is considered to be the model water body for both steps 1 and 2. In step 3, the FOCUS concept uses 10 realistic worst-case scenarios, which are assumed to cover approximately 33% of the total agricultural area in the European Union.[6] In addition, site-specific environmental parameters such as soil type, slope, climatic conditions (e.g., temperature and precipitation), and three different water bodies (i.e., pond, ditch, and stream) that are typical for each of the 10 scenarios are included. The step 3 exposure assessment uses mechanistic models to consider pesticide leaching via drainage,[7] surface runoff,[8] and spray drift as well as fate and transport processes in the respective water bodies.[9] FOCUS step 4 includes mitigation options with different levels of complexity[10] such as no-spray buffer zones or vegetated filter strips. The PECs in FOCUS step 1 and 2 play a minor role in the regulatory risk assessment of insecticides in the European Union. Of the 29 insecticides listed on Annex I of E.U. Directive 1107/2009[4] (for which the European Food Safety Authority risk assessment was publicly available), the risk estimation for 24 insecticide compounds was based on the FOCUS step 3 (four compounds) and step 4 (20 compounds) PEC calculations. The FOCUS surface water working group claims that the highest PEC in surface water (PEC_{sw}) estimates from the 10 scenarios would represent at least the 90th percentile (worst-case) for surface water exposures.[6]

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To the best of our knowledge, no study has compared a large number of pesticide field exposure data across a wide range of situations with the PECs derived from the complete FOCUS modeling approach. Hence, this study aimed to evaluate the PEC predictions by using measured pesticide concentrations from field studies.

In detail, we tested the following four hypotheses using 122 insecticide concentrations extracted from field monitoring studies:

(1) A maximum of 10% of the FOCUS step 3 PECs underestimate the measured field concentrations (MFCs).
(2) The calculated FOCUS PECs exhibit a high correlation with the measured insecticide concentrations in water and sediment. The degree of correlation improves from step 1 to step 4.
(3) The predictive capability of the FOCUS exposure model is similar across all insecticide substance classes.
(4) The PECs that resulted from step 3 simulations with realistic input data are lower than those resulting from FOCUS step 3 standard simulations, and the correlation of PECs with respective MFCs increased relative to FOCUS step 3 standard calculations.

MATERIALS AND METHODS

Selection of Insecticide Field Studies. The field studies (n = 22; Table S1, Supporting Information) that reported insecticide concentrations in lotic surface water resulting from agricultural non-point-source pollution (i.e., spray drift, edge-of-field runoff, drainage) were selected from the studies listed in a review by Schulz[11] and from multiple literature databases (i.e., ISI Web of Science, BIOSIS Previews, CAB Abstracts). Only studies containing detailed information on site-specific parameters regarding climate, landscape characteristics, agricultural pesticide use, crop conditions, and entry routes were selected for the simulation of PECs in the surface water and the sediment. Five organophosphorus insecticides that are important in terms of global application rates,[12] and the organochlorine insecticide endosulfan were included in this study. Furthermore, 10 pyrethroid compounds were considered in this analysis, as pyrethroids are one of the most important types of modern insecticides.[13,14] The selected substances are shown in Table S2 (Supporting Information). If multiple insecticide concentrations were reported in a publication, only the peak concentrations that originated from different entry events were classified as separate events; therefore, multiple concentrations in one publication can be regarded as independent. In these investigations, insecticide concentrations were measured in three European countries (France, Germany, and Italy), the United States, South Africa, and Argentina between 1995 and 2007. The respective water bodies were comparably small; that is, their catchment sizes ranged from 0.1 to 700 km^2. The majority of water bodies (approximately 90%) had catchment areas <190 km^2.

Overview of FOCUS Model Calculations. All of the insecticide concentrations that were extracted from field studies (as described above) were compared to PEC calculations using the tiered FOCUS surface water approach in accordance with E.U. Directive 1107/2009. In detail, the PEC values were derived from FOCUS step 1, 2, 3, and 4 calculations (see Table 1 and FOCUS surface water report[6]), which were also calculated within the exposure assessment in the regulatory pesticide registration. These PEC calculations were designated as FOCUS standard calculations.

Table 1. Overview of FOCUS Tiers and Their Characteristics Used for Comparison with Actual Field Data[a]

FOCUS tier	models used	characteristic	adaptations made
step 1 standard	FOCUS steps 1 and 2	extreme worst-case	no
step 2 standard	FOCUS steps 1 and 2	worst-case	no
step 3 standard	SWASH[b]	realistic worst-case	no
step 3 realistic[c]	SWASH[b]	realistic	yes
step 4 standard	SWAN	realistic worst-case	no

[a]See text for details. [b]Includes PRZM, MACRO, and TOXSWA. [c]FOCUS calculations using appropriate step 3 scenarios and information from actual insecticide monitoring field studies.

In addition to the standard FOCUS simulations, step 3 calculations were also performed by adapting the model input data to the actual field conditions; these calculations were designated as FOCUS realistic calculations. FOCUS steps 1−2 model version 1.1[6] was used to calculate the tier 1 and tier 2 PECs in surface water and sediment. FOCUS step 3 standard and realistic simulations were performed by use of MACRO version 4.3b,[7] PRZM version 3.2.1b,[8] and TOXSWA version 2.1.3.[9] These different models are integrated into the SWASH shell version 3.1.2.[6] Step 4 calculations were made with SWAN version 1.1.3[15] by taking the mitigation options into account (see below for details on all calculations).

Input Parameters for PEC Calculations Using FOCUS. *FOCUS Standard Scenarios (Steps 1−4).* FOCUS exposure calculations rely on several input parameters related to pesticides, applications, crop type, climate, and landscape.[6] The input parameters for the steps and their sources are provided in Table 2. If no crop type was specified in a field study, the crops commonly grown in the specific study region and for which the use of the particular insecticide was permitted were selected. If several crops were cultivated in an agricultural area where a field study was conducted, then multiple FOCUS PEC calculations were performed with all possible crop and scenario combinations. Therefore, a total of approximately 250 step 1 and 2 FOCUS calculations, as well as approximately 1200 step 3 and 4 calculations, were conducted, and the maximum PECs (n = 122 cases) were subsequently compared to the actual insecticide concentrations that have been measured in the field (see Data Analysis section for details). If the field concentrations were measured at specific time periods after distinct entry events (28 out of 122 cases), then to account for degradation and downstream losses, this aspect were also considered instead of simply using the maximum PECs for comparison with MFCs.

FOCUS Step 3 Realistic Calculations. FOCUS step 3 realistic calculations were performed by use of all available realistic field study information regarding insecticide use patterns, climatic conditions, landscape, and water body characteristics (see also Table S4, Supporting Information). If the reported field conditions differed from the FOCUS scenario assumptions, then the standard parameters and scenario conditions of the FOCUS model were adjusted.

Table 2. Description and Source of FOCUS Input Parameters

category	relevant FOCUS step	parameter	source[a]
physicochemical insecticide properties[b]	steps 1−3	K_{OC}, DT_{50}, water solubility, etc.	Footprint Pesticide Property Database[16] according to FOCUS[6] or from E.U. registration documents[17]
application data[c]	steps 1−4	application rate,[d] number and interval of applications, application timing	E.U. registration documents according to GAP;[17] U.S. RED documents[18]
scenario	step 2	northern or southern Europe	selected according to field study information
scenario	step 3	D1−D6, R1−R4[e]	selected according to field study information
cultivated crops	steps 1−3	maize, cereals, fruit crops, etc.	selected according to field study information
water body	step 3	ditch, stream	selected according to field study information
mitigation option[c]	step 4	no-spray buffer zone, vegetated filter strip	GAP from E.U. registration documents;[17] U.S. RED documents[18]

[a]GAP, good agricultural practice; RED, registration eligibility decision. [b]All insecticide parameters used for FOCUS modeling are given in Table S2 (Supporting Information). [c]For field studies conducted in the European Union, information was taken from E.U. registration documents or producer product labeling. For field studies conducted elsewhere and for European studies where no other source was available, information was taken from U.S. RED documents. [d]Application rates used are given in Table S3 (Supporting Information). [e]D1−D6 are the standard drainage scenarios implemented in FOCUS step 3 for different locations in Europe, and R1−R4 are the standard runoff scenarios.

For the field studies that reported surface runoff as an insecticide exposure pathway, insecticide application was simulated as a granular application to exclude spray drift as an entry route for the PEC calculations. The study information on insecticide application patterns were included in FOCUS calculations via the application definition section from the FOCUS SWASH program, which selects the application dates within a user-defined application window.[6] The exact application dates were included in the MACRO, PRZM, and TOXSWA input files if the time interval between the application date and the precipitation events was clearly identifiable in the field monitoring studies.

The landscape and water body characteristics (e.g., field size, slope, distance between field and water body), which affect the drainage or runoff inputs, were included in the PRZM and MACRO input files after the project definition in SWASH. Furthermore, user-defined water bodies were included in the SWASH database for simulation of the insecticide fate and transport in TOXSWA. To this end, the individual hydraulic characteristics of the respective water bodies were extracted from the publications. The available temperature or precipitation data (as reported in field studies) were included in the PRZM or MACRO climatic input files and were considered in TOXSWA by defining new site-specific scenarios. Details on FOCUS step 3 realistic calculation adaptations are shown in Table S4 (Supporting Information). Changes in the application scenario (e.g., application rate; $n = 5$) were applied to 19 of the 22 field study simulations. More realistic climate data were available for 13 studies. Characteristics from the water body (e.g., water body width) and the surrounding agricultural areas (e.g., field size) were used to realistically simulate the insecticide concentration levels from 11 field studies.

The final PEC comparisons (resulting from FOCUS step 3 realistic calculations with MFCs) were also based on the maximum PEC values. However, in accordance with the PEC comparisons that resulted from the standard calculations, the actual field concentrations (measured at a specific date after a relevant entry event) were also compared to step 3 realistic PECs, which were calculated for these specific data (surface water $n = 15$; sediment $n = 13$) to account for the degradation process, the insecticide fate, and the downstream loss.

Data Analysis. Generally, the maximum PECs were compared with the respective MFCs if multiple PECs were available from the FOCUS calculations for one event, that is, when different crops or scenarios were regarded as potentially relevant for the respective field conditions. The effects of different insecticide substance classes (i.e., organophosphate, organochlorine, pyrethroid) and water body size [i.e., water body width <1 m, water body width >1 m (up to ca. 4.5 m), or unknown water body size; Supporting Information] on the ratio of simulated to measured concentration (PEC divided by MFC) were analyzed by two separate single-factor analysis of variance (ANOVA) tests followed by Tukey's honestly significant differences (HSD) post hoc test for pairwise multiple comparisons. The numerical data (PEC/MFC ratio) used in the ANOVA tests were transformed ($\ln[x]$) prior to the statistical analysis to satisfy the assumption of normally distributed residuals and homogeneity of variance. All statistical analyses and graphics were made with the open-source software package R (www.r-project.org), version 2.11.1.[19]

RESULTS

Comparison between MFC and PEC from FOCUS Standard Scenarios (Steps 1−4). Figure 1 shows the relationship between PECs and MFCs in surface water ($n = 77$) and sediment ($n = 45$). A comparison of FOCUS step 1 PECs and MFCs showed that the sediment and water MFCs were generally overpredicted up to 32 000 times (median: 10^2) (Figure 1a, Table 3). Only 4% of the simulated water concentrations underestimated the real concentrations. All of the PEC in sediment (PEC_{sed}) estimates from FOCUS step 1 were higher than the measured sediment concentrations. In FOCUS step 2 assessments, most of the PEC_{sw} and PEC_{sed} values were higher than the field concentrations (Figure 1b, Table 3). However, 13% of the sediment and 14% of the water predictions underestimated the respective MFCs up to 15 times, while the median concentrations showed a general overestimation of 13 and 35 times in sediment and water, respectively (Figure 1b, Table 3). Most (77%) of the simulated water concentrations resulting from step 3 were greater than the concentrations detected in the field, with a median PEC to MFC factor greater than 10. However, 23% of the PEC_{sw} values underestimated the insecticide field concentrations (by more than 10 times in 4% of cases) in water. In addition, 42% of all simulated FOCUS step 3 sediment concentrations underestimated the MFC in sediment (MFC_{sed}) (Table 3), while the median values coincided comparably well (Figure 1c). For step 4 calculations, approximately a third (i.e., 31%) of the simulated water concentrations underestimated the field concentrations and 6.5% were underestimated by more than 10 times. In

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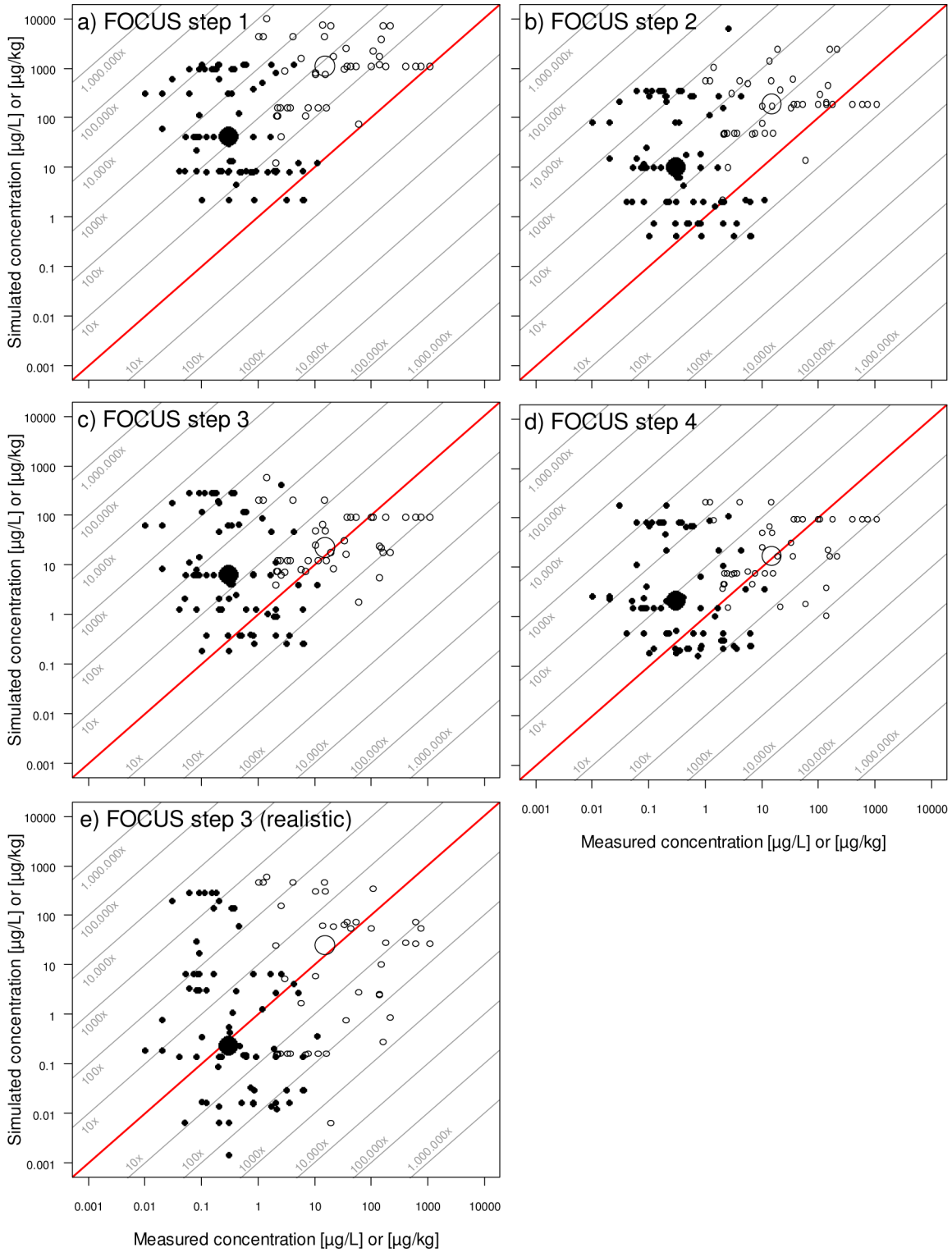

Figure 1. Relationship between simulated and measured insecticide concentrations for FOCUS standard scenarios and FOCUS step 3 realistic calculations using information from field studies. (●) Water (n = 77); (○) sediment (n = 45); larger circles, overall medians. The 45° line denotes identity between PEC and MFC. The gray lines indicate over- and underestimation by orders of magnitude. The simulated concentrations are displayed on the y-axis so that the MFC overestimations are plotted above the 45° line.

addition, 49% of all PEC_{sed} values calculated by step 4 underestimated the MFC_{sed} values by up to 130 times (Figure 1d, Table 3).

We also found that the underestimation rate for MFC in surface water (MFC_{sw}) is even higher (33.3% of FOCUS step 3 PEC_{sw} exceedances instead of 23% for complete data; Table 3) when the evaluated data set is restricted to only the E.U. data. In addition, Figure 1 clearly shows that there is no obvious relationship between the simulated and measured insecticide concentrations for all of the FOCUS steps.

Furthermore, our analysis showed that, in all of the FOCUS standard steps, the pyrethroids (n = 17) had significantly lower

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Table 3. Over- and Underprediction and Adequately Matching Data for FOCUS Standard and Realistic Simulations[a]

	surface water		sediment	
FOCUS tiers	overprediction (PEC > MFC), %	underprediction (PEC < MFC), %	overprediction (PEC > MFC), %	underprediction (PEC < MFC), %
step 1	96	4	100	0
step 2	86	14	87	13
step 3	77	23	58	42
step 3 (realistic)[b]	57	43	22	78
step 4	69	31	51	49

[a]PEC, predicted environmental concentration; MFC, measured field concentration. [b]FOCUS calculations using appropriate step 3 scenarios and information from insecticide field studies.

ratios of PEC to MFC and thus higher levels of real-world data underestimation than the organophosphates (n = 55) and the organochlorines (n = 5) (organochlorine−pyrethroid step 4, p = 0.02; all other p < 0.001, see Supporting Information, Figure S1); however, there was no significant difference between organochlorines and organophosphates.

Comparison between MFC and PEC from FOCUS Step 3 Realistic. A considerable proportion of all calculated FOCUS step 3 realistic PECs underestimated MFCs for water (43%) and sediment (78%) (Table 3, Figure 1e). Approximately 26% of PEC_{sw} and 51% of PEC_{sed} values were more than 10 times lower in FOCUS step 3 realistic simulations than the MFCs (Figure 1e). In addition, 12% of PEC_{sw} and 7% of PEC_{sed} cases exceeded the MFCs by more than 100 times (Figure 1e).

DISCUSSION

Protectiveness of FOCUS Predictions. Generally, the degree of conservatism should decrease from FOCUS steps 1 to 4, which is in agreement with our results comparing PEC and MFC values. Consequently, the percentage of insecticide MFCs in surface water that exceed the PECs increased from 4% for step 1 to 31% for step 4 (Figure 1, Table 3).

FOCUS[6] states that uncertainty will always prevail "to some degree in environmental risk assessment"; however, the use of the FOCUS scenarios as part of the E.U. registration process "provides a mechanism for assessing pesticide PECs in surface water and sediment with an acceptable degree of uncertainty". For several reasons, our study results question whether the degree of uncertainty of the regulatory exposure model outcomes generated by the FOCUS is acceptable. First, 23% of PEC_{sw} and 42% of PEC_{sed} values that resulted from step 3 calculations underpredicted the corresponding MFCs. This rejects our first hypothesis, which states that a maximum of 10% of the calculated FOCUS step 3 PECs would underestimate the field data. The ≤10% exceedance value had also been hypothesized as a quality threshold by the FOCUS working group.[6] A similar situation holds true for FOCUS step 4 results, as almost a third of the PEC_{sw} values underpredicted the insecticide MFCs (Table 3). This result is remarkable when it is considered that FOCUS step 4 is the most realistic standard tier available in European regulatory exposure modeling and is almost exclusively used in risk assessment for insecticides currently registered in the European Union. In addition, this is the first study demonstrating that the field concentrations of insecticides can even exceed the FOCUS step 1 (surface water) and 2 (surface water and sediment) PECs (Figure 1, Table 3).

Overall, these results indicate that the FOCUS modeling approach is not reliable in predicting insecticide concentrations when compared to real-world surface water situations. This result also means that unacceptable ecological effects could arise from agricultural insecticide uses, which are not assessed by the regulatory risk assessment.[20] The fact that we are not aware of this situation is somewhat surprising, given Hendley's[21] claim in 2003 that monitoring initiatives should be performed and used explicitly for exposure model validation within a so-called "moditoring" approach.

In addition to model inaccuracies (see below), the underestimation of insecticide field concentrations by the respective PECs might also be attributed to farmers' malpractice during the insecticide application, for example, nonadherence to no-spray buffer zones. However, this malpractice would not explain the 23% underestimation of MFC_{sw} values resulting from FOCUS step 3 calculations, as this step does not include any pesticide application restrictions for farmers (e.g., no-spray buffer zones). Consequently, this suggests that a theoretical maximum of only 8% (i.e., the difference between 23% and 31% underestimations of MFCs in steps 3 and 4, respectively) of cases in which FOCUS step 4 PEC_{sw} underestimates the MFC_{sw} could be attributed to farmers' malpractice. Nevertheless, it is possible that farmers do not adhere to the required application rates.

Generally, it can be argued that the FOCUS modeling approach is valid only for the pesticide registration process in the European Union and respective European agricultural settings, so that an evaluation of the FOCUS PECs should include only the insecticide concentrations measured within the European Union. However, comparison of step 3 PEC_{sw} to MFC_{sw} values (derived only from E.U. studies) showed that eight of 24 (33.3%) field concentrations were underestimated, which is higher than the average of 23% derived from the global data (Figure 1, Table 3). This result clearly indicates that the FOCUS models also failed to predict protective insecticide field concentrations for conditions in Europe.

Quality of FOCUS Predictions. Predicted concentrations should be protective,[6] and the exposure model simulations should also provide some degree of realistic estimates of field concentrations, that is, there should ideally be a close relationship between measured and predicted concentrations. However, the results of our study show that the number of matches between predicted and measured concentrations was generally low. If a difference between predicted and measured concentrations of ±10% is regarded as adequate,[6,22] up to 6% of step 2 PECs in surface water and 9% of step 3 PECs in sediment matched the MFCs. In total, 97.7% of the step 3 PECs were not within ±10% of the MFCs. Even when the performance threshold is set at ±30% to account for uncertainties in the field measurements, 92.6% of step 3 PECs did not match the MFCs in surface water and sediment. In contrast to our second hypothesis, Figure 1 shows that there is no positive relationship in terms of a statistically significant

slope >0 in a linear regression model between predicted and measured concentrations. For all FOCUS steps, the data points form a rectangular cluster that spans several orders of magnitude on both axes. The complete absence of a relationship between the predicted and measured data highlights the importance of the inherent FOCUS model restrictions. This model weakness appears instrumental in the results of our study and needs to be urgently addressed rather than focusing only on the problems associated with farming practices (discussed above). In addition, the relationship did not improve from FOCUS step 1 to step 4 (Figure 1).

The low quality of FOCUS predictions, as described here, is in contrast to the results derived from a series of test runs using FOCUS step 3 models and scenarios in which generally good (although not quantified) agreement between predicted and measured concentrations in drainflow and runoff had been declared by the FOCUS group.[6] However, only a few field studies have compared predicted environmental concentrations and measured field data. For example, Padovani and Capri[23] showed that the PECs derived from TOXSWA 1.2 (used in Dutch registration process) accurately predicted the measured pesticide concentrations that resulted from spray drift input, as measured and predicted concentrations were below the detection limit in almost all cases. Furthermore, Singh and Jones[24] demonstrated that the U.S. Environmental Protection Agency (EPA) PRZM model provides a "reasonable estimate" of the edge-of-field chemical runoff (n = 17), as the simulated data were within an order of magnitude of the measured data. In addition, Jackson et al.[25] compared predicted pesticide concentrations (n = 40) in drinking water reservoirs (calculated with the U.S. EPA's pesticide exposure models, FIRST and PRZM/EXAMS) with the monitoring data and found a general overestimation of field concentrations by several orders of magnitude. Until now, no studies have compared the actual field concentrations of pesticides in more than 40 cases. Hence, the study presented here with n = 122 from 22 different field studies is the largest study to evaluate the FOCUS approach.

Although FOCUS steps 3 and 4 are regarded as sophisticated, higher-tier pesticide exposure calculations, several inherent restrictions and model weaknesses exist, which may partly explain the PEC calculation inaccuracies. First, the pesticide exposure resulting from the upstream fields is integrated in a too-simplified manner, as a constant additional pesticide loading of 20% irrespective of upstream conditions is assumed. A further important model weakness is the absence of hourly weather data. The standard daily runoff fluxes calculated by PRZM are translated to hourly data by assuming a peak runoff rate of 2 mm/h. For example a 16 mm daily runoff event translates into an eight hour runoff loading of 2 mm/h,[6] although it is possible that during heavy rainfall events, a large proportion of the 16 mm daily runoff occurs in a considerably shorter time period. This pragmatic translation may not realistically reflect the peak pesticide concentrations,[26] particularly during extreme rainfall events.[27] Moreover, the fact that surface water exposure caused by runoff and drainage entries cannot be simulated simultaneously by the FOCUS model is unrealistic and may result in an underestimation of the field concentrations.[28] Even if the PEC_{sed} generally plays a minor role in regulatory risk assessment due to the lack of adequate sediment toxicity data for benthic organisms, note that the simplified assumptions underlying FOCUS PEC_{sed} calculations (i.e., identical sediment layer properties across all step 3 scenarios) could result in high uncertainties.

Evaluation of Factors Influencing PEC to MFC Ratios. Our results show that for low (i.e., < 0.5 μg/L) water-phase insecticide field concentrations, the PECs are higher than the MFCs in all of the FOCUS standard steps (Figure 1a–d). The reason for this dicrepancy is that most of the MFC_{sw} were compared to initial PEC_{sw} values, although the latter most likely did not represent the peak concentrations that are commonly detected when an event-triggered sampling is used.[20,27] This explanation is corroborated by Figure 2, which shows that 50%

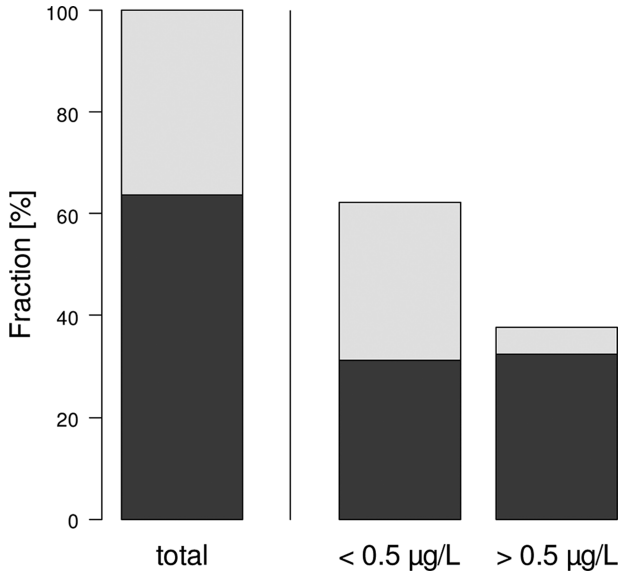

Figure 2. Fraction of insecticide surface water concentrations that were detected by event-related sampling (black bars) for all (n = 77) concentrations as well as for concentrations <0.5 μg/L (n = 48) and >0.5 μg/L (n = 29). Gray bars denote non-event-related sampling. See also Supporting Information for sampling details of individual field studies.

of the 48 MFC_{sw} values below 0.5 μg/L were obtained via an event-related sampling approach, which was the case for 86% of the 29 insecticide concentrations >0.5 μg/L. This result suggests that the field concentrations represented by the MFC_{sw} values used here are still lower than the concentrations present in the field. Consequently, the degree to which the FOCUS PECs underestimate the MFCs could be considerably higher. When only the field concentrations that were measured by event-triggered sampling are analyzed, a much higher number (i.e., 18 of 49 MFC_{sw}; 37%) of field concentrations were underestimated by step 3 PEC_{sw}.

Our third hypothesis (that the predictive capability of the FOCUS modeling approach is similar for all substance classes) was not confirmed by our analysis. Compared to organochlorines and organophosphates, highly toxic pyrethroids had significantly lower ratios of PEC_{sw} to MFC_{sw} for all FOCUS standard steps. Although the sample size for this analysis is rather low for organochlorines, this suggests that the FOCUS model particularly underpredicted the pyrethroid MFCs in surface water. This result is remarkable, as over the past decades pyrethroids have become increasingly important agricultural insecticides.[29] Generally, synthetic pyrethroids are highly hydrophobic and characterized by low water solubility and have high organic carbon–water partitioning coefficient (K_{OC}) values, which lead to a rapid and strong sorption to soil and sediment in the environment.[30,31] Luo and Zhang[32] stated that

PRZM is known to inadequately predict the pesticide transport associated with soil erosion. This assertion may explain the underestimation of insecticide PECs arising from runoff entries for strongly sorbing pyrethroids, as the pesticides associated with eroded soils are removed only from the uppermost soil compartment.[33] In addition, Jones and Mangels[34] list several PRZM deficiencies (e.g., overestimation of downward movement, underestimation of pesticide persistence in soil) that could also lead to the underestimation of field concentrations.

As the K_{OC} value is a key input parameter for exposure modeling, in addition to data used that were published in the Footprint Pesticide Property Database,[16] we recalculated the PECs with the K_{OC} values from EPISUITE 4.1[35] for the substances for which K_{OC} values showed a large variance. However, we detected only small differences in the amount of surface water underestimation in step 1 (from 4% to 5%) and for the sediment in step 3 (from 42% to 44%). In addition, we found no significant differences between the PEC/MFC ratios calculated with K_{OC} values from EPISUITE 4.1 and the Footprint Pesticide Property Database (Supporting Information). Furthermore, we recalculated the PEC values for bifenthrin and fenvalerate using the degradation half times (DT_{50}) for soil from the American Crop Protection Association (ARS) Pesticide Properties Database,[36] which differed considerably from the Footprint[16] values; however, we found no change in the amount of overestimation or underestimation for the FOCUS realistic calculations (Supporting Information). Therefore, we concluded that the model outcome for the investigated substances was insensitive to the range of reported K_{OC} values and half-lives. Note that the experimental K_{OC} values for strongly hydrophobic substances might be biased toward having particularly low values due to the lack of complete phase separation during the experimental setup. A detailed sensitivity analysis is needed to clarify the general influence of physicochemical substance properties on model outcomes.

Evaluation of FOCUS Realistic Simulations. The FOCUS surface water working group notes that the scenarios used in the E.U. pesticide registration process "do not mimic specific fields, and nor are they necessarily representative of the agriculture at the location or the Member State after which they are named. (...) crops or situations have been adjusted with the intention of making the scenario more appropriate to represent a realistic worst-case for a wider area".[6] To overcome this generalizing nature of the FOCUS standard scenarios, we performed realistic FOCUS step 3 calculations using all site and insecticide use characteristics available from scientific field studies. The results of FOCUS step 3 realistic calculations showed that, with these adaptations, 43% (instead of 23%) of calculated PEC_{sw} and PEC_{sed} values underestimated the MFCs (Figure 1, Table 3). The substitution of worst-case assumptions by real-world data in step 3 realistic calculations explains the generally lower PECs compared to step 3 standard calculations (Figure 1). Realistic step 3 PEC values underestimate the MFCs to a larger extent, despite the use of more realistic (i.e., lower) application rates, which suggests that the emission rates are not a likely cause of our overall study results.

Overall, our fourth hypothesis (stating that the PECs resulting from step 3 realistic calculations are lower than the PECs resulting from step 3 standard calculations) was confirmed by our results. More importantly, the relationship between the PEC and the MFC did not improve by using more realistic entry data for step 3. Again, this result indicates that the FOCUS modeling approach is most likely due to an inappropriate mechanistic representation of the relevant processes not capable of predicting the actual field exposure levels.

In conclusion, our study clearly revealed the need for further targeted modification and calibration of the central processes of the FOCUS exposure models. It appears that further testing is necessary to investigate factors that may potentially influence the model outcomes and to reassess the adequacy of the model input variables (see Blenkinsop et al.[37] for development of alternative FOCUS climate scenarios). Beyond that, our data provide evidence to recommend a further safety or assessment factor for the exposure side of pesticide risk assessment to address the current uncertainties, unless it is clearly demonstrated with sufficient probability that all of the possible field exposures are covered by regulatory models. If we continue to use the current FOCUS scenarios to assess the exposure of insecticides, then FOCUS step 1 data should be used, or FOCUS step 3 or step 4 results must be accompanied by a general safety factor of about 10 to consider the claims originally made when the FOCUS models were implemented.

■ ASSOCIATED CONTENT

Supporting Information

Additional text, four tables, and two figures with information on selected field studies and modeling input parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Schwarzenbach, R. P.; Escher, B. I.; Fenner, K.; Hofstetter, T. B.; Johnson, C. A.; von Gunten, U.; Wehrli, B. The challenge of micropollutants in aquatic systems. *Science* **2006**, *313*, 1072−1077.

(2) Brock, T., Alix, A., Brown, C. D., Capri, E., Gottesbüren, B., Heimbach, F., Lythgo, C., Schulz, R., Streloke, M., Eds. *Linking Aquatic Exposure and Effects: Risk Assessment of Pesticides*; CRC Press: Boca Raton, FL, 2009.

(3) Schäfer, R. B.; Von Der Ohe, P.; Kühne, R.; Schüürmann, G.; Liess, M. Occurrence of 331 organic pollutants in four rivers of North Germany between 1994 and 2004 and risk assessment for algae, invertebrates and fish. *Environ. Sci. Technol.* **2011**, *45*, 6167−6174.

(4) European Commission (EC) Regulation 1107/2009 of the European Parliament and the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Off. J. Eur. Union* **2009**, *309*, 1−50.

(5) Adriaanse, P. I.; Allen, R.; Gouy, V.; Hollis, J. M.; Hosang, J.; Jarvis, T.; Klein, M.; Layton, R.; Linders, J.; Schäfer, H.; Smeets, L.; Yon, D. Surface water models and European Union registration of plant protection products. *Final report of the work of the regulatory*

modelling working group on surface water models of FOCUS (FOrum for the Co-ordination of pesticide fate models and their USe), 1997.
(6) FOCUS. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. *Report of the FOCUS working group on surface water scenarios*, EC Document Reference SANCO/4802/2001-rev.2, 2001.
(7) Jarvis, N. J. The MACRO model (version 4.3). Technical description. http://www-mv.slu.se/bgf/Macrohtm/macro43b/TechMacro43.pdf.
(8) Carsel, R. F.; Imhoff, J. C.; Hummel, P. R.; Chaplick, J. M.; Donigian, A. S. *PRZM-3, A model of predicting pesticide and nitrogen fate in the crop root and unsaturated soil zones: User manual for release 3.0.*; GA30605-2720; National Exposure Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency: Athens, GA, 1998.
(9) Adriaanse, P. I.; Beltman, W. H. J. *Transient water flow in TOXSWA model (FOCUS versions); concepts and mathematical description*; WOt-rapport No. 101; Statutory Research Tasks Unit for Nature and the Environment, Wageningen, The Netherlands, 2009.
(10) FOCUS. Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. *Report of the Focus Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment*; EC Document Reference SANCO/10422/2005 v2.0, 2007.
(11) Schulz, R. Field studies on exposure, effects and risk mitigation of aquatic nonpoint-source insecticide pollution - A review. *J. Environ. Qual.* **2004**, *33*, 419−448.
(12) Gianessi, L.; Reigner, N. Pesticide use in U.S. crop production: 2002 with comparison to 1992 & 1997; Washington, DC, 2006.
(13) Adam, O.; Degiorgi, F.; Crini, G.; Badot, P. M. High sensitivity of *Gammarus* sp. juveniles to deltamethrin: Outcomes for risk assessment. *Ecotoxicol. Environ. Saf.* **2010**, *73*, 1402−1407.
(14) Amweg, E. L.; Weston, D. P.; Ureda, N. M. Use and toxicity of pyrethroid pesticides in the Central Valley, California, USA. *Environ. Toxicol. Chem.* **2005**, *24*, 966−972.
(15) ECPA; Tessella Support services plc. Surface water assessment enabler (SWAN) v.1.1.4, dd. 27 March 2008. Supported Tool Versions: MACRO shell, 4.4.2; PRZM shell, 2.6; TOXSWA shell, 2.5; 2008.
(16) The FOOTPRINT Pesticide Properties Database; The Agricultural & Environmental Research Unit (AERU) at the University of Hertfordshire, Hatfield, Herts, U.K., 2010; http://sitem.herts.ac.uk/aeru/footprint/en/index.htm.
(17) DG SANCO. E.U. Pesticide Database, 2008; http://ec.europa.eu/sanco_pesticides/public/index.cfm.
(18) U.S. EPA. Pesticide Registration Status, 2011; http://www.epa.gov/opp00001/reregistration/status.htm.
(19) R Development Core Team. R: A language and environment for statistical computing, reference index version 2.11.1; www.r-project.org (May 31, 2011)
(20) Schäfer, R. B.; Ohe, P. V. D.; Rasmussen, J.; Kefford, J. B.; Beketov, M.; Schulz, R.; Liess, M. Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environ. Sci. Technol.* **2012**, *46*, 5134−5142.
(21) Hendley, P. Advances in validation of environmental exposure model predictions for regulatory purposes. In *Chemistry of crop protection*; Voss, G., Ramos, G., Eds.; Wiley−VCH Verlag: Weinheim, Germany, 2003.
(22) U.S. EPA. Model accuracy and uncertainty. Memorandum, 1988; http://www.epa.gov/region7/air/nsr/nsrmemos/modelau.pdf.
(23) Padovani, L.; Capri, E. Chlorpyrifos-methyl dissipation in a small adjacent water body following application to citrus. *Chemosphere* **2005**, *58*, 1219−1229.
(24) Singh, P.; Jones, R. L. Comparison of pesticide root zone model 3.12: Runoff predictions with field data. *Environ. Toxicol. Chem.* **2002**, *21*, 1545−1551.
(25) Jackson, S.; Hendley, P.; Jones, R.; Poletika, N.; Russell, M. Comparison of regulatory method estimated drinking water exposure concentrations with monitoring results from surface drinking water supplies. *J. Agric. Food Chem.* **2005**, *53*, 8840−8847.
(26) Mackay, N. Capabilities and limitations of models. In *Linking aquatic exposure and effects: Risk assessment of pesticides*; Brock, T., Alix, A., Brown, C., Capri, E., Gottesbüren, B., Heimbach, F., Lythgo, C., Schulz, R., Streloke, M., Eds.; CRC Press: Boca Raton, FL, 2009.
(27) Schulz, R. Rainfall-induced sediment and pesticide input from orchards into the Lourens River, Western Cape, South Africa: importance of a single event. *Water Res.* **2001**, *35*, 1869−1876.
(28) Schottler, S. P.; Eisenreich, S. J.; Capel, P. D. Atrazine, alachlor and cyananzine in a large agricultural river system. *Environ. Sci. Technol.* **1994**, *28*, 1079−1089.
(29) Hendley, P., Weston, D. P., Gan, J., Spurlock, F., Eds. *Synthetic pyrethroids: Occurrence and behavior in aquatic environments*; ACS Symposium Series *991*; American Chemical Society: Washington, DC, 2008.
(30) Domagalski, J. L.; Weston, D. P.; Zhang, M. H.; Hladik, M. Pyrethroid insecticide concentrations and toxicity in streambed sediments and loads in surface waters of the San Joaquin Valley, California, USA. *Environ. Toxicol. Chem.* **2010**, *29*, 813−823.
(31) Hill, I. R. Aquatic organisms and pyrethroids. *Pestic. Sci.* **1989**, *27*, 429−465.
(32) Luo, Y. Z.; Zhang, M. H. Environmental modeling and exposure assessment of sediment-associated pyrethroids in an agricultural watershed. *Plos ONE* **2011**, *6*, No. e15794.
(33) U.S. EPA. Pesticide Root Zone model (PRZM) release note, 2012; http://www.epa.gov/ceampubl/gwater/przm3/prz3reln.html.
(34) Jones, R. L.; Mangels, G. Review of the validation of models used in federal insecticide, fungicide, and rodenticide act environmental exposure assessments. *Environ. Toxicol. Chem.* **2002**, *21*, 1535−1544.
(35) *Estimation Programs Interface Suite for Microsoft Windows, v 4.10*. U.S. Environmental Protection Agency, Washington, DC, 2012.
(36) Agricultural Research Service (ARS). Pesticide Properties Database, 2012; http://www.ars.usda.gov/Services/docs.htm?docid=14199
(37) Blenkinsop, S.; Fowler, H. J.; Dubus, I. G.; Nolan, B. T.; Hollis, J. M. Developing climatic scenarios for pesticide fate modelling in Europe. *Environ. Pollut.* **2008**, *154*, 219−231.

Supporting Information for:

Regulatory FOCUS Surface Water Models Fail to Predict Insecticide Concentrations in the Field

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Table S1. Field studies (n = 22) selected for comparison between measured and simulated insecticide concentrations (n = 122) in agricultural surface waters and characteristics of insecticide exposure measured in the field.

Reference	Country	Insecticide compounds	Entry pathway	Sampling interval	Comparis-ons of PEC & MFC	Analytical method	LOD / LOQ (µg/L or µg/kg)	Analytical recovery (%)	Range of LOD or LOQ / MFC
Anderson et al. (2006)[1]	USA	permethrin chlorpyrifos esfenvalerate, λ-cyhalothrin	runoff	daily	11[a] / 3[b]	GC/ECD ELISA GC/ECD GC/ECD	- / - 0.05 / -[a] - / - - / -	-	- 0.02-0.96[a] - -
Anderson et al. (2002)[2]	USA	chlorpyrifos, diazinon	runoff	monthly	12[a] / 0[b]	ELISA	0.08 / -[a] 0.03 / -[a]	-	0.22-1.3[a] 0.15-1[a]
Berenzen et al. (2005)[3]	Germany	parathion	runoff	event	3[a] / 0[b]	GC/ECD, GC/MS	0.05 / -[a]	97-99[a]	0.17-1[a]
Black et al. (2000)[4]	USA	endosulfan	nonpoint source	single	0[a] / 1[b]	GC/ECD	- / 1.0[b]	-	0.71[b]
Capri et al. (2005)[5]	Italy	chlorpyrifos	runoff, spray drift	1h - 2d	2[a] / 0[b]	GC/NPD	- / 0.05[a]	77.4-106.6[a]	0.14-0.16[a]
Dabrowski et al. (2006)[6]	South Africa	azinphos-methyl	runoff, spray drift	event	3[a] / 3[b]	GC/ECD, GC/NPD, GC/FPD	0.01 / -[ab]	79-106[ab]	< 0.01[ab]
Dabrowski et al. (2002)[7]	South Africa	azinphos-methyl, chlorpyrifos, endosulfan, deltamethrin	runoff	event	9[a] / 0[b]	GC/ECD, GC/NPD, GC/FPD	0.01 / -[a]	79-106[a]	0.02[a] 0.05[a] 0.01[a] 0.03-1[a]
Domagalski et al. (2010)[8]	USA	bifenthrin cyfluthrin cypermethrin, esfenvalerate permethrin	runoff	event	0[a] / 17[b]	GC/MS	- / 2.2[b] - / 2[b] - / 2.6[b] - / 2.1[b] - / 1[b]	97.4[b] 82.3[b] 86.6[b] 82.5[b] 92.9[b]	0.14-1[b] 0.29-0.95[b] 0.46[b] 0.72[b] 0.07-1[b]
Gormley et al. (2005)[9]	USA	azinphos-methyl	runoff	daily	1[a] / 0[b]	-	-	-	-
Jergentz et al. (2004)[10]	Argentina	endosulfan	nonpoint source	event	0[a] / 1[b]	GC/ECD, GC/FPD	2 / -[b]	-	0.1[b]

PEC: Predicted Environmental Concentration; MFC: Measured Field Concentration; LOD: Limit of Detection; LOQ: Limit of Quantification;
[a]: in surface water; [b]: in sediment

Table S1. (continued)

Reference	Country	Insecticide compounds	Entry pathway	Sampling interval	Comparis-ons of PEC & MFC	Analytical method	LOD / LOQ (µg/L or µg/kg)	Analytical recovery (%)	Range of LOD or LOQ / MFC
Jergentz et al. (2005)[11]	Argentina	cypermethrin chlorpyrifos	runoff	event	2[a] / 1[b]	GC/ECD, GC/FPD	0.05 / -[a] 0.01 / -[a]; 2 / -[b]	-	0.07[a] 0.02[a]; 0.15[b]
Liess et al. (1999)[12]	Germany	parathion fenvalerate	runoff	event	12[a] / 0[b]	GC/ECD, GC/MS	- / 0.02[a] -/ 0.1[a]	-	< 0.01-0.5[a] 0.02-0.12[a]
Marino and Ronco (2005)[13]	Argentina	chlorpyrifos cypermethrin	spray drift, runoff	event	10[a] / 12[b]	HPLC, GC/ECD	0.00001 / -[ab]	-	< 0.01[ab]
Neumann et al. (2002)[14]	Germany	parathion fenvalerate	runoff	event	2[a] / 0[b]	GC/NPD, GC/MS	0.1-0.5 / -[a]	-	-
Padovani and Capri (2005)[15]	Italy	chlorpyrifos-methyl	spray drift	event	1[a] / 0[b]	GC/MS	- / 0.05[a]	-	0.625[a]
Poissant et al. (2008)[16]	Canada	chlorpyrifos	runoff	event	1[a] / 0[b]	GC/MS	0.03 / -[a]	-	0.5[a]
Schäfer et al. (2008)[17]	France	endosulfan	runoff	event	0[a] / 1[b]	GC/MS	- / 0.125[b]	-	< 0.01[b]
Schulz (2003)[18]	South Africa	azinphos-methyl	runoff	event	1[a] / 0[b]	GC/ECD, GC/NPD, GC/FPD	- / 0.01[a]	79-106[a]	0.5[a]
Schulz (2005)[19]	Germany	parathion fenvalerate	runoff	event	2[a] / 0[b]	GC/ECD, GC/MS	- / 0.01-0.05[a]	-	-
Smalling et al. (2007)[20]	USA	chlorpyrifos bifenthrin, tau-fluvalinate	runoff	event/ weekly	0[a] / 3[b]	GC/MS	- / 0.6-7.9[b]	80-120[b]	-
Suess et al. (2006)[21]	Germany	β-cyfluthrin parathion	spray drift	weekly	2[a] / 0[b]	GC/MS, LC/MS/MS	- / 0.05[a]	70-110[a]	0.12-0.6[a]
Wan et al. (2006)[22]	Canada	chlorpyrifos endosulfan diazinon	runoff	event	3[a] / 3[b]	GC/ECD, GC/MS	- / 0.1[a]; - / 30[b] - / 0.1[a]; - / 10[b] - / 0.01[a]; - / 20[b]	89[a]; 107[b] 93[a]; 104[b] 100[a]; 81[b]	5[a]; 0.2[b] 0.3[a]; 0.07[b] < 0.01[a]; 0.57[b]

PEC: Predicted Environmental Concentration; MFC: Measured Field Concentration; LOD: Limit of Detection; LOQ: Limit of Quantification;
[a]: in surface water; [b]: in sediment

Table S2. Insecticides parameters used for FOCUS modeling. Physicochemical data were taken from the FOOTPRINT pesticide database[23].

		Azinphos-methyl		Bifenthrin		Chlorpyrifos[a]		Clorpyrifos-methyl	
	Unit	Value	Note	Value	Note	Value	Note	Value	Note
Molar mass	g/mol	317.32		422.88		350.89		322.53	
Saturated vapour pressure	mPa	5.00E-04	at 25°C	0.0178	at 25°C	1.43	at 25°C	3	at 25°C
Molar enthalpy of vaporisation	J/mol	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default
Solubility in water	mg/L	28	at 20°C	0.001	at 20°C	1.05	at 20°C	2.74	at 20°C
Molar enthalpy of dissulution	J/mol	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default
Diffusion coefficient in water	m²/d	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default
Diffusion coefficient in air	m²/d	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default
Koc	L/kg	1000		236610		8151.31		4645	
Freundlich exponent		0.9	default	0.9	default	0.9	default	1.28	
Ref. Concentration in liquid phase	g/m ³	1	FOCUS default	1	FOCUS default	1	FOCUS default	1	FOCUS default
Factor for the uptake by plant roots in soil		0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default
Wash-off factor from crop	1/mm	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default
Half-life time water	d	50	aqueous hydrolysis[b]	1000	default	21	aqueous hydrolysis[b]	21	aqueous hydrolysis[b]
Half-life time soil	d	10		26		74	at 20°C	3	
Half-life time sediment	d	1000	default	251	system	51		14	system
Half-life time crop	d	10	FOCUS default	10	FOCUS default	10	FOCUS default	10	FOCUS default
Activation energy	J/mol	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default
Exponent	1/K	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default
Q10 factor		2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured at pF		2	FOCUS default	2	FOCUS default	2	FOCUS default	2	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured ar moisture content	%	100	FOCUS default	100	FOCUS default	100	FOCUS default	100	FOCUS default
Use bi-phase degradation	y/n	n	FOCUS default	n	FOCUS default	n	FOCUS default	n	FOCUS default

[a]: Data were taken from the European review report

[b]: FOCUS requires the water phase only $DegT_{50}$ from water-sediment studies as water DT_{50} but the aqueous hydrolysis value were taken in the most cases to represent worst case

Table S2. (continued)

		Cyfluthrin		β-Cyfluthrin		λ-Cyhalothrin		Cypermethrin[a]	
	Unit	Value	Note	Value	Note	Value	Note	Value	Note
Molar mass	g/mol	434.3		434.29		449.85		416.3	
Saturated vapour pressure	mPa	0.0003	at 25°C	0.000056	at 25°C	0.0002	at 25°C	0.00023	at 25°C
Molar enthalpy of vaporisation	J/mol	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default
Solubility in water	mg/L	0.0066	at 20°C	0.0012	at 20°C	0.005	at 20°C	0.009	at 20°C
Molar enthalpy of dissulution	J/mol	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default
Diffusion coefficient in water	m²/d	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default
Diffusion coefficient in air	m²/d	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default
Koc	L/kg	64300		64300		157000		26492	
Freundlich exponent		1.1		0.9	default	1.1		1	
Ref. Concentration in liquid phase	g/m ³	1	FOCUS default	1	FOCUS default	1	FOCUS default	1	FOCUS default
Factor for the uptake by plant roots in soil		0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default
Wash-off factor from crop	1/mm	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default
Half-life time water	d	215	aqueous hydrolysis[b]	215	aqueous hydrolysis[b]	1000	default	3	
Half-life time soil	d	33		13		25		60	
Half-life time sediment	d	8	system	3	system	12	system	17	system
Half-life time crop	d	10	FOCUS default	10	FOCUS default	10	FOCUS default	10	FOCUS default
Activation energy	J/mol	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default
Exponent	1/K	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default
Q10 factor		2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured at pF		2	FOCUS default	2	FOCUS default	2	FOCUS default	2	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured ar moisture content	%	100	FOCUS default	100	FOCUS default	100	FOCUS default	100	FOCUS default
Use bi-phase degradation	y/n	n	FOCUS default	n	FOCUS default	N	FOCUS default	n	FOCUS default

[a]: Data were taken from the European review report

[b]: FOCUS requires the water phase only $DegT_{50}$ from water-sediment studies as water DT_{50} but the aqueous hydrolysis value were taken in the most cases to represent worst case

Table S2. (continued)

		Deltamethrin		Diazinon		α-Endosulfan[a]		β-Endosulfan[a]	
	Unit	Value	Note	Value	Note	Value	Note	Value	Note
Molar mass	g/mol	505.2		304.35		406.93		406.93	
Saturated vapour pressure	mPa	0.0000124	at 25°C	11.97	at 25°C	1.05E+00	at 25°C	0.138	at 25°C
Molar enthalpy of vaporisation	J/mol	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default
Solubility in water	mg/L	0.0002	at 20°C	60	at 20°C	0.41		0.23	at 20°C
Molar enthalpy of dissulution	J/mol	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default
Diffusion coefficient in water	m²/d	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default
Diffusion coefficient in air	m²/d	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default
Koc	L/kg	10240000		643		7969		8612	
Freundlich exponent		1.1		1.02		0.9	default	0.9	default
Ref. Concentration in liquid phase	g/m ³	1	FOCUS default	1	FOCUS default	1	FOCUS default	1	FOCUS default
Factor for the uptake by plant roots in soil		0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default
Wash-off factor from crop	1/mm	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default
Half-life time water	d	17	water phase only	138	aqueous hydrolysis[b]	19		10.7	
Half-life time soil	d	13		9.1		37		37	
Half-life time sediment	d	65	system	10.4	system	21	system	21	system
Half-life time crop	d	10	FOCUS default	10	FOCUS default	10	FOCUS default	10	FOCUS default
Activation energy	J/mol	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default
Exponent	1/K	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default
Q10 factor		2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured at pF		2	FOCUS default	2	FOCUS default	2	FOCUS default	2	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured ar moisture content	%	100	FOCUS default	100	FOCUS default	100	FOCUS default	100	FOCUS default
Use bi-phase degradation	y/n	n	FOCUS default	n	FOCUS default	n	FOCUS default	n	FOCUS default

[a]: Data were taken from the European review report
[b]: FOCUS requires the water phase only $DegT_{50}$ from water-sediment studies as water DT_{50} but the aqueous hydrolysis value were taken in the most cases to represent worst case

Table S2. (continued)

		Esfenvalerate		Fenvalerate		Parathion		Permethrin	
	Unit	Value	Note	Value	Note	Value	Note	Value	Note
Molar mass	g/mol	419.9		419.9		291.3		391.3	
Saturated vapour pressure	mPa	0.0000012	at 25°C	0.0192	at 25°C	0.89	at 25°C	0.002	at 25°C
Molar enthalpy of vaporisation	J/mol	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default	95000	FOCUS default
Solubility in water	mg/L	0.001	at 20°C	0.001	at 20°C	12.4	at 20°C	0.2	at 20°C
Molar enthalpy of dissulution	J/mol	5300	FOCUS default	27000	FOCUS default	27000	FOCUS default	27000	FOCUS default
Diffusion coefficient in water	m²/d	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default	4.30E-05	FOCUS default
Diffusion coefficient in air	m²/d	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default	0.43	FOCUS default
Koc	L/kg	5300		5273		7660		100000	
Freundlich exponent		1.07	default	0.96		0.95		0.99	
Ref. Concentration in liquid phase	g/m ³	1	FOCUS default	1	FOCUS default	1	FOCUS default	1	FOCUS default
Factor for the uptake by plant roots in soil		0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default	0.5	FOCUS default
Wash-off factor from crop	1/mm	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default	0.05	FOCUS default
Half-life time water	d	10	aqueous hydrolysis[b]	115	aqueous hydrolysis[b]	260	aqueous hydrolysis[b]	31	aqueous hydrolysis[b]
Half-life time soil	d	44		40		49		13	
Half-life time sediment	d	71	system	1000	default	4.3	system	40	system
Half-life time crop	d	10	FOCUS default	10	FOCUS default	10	FOCUS default	10	FOCUS default
Activation energy	J/mol	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default	65400	FOCUS default
Exponent	1/K	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default	0.0948	FOCUS default
Q10 factor		2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default	2.58	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured at pF		2	FOCUS default	2	FOCUS default	2	FOCUS default	2	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default	0.7	FOCUS default
Half-life measured ar moisture content	%	100	FOCUS default	100	FOCUS default	100	FOCUS default	100	FOCUS default
Use bi-phase degradation	y/n	n	FOCUS default	n	FOCUS default	n	FOCUS default	n	FOCUS default

[a]: Data were taken from the European review report
[b]: FOCUS requires the water phase only $DegT_{50}$ from water-sediment studies as water DT_{50} but the aqueous hydrolysis value were taken in the most cases to represent worst case

Table S2. (continued)

		Tau-fluvalinate	
	Unit	Value	Note
Molar mass	g/mol	502.9	
Saturated vapour pressure	mPa	9.00E-08	at 25°C
Molar enthalpy of vaporisation	J/mol	95000	FOCUS default
Solubility in water	mg/L	0.00103	at 20°C
Molar enthalpy of dissulution	J/mol	27000	FOCUS default
Diffusion coefficient in water	m²/d	4.30E-05	FOCUS default
Diffusion coefficient in air	m²/d	0.43	FOCUS default
Koc	L/kg	639154	
Freundlich exponent		0.9	
Ref. Concentration in liquid phase	g/m ³	1	FOCUS default
Factor for the uptake by plant roots in soil		0.5	FOCUS default
Wash-off factor from crop	1/mm	0.05	FOCUS default
Half-life time water	d	22.5	aqueous hydrolysis[b]
Half-life time soil	d	4	
Half-life time sediment	d	48	system
Half-life time crop	d	10	FOCUS default
Activation energy	J/mol	65400	FOCUS default
Exponent	1/K	0.0948	FOCUS default
Q10 factor		2.58	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default
Half-life measured at pF		2	FOCUS default
Exponent for the effect of water content		0.7	FOCUS default
Half-life measured ar moisture content	%	100	FOCUS default
Use bi-phase degradation	y/n	n	FOCUS default

[a]: Data were taken from the European review report
[b]: FOCUS requires the water phase only $DegT_{50}$ from water-sediment studies as water DT_{50} but the aqueous hydrolysis value were taken in the most cases to represent worst case

Table S3. Insecticide application rates used for modelling

Reference	Insecticide compounds	Total application rate per season (kg active ingredient /ha)[a]
Anderson et al. (2006)[1]	permethrin	0.8968
	chlorpyrifos	1.1209
	esfenvalerate	0.448
	λ-cyhalothrin	0.03
Anderson et al. (2002)[2]	chlorpyrifos	7.846
	diazinon	2.242
Berenzen et al. (2005)[3]	parathion	0.225
Black et al. (2000)[4]	endosulfan	1.6812
Capri et al. (2005)[5]	chlorpyrifos	0.248
Dabrowski et al. (2006)[6]	azinphos-methyl	5.044
Dabrowski et al. (2002)[7]	azinphos-methyl	5.044
	chlorpyrifos	2.242
	endosulfan	2.6898
	deltamethrin	0.084
Domagalski et al. (2010)[8]	bifenthrin	0.1
	cyfluthrin	0.045
	cypermethrin	0.672
	esfenvalerate	0.224
	permethrin	1.792
Gormley et al. (2005)[9]	azinphos-methyl	2.5218
Jergentz et al. (2004)[10]	endosulfan	0.782
Jergentz et al. (2005)[11]	cypermethrin	0.336
	chlorpyrifos	3.36
Liess et al. (1999)[12]	parathion	0.225
	fenvalerate	0.045
Marino and Ronco (2005)[13]	chlorpyrifos	3.36
	cypermethrin	0.448
Neumann et al. (2002)[14]	parathion	0.225
	fenvalerate	0.045
Padovani and Capri (2005)[15]	chlorpyrifos-methyl	1.238
Poissant et al. (2008)[16]	chlorpyrifos	8.406
Schäfer et al. (2008)[17]	endosulfan	0.525
Schulz (2003)[18]	azinphos-methyl	5.0439
Schulz (2005)[19]	parathion	0.225
	fenvalerate	0.045
Smalling et al. (2007)[20]	chlorpyrifos	10.0878
	bifenthrin	0.3363
	tau-fluvalinate	0.3362
Suess et al. (2006)[21]	β-cyfluthrin	0.045
	parathion	0.9
Wan et al. (2006)[22]	chlorpyrifos	1.6812
	endosulfan	0.784
	diazinon	2.242

[a] For field studies conducted in the EU, information was taken from EU registration documents or producer product labelling. For field studies conducted elsewhere and for European studies where no other source was available, information was taken from US RED documents.

Table S4. Information about adaptations made for FOCUS step 3 realistic calculations

Ref-erence	Climate	Landscape and water body	Application
1	Only irrigation[a]	Water body width; additional ditch scenario	-
2	Only irrigation[a]	Water body width; additional ditch scenario	-
2	Specific precipitation events included	-	Application rate; granular application[b]
4	Selection of specific climate scenario	-	-
5		Water body width; base flow; distance between water body and crop	Application rate; specific spray deposition rates[c]
6	Specific precipitation events included	Water body width; base flow; size upstream catchment; distance between water body and crop	Application rate; specific spray deposition rates[c]
7	Specific precipitation events included	-	Granular application[b]
8	Only irrigation[a]	-	Granular application[b]
9	-	-	Granular application[b]
10	Location specific climatic scenario included	Water body width and depth	Granular application[b]
11	Location specific climatic scenario included	-	Granular application[b]
12	-	-	Application rate; granular application[b]
13	Location specific climatic scenario included	-	Specific application dates as mentioned in field study
14	-	-	Granular application[b]
15	-	Water body width and length; size upstream catchment; base flow; distance between water body and crop	Application rate; specific spray deposition rates[c]

[a]: No precipitation in summer months but periodical irrigation
[b]: granular application to exclude spray drift as runoff was the relevant entry route
[c]: specific spray deposition rates for different distances from edge of field to water body for spray drift entries included

Table S4. (continued)

Reference	Climate	Landscape and water body	Application
16	-	-	Granular application[b]
17	-	Water body width; base flow	Granular application[b]
18	Specific precipitation events included	Water body width; base flow	Granular application[b]
19	Specific precipitation events included	Water body width; base flow	Granular application[b]
20	Only irrigation[a]	-	-
21	-	Water body width; base flow; distance between water body and crop	Specific spray deposition rates[c]
22		Water body width	Granular application[b]

[a]: No precipitation in summer months but periodical irrigation
[b]: granular application to exclude spray drift as runoff was the relevant entry route
[c]: specific spray deposition rates for different distances from edge of field to water body for spray drift entries included

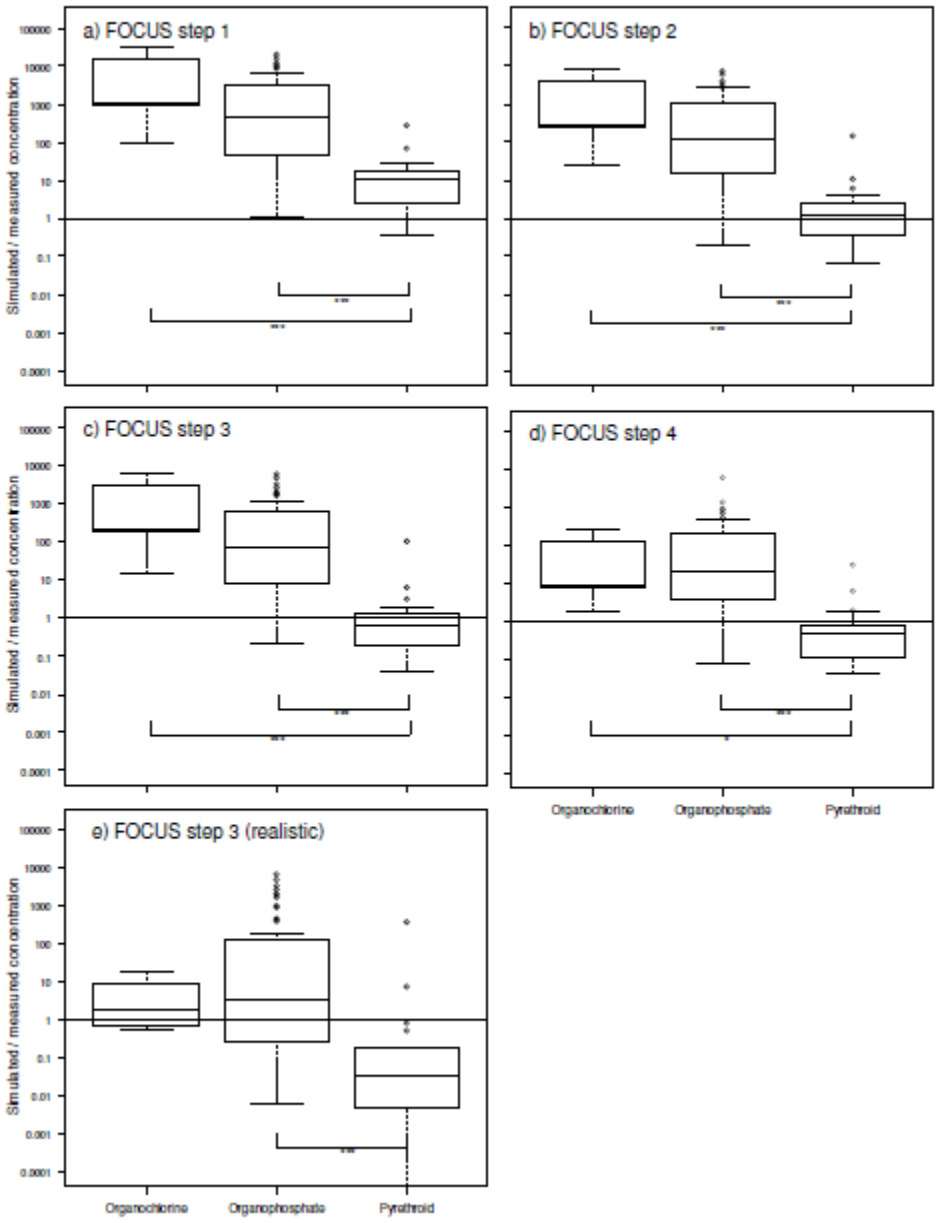

Fig. S1. Boxplots of simulated to measured concentration ratios in the water phase for different insecticide classes for all FOCUS steps; (organochlorine: n = 5, organophosphate: n = 55, pyrethroids: n = 17). Asterisks indicate significant differences (ANOVA, Tukey's HSD post hoc test; ***: $p < 0.001$; **: $p < 0.01$; *: $p < 0.05$).

Text S1. Influence of water body size on the ratio between simulated and measured concentrations

Although the FOCUS surface water group declared that the TOXSWA model is only valid for small water bodies,[28] our analysis showed that there was no significant difference in the ratio between simulated and measured concentrations for different water body sizes (< 1m compared to those > 1m and < 4.5 m). However, due to the low sample size (n = 6) the power of this analysis is quite low. Although exact widths were often not available, the vast majority (approximately 90%) of investigated water bodies were rather small as indicated by their catchment sizes so that the FOCUS requirements (i.e., valid only for small water bodies) were generally achieved. If only MFC from small water bodies were used, the degree of underestimation of MFC by PECs would even increase, as small water bodies generally exhibit higher insecticide exposure levels.[29]

Text S2. Uncertainties in K_{OC}-values and degradation half-times from FOOTPRINT PPDB

We selected the organic carbon water partitioning coefficients (K_{OC}) from the Footprint pesticide database[23], since for insecticides which are authorised for the use in the European Union under the EU Directive 1107/2009[24], the Footprint values represent those published in the official EU registration documents. Since these values are regularly used in the regulatory FOCUS calculations, which we aimed to evaluate with this study, we also used them here. Nevertheless, these values may only be an approximation of real values. In order to explore whether model algorithms or physicochemical model input parameters are responsible for the observed model prediction inadequacies, we performed calculations using alternative physicochemical parameters.

We compared the used K_{OC} (Footprint) values with those calculated from EPISUITE 4.1[25] using molecular connectivity index (MCI)-method and the empirical EPISUITE 4.1 values. In addition, we compared the used Footprint K_{OC}s with K_{OC}s published in the Agricultural Research Service (ARS) Pesticide Properties Database[26] derived from the US pesticide regulation. Figure S2 shows the relationship of K_{OC}s from the different sources.

The empirical values from EPISUITE 4.1 (Figure S2a) and from the ARS PPD (Figure S2b) matched comparably well (r = 0.91, r = 0.92) with the used values from the Footprint database as used in this study. In contrast, the relationship of the latter with the values of EPISUITE

4.1 using the MCI-method (Figure S2c) was much lower (r = 0.37) but still significant. We identified deltamethrin as an outlier as it showed deviations from the linear model greater 2 x standard deviation. Excluding deltamethrin from the linear regression, increased the r value to 0.56. We therefore decided to recalculate the PECs for all MFCs of deltamethrin using the K_{OC} values from EPISUTE 4.1 (MCI method). Nevertheless, the recalculations for deltamethrin did not result in a difference in the amount of over- and underpredictions, the respective values remained at 77 and 23%.

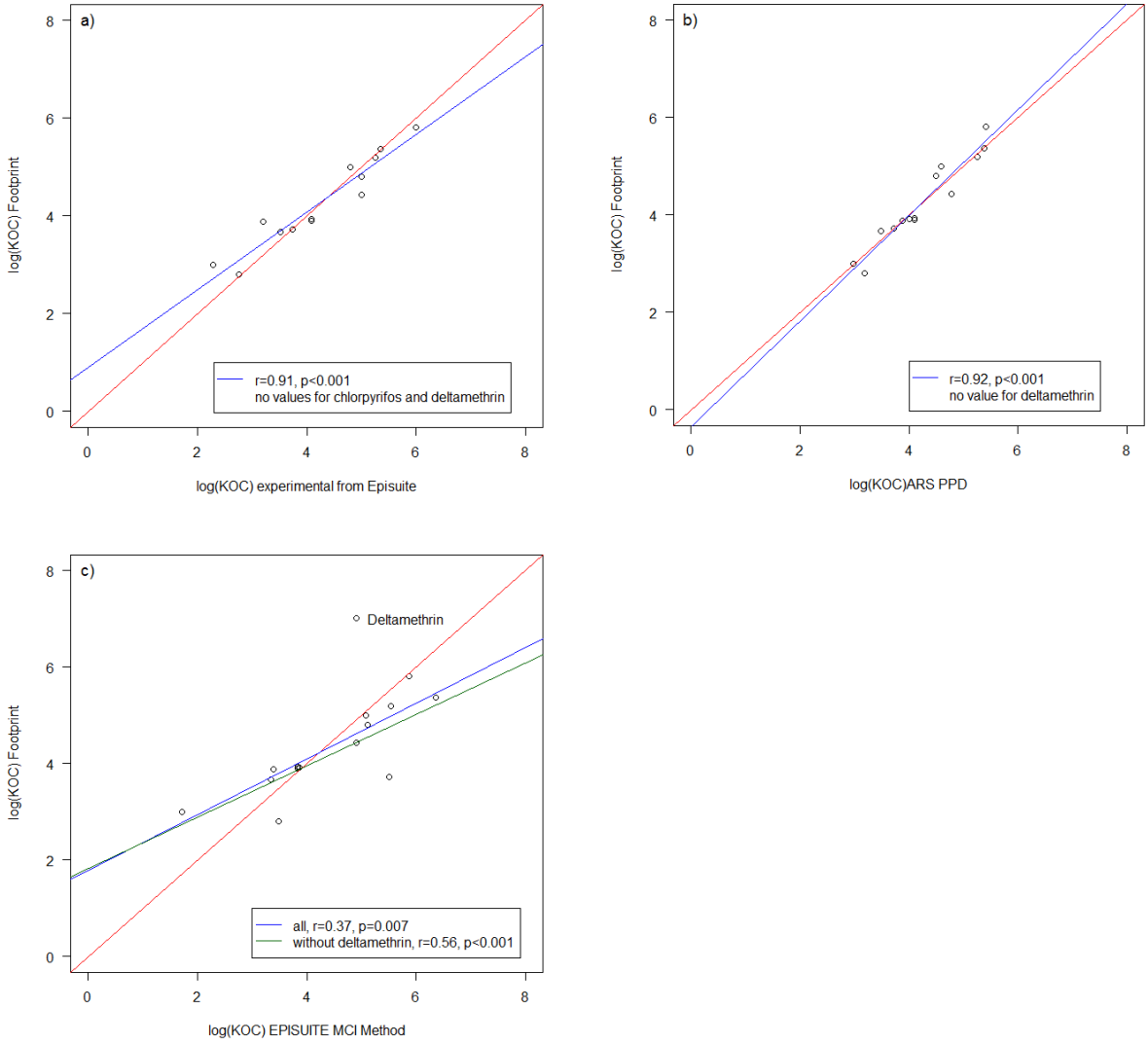

Figure S2. Relationship between log (KOC) values from Footprint Pesticide Property Database used in this study and log (KOC) values from a) EPISUITE 4.1 experimental, b) ARS Pesticide Property Database, and c) EPISUITE 4.1 calculated with the MCI method. The green line in (c) provides the relationship excluding deltamethrin. The 45 degree (red) line denotes identity between the KOC values.

In addition, we recalculated the PEC values for azinphos-methyl, bifenthrin, esfenvalerate and fenvalerate using the EPISUITE K_{OC}-values, as the relationship between the Footprint and EPISUITE values for these compounds showed differences > 1 from the 1:1 relationship, even if these values were not identified as outliers in the linear regression using the > 2 SD criterion.

The recalculation resulted only in minor changes. Surface water step 1 and sediment step 3 underpredictions changed from 4 to 5% and from 42 to 44%, respectively. All other values remained the same.

Differences in K_{OC} led only to minor changes and are thus considered here to be of minor relevance for the detected general model prediction inadequacies.

In addition, the degradation half-times (DT_{50}) are considered to be important substance parameters. In our study, in most cases the maximum (and thus initial) PECs were used for the comparison with measured concentration. Therefore, only the degradation in soil is relevant.

In the FOCUS step 3 surface water approach, a strong precipitation event is assumed within a 10-day period after application, resulting in exposure of water bodies.[28] In our study, the simulated mean time between insecticide application and the time at which the relevant PECs occurred in surface water was 1.1 days and the 90^{th} percentile value was 4 days for all step 3 standard calculations. As a result of this relative short time between application and water entry, the DT_{50} in soil was considered to be of minor relevance for the standard calculations.

Regarding the step 3 realistic calculations, the DT_{50} soil is of greater concern as the mean time between application and respective maximum PEC was 19 days and in contrast to the step 3 standard calculations, runoff is the major input pathway. We compared the used Footprint DT_{50} soil values with those from the ARS PPD. Only the DT_{50} soil values for bifenthrin and fenvalerate showed a major difference (> 25d) to the 1:1 relationship. We therefore recalculated the step 3 realistic PECs for these two substances, but no difference between the PECs ($p = 0.1$) and between the ratio of measured and simulated concentrations ($p = 0.25$) were found. In addition, the recalculated PECs for bifenthrin and fenvalerate did not alter the amount of over- and underpredictions of MFC.

References

(1) Anderson, B. S.; Phillips, B. M.; Hunt, J. W.; Worcester, K.; Adams, M.; Kapellas, N.; Tjeerdema, R. S. Evidence of pesticide impacts in the Santa Maria River watershed, California, USA. *Environ. Toxicol. Chem.* **2006,** *2*, 1160-1170.

(2) Anderson, B. S.; De Vlaming, V.; Larsen, K.; Deanovic, L. S.; Birosik, S.; Smith, D. J.; Hunt, J. W.; Phillips, B. M.; Tjeerdema, R. S. Causes of ambient toxicity in the Calleguas Creek watershed of southern California. *Environ. Monit. Assess.* **2002**, *78*, 131-151.

(3) Berenzen, N.; Lentzen-Godding, A.; Probst, M.; Schulz, H.; Schulz, R.; Liess, M. A comparison of predicted and measured levels of runoff-related pesticide concentrations in small lowland streams on a landscape level. *Chemosphere* **2005**, *58*, 683-691.

(4) Black, R. W.; Haggland, A. L.; Voss, F. D. Predicting the probability of detecting organochlorine pesticides and polychlorinated biphenyls in stream systems on the basis of land use in the pacific northwest, USA. *Environ. Toxicol. Chem.* **2000**, *19*, 1044-1054.

(5) Capri, E.; Balderacchi, M.; Yon, D.; Reeves, G. Deposition and dissipation of chlorpyrifos in surface water following vineyard applications in northern Italy. *Environ. Toxicol. Chem.* **2005**, *2*, 852-860.

(6) Dabrowski, J. M.; Bennett, E. R.; Bollen, A.; Schulz, R. Mitigation of azinphos-methyl in a vegetated stream: comparison of runoff- and spray-drift. *Chemosphere* **2006**, *62*, 204-212.

(7) Dabrowski, J. M.; Peall, S. K. C.; Reinecke, A. J.; Liess, M.; Schulz, R. Runoff-related pesticide input into the Lourens River, South Africa: Basic data for exposure assessment and risk mitigation at the catchment scale. *Water Air Soil Poll.* **2002**, *135*, 265-283.

(8) Domagalski, J. L.; Weston, D. P.; Zhang, M. H.; Hladik, M. Pyrethroid insecticide concentrations and toxicity in streambed sediments and loads in surface waters of the San Joaquin Valley, California, USA. *Environ. Toxicol. Chem.* **2010**, *29*, 813-823.

(9) Gormley, K. L.; Teather, K. L.; Guignion, D. L. Changes in salmonid communities associated with pesticide runoff events. *Ecotoxicology* **2005**, *14*, 671-678.

(10) Jergentz, S.; Mugni, H.; Bonetto, C.; Schulz, R. Runoff-related endosulfan contamination and aquatic macroinvertebrate response in rural basins near Buenos Aires, Argentina. *Arch. Environ. Contam. Toxicol.* **2004**, *46*, 345-352.

(11) Jergentz, S.; Mugni, H.; Bonetto, C.; Schulz, R. Assessment of insecticide contamination in runoff and stream water of small agricultural streams in the main soybean area of Argentina. *Chemosphere* **2005**, *6*, 817-826.

(12) Liess, M.; Schulz, R.; Liess, M. H.-D.; Rother, B.; Kreuzig, R. Determination of insecticide contamination in agricultural headwater streams. *Water Res.* **1999**, *33*, 239-247.

(13) Marino, D.; Ronco, A. Cypermethrin and chlorpyrifos concentration levels in surface water bodies of the Pampa Ondulada, Argentina. *Bull. Environ. Contam. Toxicol.* **2005**, *75*, 820-826.

(14) Neumann, M.; Schulz, R.; Schäfer, K.; Müller, W.; Mannheller, W.; Liess, M. The significance of entry routes as point and non-point sources of pesticides in small streams. *Water Res.* **2002**, *36*, 835-842.

(15) Padovani, L.; Capri, E. Chlorpyrifos-methyl dissipation in a small adjacent water body following application to citrus. *Chemosphere* **2005**, *58*, 1219-1229.

(16) Poissant, L.; Beauvais, C.; Lafrance, P.; Deblois, C. Pesticides in fluvial wetlands catchments under intensive agricultural activities. *Sci. Total Environ.* **2008**, *404*, 182-195.

(17) Schäfer, R. B.; Mueller, R.; Brack, W.; Wenzel, K. D.; Streck, G.; Ruck, W.; Liess, M. Determination of 10 particle-associated multiclass polar and semi-polar pesticides from small streams using accelerated solvent extraction. *Chemosphere* **2008**, *70*, 1952-1960.

(18) Schulz, R. Using a freshwater amphipod in situ bioassay as a sensitive tool to detect pesticide effects in the field. *Environ. Toxicol. Chem.* **2003**, *22*, 1172-1176.

(19) Schulz, R. Aquatic in situ bioassays to detect agricultural non-point source pesticide pollution: a link between laboratory and field. In *Techniques in Aquatic Toxicology*; Ostrander, G. K., Ed.; CRC Press LLC: Boca Raton 2005; Vol. 2, pp 427.

(20) Smalling, K. L.; Orlando, J. L.; Kuivila, K. M. Occurrence of pesticides in water, sediment, and soil from the Yolo Bypass, California. *San Francisco Estuary and Watershed Science* **2007**, *5*, 1-17.

(21) Süß, A.; Bischoff, G.; Mueller, A. C. W.; Buhr, L. Chemical and biological monitoring of the load of plant protection products and of zoocoenoses in ditches of the orchard region „Altes Land“ [in german]. *Nachr.bl. Dtsch. Pflanzenschutzd.* **2006**, *58*, 28-42.

(22) Wan, M. T.; Kuo, J. N.; McPherson, B.; Pasternak, J. Agricultural pesticide residues in farm ditches of the Lower Fraser Valley, British Columbia, Canada. *J. Environ. Sci. Health B* **2006**, *41*, 647-669.

(23) The FOOTPRINT Pesticide Properties Database, Hatfield, Herts, UK: The Agricultural & Environmental Research Unit (AERU) at the University of Hertfordshire: 2010; http://sitem.herts.ac.uk/aeru/footprint/index2.htm.

(24) European Commission. Regulation (EC) No 1107/2009 of the European Parliament and the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Off. J. Eur. Union* **2009**, *309*, 1-50.

(25) US EPA. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10. United States Environmental Protection Agency, 2012, Washington, DC, USA.

(26) The Agricultural Research Service (ARS) Pesticide Properties Database, http://www.ars.usda.gov/Services/docs.htm?docid=14199

(28) FOCUS. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS working group on surface water scenarios, EC Document Reference SANCO/4802/2001-rev.2. 2001, pp 245.

(29) Schulz, R. Field studies on exposure, effects and risk mitigation of aquatic nonpoint-source insecticide pollution - A review. *J. Environ. Qual*. **2004**, *33*, 419-448.