Environmental contaminants in birds of prey from Germany: insights into current threats

Inaugural-Dissertation
to obtain the academic degree
Doctor rerum naturalium (Dr. rer. nat.)

Submitted to the Department of Biology, Chemistry, Pharmacy
of the Freie Universität Berlin

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2022

This dissertation was conducted at the Leibniz Institute for Zoo and Wildlife Research in Berlin from June 2018 to September 2021 under the supervision of Dr. Oliver Krone and is submitted to the Department of Biology, Chemistry, Pharmacy of the Freie Universität of Berlin.

1st reviewer: Dr. Oliver Krone
2nd reviewer: Prof. Dr. Peter Robin Hiesinger

Date of defense: 20.04.2023

Acknowledgements

First of all, I like to thank Oliver Krone for giving me the opportunity to conduct my dissertation on birds of prey at the Leibniz Institute for Zoo and Wildlife Research (IZW). I am very grateful for the supervision and support I received during my doctoral studies. I also want to thank Detlef Schenke for supervising the analytical part of this thesis at the Julius-Kühn Institut (JKI).

A special thanks go to Richard Shore for giving me the opportunity to conduct a part of my research at the UK Centre for Ecology and Hydrology. Your impact on my personal and professional development won't be forgotten.

I also would like to thank Gabriele Treu for supporting me during my doctoral studies and for providing critical information from a regulatory perspective. I also acknowledge the reviewers of this dissertation, Oliver Krone and Peter Robin Hiesinger, for their willingness and time to review this thesis. I thank the World Wide Fund for Nature, Germany, for enabling this doctoral thesis and especially for providing an extension due to the COVID-19 pandemic. I further acknowledge the Klara Samariter Foundation for supporting the analysis and fieldwork of this thesis.

From the IZW, I acknowledge Manuela Merling de Chapa for supporting me during my fieldwork. I am also thankful for the statistical support I received from Alexandre Courtiol and Heribert Hofer. Further, I am grateful for the assistance I received during my thesis, particularly from Susanne Auls and Sabine Schiller (IZW), as well as from Martina Hoffmann and Ina Stachewicz-Voigt (JKI).

A special thank goes to Nikolaos Thomaidis and the Trace Analysis and Mass Spectrometry Group for a great collaboration and the possibility of receiving analytical training at the University of Athens. I also would like to thank Jan Koschorreck from the German Environment Agency (UBA) for supporting my academic career while also working at UBA. Further, I acknowledge Veerle Jaspers for sparking my interest in raptor ecotoxicology and encouraging me to apply for doctoral positions.

Lastly, I like to thank my family for supporting me and for giving me the opportunity to pursue an academic career. I also want to thank all my colleagues and friends I met along the way who made this journey unforgettable. I will always look back at my time with joy and hope to meet you again in and outside the field of wildlife biology.

Declaration of Independence

Herewith I certify that I have prepared and written my thesis independently and that I have not used any sources and aids other than those indicated by me. I also declare that I have not submitted the dissertation in this or any other form to any other institution as a dissertation.

This dissertation is based on the following manuscripts:

Badry A, Krone O, Jaspers VLB, Mateo R, García-Fernández A, Leivits M, Shore RF (2020). **Towards harmonisation of chemical monitoring using avian apex predators: Identification of key species for pan-European biomonitoring**. Science of The Total Environment; 731: 139198.
https://doi.org/10.1016/j.scitotenv.2020.139198

Chapter 2

Badry A, Schenke D, Treu G, Krone O (2021). **Linking landscape composition and biological factors with exposure levels of rodenticides and agrochemicals in avian apex predators from Germany**. Environmental Research 193: 110602:
https://doi.org/10.1016/j.envres.2020.110602

Chapter 3

Badry A[1], Treu G[1], Gkotsis G, Nika MC, Alygizakis N, Thomaidis NS, Voigt CC, Krone O (2022). **Ecological and spatial variations of legacy and emerging contaminants in white-tailed sea eagles from Germany: Implications for prioritisation and future risk management**. Environment International 158: 106934:
https://doi.org/10.1016/j.envint.2021.106934
[1] shared first authorship

Chapter 4

Badry A, Schenke D, Brücher H, Chakarov N, Grünkorn T, Illner H, Krüger O, Marczak T, Müskens G, Nachtigall W, Zollinger R, Treu G, Krone O (2022). **Spatial variation of rodenticides and emerging contaminants in blood of raptor nestlings from Germany**. Environmental Science and Pollution Research.
https://doi.org/10.1007/s11356-022-20089-1

Chapter 5

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List of Abbreviations

AR	Anticoagulant rodenticide
CECs	Contaminants of emerging concern
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
EC_{50}	Half maximal effective concentration
ERBFacility	European Raptor Biomonitoring Facility
EU	European Union
EURAPMON	Research and Monitoring for and with Raptors in Europe
FGAR	First generation anticoagulant rodenticide
GC	Gas chromatography

Hg	Mercury
HMP	Human medicinal product
HRMS	High resolution mass spectrometer
LC	Liquid chromatography
MP	Medicinal product
MSFD	Marine Strategy Framework Directive
NSAID	Non-steroidal anti-inflammatory drug
NTS	Non-target screening
OECD	Organisation for Economic Co-operation and Development
Pb	Lead
PBT	Persistence, bioaccumulation, and toxicity
PCBs	Polychlorinated biphenyls
PEC	Predicted environmental concentration
PFAA	Perfluoroalkyl acid
PFAS	Per- and polyfluoroalkyl substances
PFCA	Perfluorinated carboxylic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctanesulfonic acid
PFSA	Perfluorosulfonic acid
PNEC	Predicted no-effect concentration
POP	Persistent organic pollutant
PPP	Plant protection product
QSAR	Quantitative structure–activity relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SGAR	Second generation anticoagulant rodenticide
t	Tonnes
TMF	Trophic magnification factor
UK	United Kingdom

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Zusammenfassung

Umweltschadstoffe haben bei vielen Prädatoren zu einem erheblichen Rückgang der Populationen während des 20. Jahrhunderts geführt. Insbesondere Greifvögel litten unter Reproduktionsstörungen und erhöhter Sterblichkeit aufgrund der Biomagnifikation persistenter organischer Schadstoffe wie Dichlordiphenyltrichlorethan (DDT) und polychlorierten Biphenylen (PCBs). Diese Auswirkungen auf Greifvögel führten in Kombination mit schädlichen Folgen für die menschliche Gesundheit zu nationalen und weltweiten Verboten dieser Stoffe. Infolgedessen begannen sich die Populationen vieler Greifvogelarten ab den 1980er Jahren zu erholen. Trotz dieser regulatorischen Fortschritte gibt es derzeit immer noch Mängel in den Chemikaliengesetzen, die zu Emissionen gefährlicher Chemikalien in die Umwelt führen. Einige dieser chemischen Klassen, wie z. B. antikoagulante Rodentizide (ARs), bedrohen nachweislich Greifvogelpopulationen durch Sekundärvergiftungen in Europa. ARs hemmen die Synthese von Gerinnungsfaktoren in der Leber von Vertebraten und werden auch in Deutschland häufig zur Kontrolle von Nagetierpopulationen eingesetzt. Für andere Substanzgruppen, die im Verdacht stehen Greifvögel zu gefährden, wie beispielsweise aktuell verwendete Pflanzenschutzmittel (PSM) oder Arzneimittel, liegen hingegen nur begrenzt Informationen in Wildtierarten vor.

Da die europäische Chemikaliengesetzgebung in den Mitgliedstaaten der Europäischen Union harmonisiert ist, muss die Überwachung der Ergebnisse z. B. von Risikominderungsmaßnahmen auf der gleichen räumlichen Ebene durchgeführt werden. Daher untersuchte der erste Teil dieser Dissertation die Eignung europäischer Greifvogelarten für europaweiteres Monitoring prioritärer Schadstoffe (Kapitel 2). Hierbei spielten neben der Verbreitung auch ökologische Kriterien wie Nahrung, Habitat und Zugverhalten eine zentrale Rolle. Da in Deutschland die Gefahren für Greifvögel durch Umweltschadstoffe, wie beispielsweise ARs, weitgehend unbekannt sind beschäftigte sich das Kernthema der Dissertation mit der Identifizierung und Charakterisierung bekannter und unbekannter Schadstoffe auf nationaler Ebene. Hierzu fokussierte ich mich zuerst auf die Lebern von Greifvogel-Totfunden, da die Leber das zentrale Stoffwechselorgan ist und daher für die Analyse von Chemikalien mit unterschiedlichen physikalisch-chemischen Eigenschaften geeignet ist (Kapitel 3 und 4). Im nächsten Schritt wurde das Blut von Greifvogel-Nestlingen analysiert, um die räumlich-zeitliche Auflösung der Schadstoffexpositionen zu verbessern (Kapitel 5). In Kapitel 3 und 5 analysierte ich die Verteilung von prioritären Schadstoffgruppen wie ARs sowie ausgewählten PSMs und Arzneimitteln in Greifvögeln aus terrestrischen und

aquatischen Nahrungsgilden. In Kapitel 4 fokussierte ich mich auf die Identifizierung von 2441 bekannten und neuauftretenden Schadstoffen in Seeadlern (*Haliaeetus albicilla*) als Indikatorart für den Ostseeraum. Für die Analysen der Lebern (Kapitel 3 und 5) wurde sowohl Flüssigchromatographie (LC) als auch Gaschromatographie (GC) mit Massenspektrometern (MS)-Kopplung verwendet. Die Analysen im Blut konzentrierte sich hingegen auf polarere, nicht volatile LC-Chemikalien (Kapitel 5).

Die Ergebnisse des zweiten Kapitels zeigten, dass sich die europaweite Artenauswahl für die meisten der betrachteten Schadstoffe auf einige wenige Arten beschränken lässt. Der Mäusebussard (*Buteo buteo*) und der Waldkauz (*Strix aluco*) waren aufgrund ihrer weiten Verbreitung, ihrer breiten Lebensraumnische und Standorttreue die geeignetsten Arten für eine Vielzahl der betrachteten Schadstoffe. Andere Arten können jedoch für bestimmte Monitoringprogramme besser geeignet sein, wie beispielsweise der Steinadler (*Aquila chrysaetos*) für Blei oder der Habicht (*Accipiter gentilis*) für Programme, die auch weitnördliche Regionen in Europa einschließen. Der ökologisch basierte Ansatz zur Identifizierung von Indikatorarten hat sich als robust erwiesen und kann leicht auf andere Schadstoffgruppen und Kontinente ausgeweitet werden. Die Ergebnisse des nationalen Greifvogel-Monitorings in Deutschland aus Kapitel 3 zeigten, dass ARs unter 30 PSMs und 7 Arzneimitteln die größte Bedrohung für Greifvögel darstellen. Urbaner Habichte und Rotmilane (*Milvus milvus*) wiesen ARs in >80 % der Lebern auf und überschritten mehrfach Toxizitätsschwellenwerte. Die häufige Detektion im Habicht als überwiegend avivore (vogelfressende) Art deutet auf eine weitreichende Nahrungsnetzkontamination im städtischen Gebiet hin. Die häufige Detektion im Rotmilan als opportunistischem Kleinsäugerjäger ist hingegen vergleichbar mit der in anderen europäischen Ländern. Interessanterweise waren auch 38 % der überwiegend piscivoren (fischfressenden) Seeadler zu ARs exponiert. Rein piscivore Fischadler zeigten hingegen keine Schadstoffexposition. Aufgrund der geringen Stichprobenzahl der Fischadler werden weitere Studien empfohlen, um den Expositionspfad von ARs in Seeadlern zu untersuchen. Unter den Arzneimitteln wurde Ibuprofen am häufigsten in den Lebern von Seeadlern (24 %) nachgewiesen. Die Ergebnisse deuten auf eine aquatische Exposition hin, die mit einer unzureichenden Abwasserbereinigung und hohen Verbrauchsmenge zusammenhängen könnte. Unter den PSMs wurde das Neonicotinoid Thiacloprid sowie das nicht mehr zugelassenen Insektizid Dimethoat (und der Metabolit Omethoat) in jeweils zwei Rotmilanen nachweisen. Die Konzentrationen von Dimethoat/Omethoat deuten auf eine vorsätzliche Vergiftung hin. Zusammen mit einer AR-Vergiftung eines weiteren Rotmilans ist folglich davon auszugehen, dass vorsätzliche

Vergiftungen eine Bedrohung für Rotmilane in Deutschland darstellen. Neben der Untersuchung chemischer Bedrohungen für drei prioritäre Schadstoffklassen (ARs, PSM, Arzneimittel), zeigten die Ergebnisse von Kapitel 4, dass insgesamt 85 der 2441 altbekannten und neuauftretenden Schadstoffe in Lebern von Seeadlern nachgewiesen wurden. Die meisten Schadstoffe waren Arzneimittel (einschließlich Transformationsprodukte), obwohl diese nicht als persistent oder bioakkumulativ eingestuft wurden. Insgesamt waren 45% der 2441 Schadstoffe Arzneimittel, da sich die Auswahl der Analyten auf die aquatische Umwelt fokussierte. Die Ergebnisse demonstrieren jedoch, dass eine unzureichende Abwasserbereinigung in Kläranlagen zu Expositionen in Spitzenprädatoren aquatischer Nahrungsnetzen führt. Altbekannte Schadstoffe wie PCBs und DDTs wurden in allen Individuen nachgewiesen, allerdings unterhalb der Toxizitätsschwellenwerte. Andere häufig nachgewiesene Schadstoffe waren Per- und Polyfluoralkylsubstanzen (PFAS), die veraltet auch als PFC abgekürzt wurden. Innerhalb der PFAS machte Perfluoroctansulfonsäure (PFOS) den Hauptteil der Kontamination aus (96,8% von $\sum_{10}$PFAS) und zeigte zusammen mit DDTs und PCBs die insgesamt höchsten Konzentrationen in den Seeadlern. Die im Vergleich zur Literatur hohen PFOS-Konzentration einiger Individuen im Einzugsgebiet der Elbe deutet auf eine Emissionsquelle in Norddeutschland hin. Die am häufigsten nachgewiesenen PSMs waren Spiroxamin (zugelassenes Fungizid) und Simazin (nicht mehr zugelassenes Herbizid), die mit erhöhten Konzentrationen in den Seeadlern aus Agrarlandschaften nachgewiesen wurden.

Bei der Analyse des Blutes der Greifvogel-Nestlinge wurde ein erweiterter LC-Ansatz des dritten Kapitels angewandt, der sich auf ARs, 90 PSMs und 7 MPs fokussierte. Ähnlich wie in Kapitel 3 waren Rotmilane besonders von der AR-Kontamination (22,6%) betroffen. Des Weiteren wurden AR-Rückstände auch in Mäusebussarden (8,6%) nachgewiesen, während bei Wiesenweihen (*Circus pygargus*), Seeadlern und Fischadlern keine Exposition im Blut zeigten. Die bodenbrütende Wiesenweihe wurde in Getreidefeldern beprobt, was unterstreicht, dass AR-Anwendungen als PSM im Untersuchungsgebiet nicht mehr relevant zu sein scheinen. Jedoch ist die Halbwertszeit von ARs im Blut geringer als in der Leber, was die Detektion erschwert. Die geringe Halbwertszeit im Blut ist in Kombination mit einer vermutlich geringeren AR-Kontamination (basierend auf Kapitel 3) für die Abwesenheit von ARs im Blut der Seeadler verantwortlich. Fischadler hingegen scheinen generell nicht belastet zu sein. Es zeigte sich, dass die Konzentrationen von ARs in terrestrischen Greifvögeln aus Nordrhein-Westfalen im Vergleich zu denen in Nordostdeutschland höher sind. Dies hängt vermutlich mit der vermehrten Biozidanwendung in Regionen mit hoher Bevölkerungsdichte und intensiver Viehzucht zusammen. Das am häufigsten im Blut der Nestlinge nachgewiesene PSM war das

Herbizid Bromoxynil (14%). Neben ARs wurde das Herbizid Bromoxynil in 14% der Nestlinge nachgewiesen. Die Median-Konzentrationen in der Wiesenweihe waren ähnlich hoch (Rotmilan) bzw. niedriger (Mäusebussard) im Vergleich zu den baumbrütenden terrestrischen Greifvögeln. Daraus wird geschlussfolgert, dass Überschneidungen in ihrer Nahrung für die beobachtete Exposition ausschlaggebend sind und nicht die direkte Exposition auf dem Feld. Ähnlich wie bei den ARs waren die Bromoxynil Konzentrationen in terrestrischen Greifvögeln aus Nordrhein-Westfalen höher als in Nordostdeutschland, was vermutlich mit dem intensiven Maisanbau in der Region zusammenhängt.

Zusammenfassend zeigen die Ergebnisse dieser Dissertation, dass Greifvögel in Deutschland einer Vielzahl verschiedener Chemikalien ausgesetzt sind. Insbesondere persistente und bioakkumulierende Schadstoffe wiesen die höchsten Konzentrationen auf. Neben den momentan zugelassenen ARs zeigte sich, dass verbotene Schadstoffe wie DDTs, PCBs und PFOS einen Hauptteil der Schadstoffbelastung ausmachen. Insbesondere ARs haben sich in städtischen Gebieten und Regionen mit intensiver Viehhaltung als Bedrohung für terrestrische Greifvögel erwiesen. Um die Auswirkungen auf besonders gefährdete Arten wie urbane Habichte und den Rotmilan zu verringern, werden zusätzliche Hygienemaßnahmen in Viehzuchtbetrieben und Städten sowie die Beschränkung der Verwendung besonders toxischer ARs im Freien empfohlen. Aufgrund der Komplexität der Bewertung toxischer Wirkungen unter Feldbedingungen empfehle ich außerdem sich zum Schutz von Greifvögeln in erster Linie auf die Persistenz und Bioakkumulation zu konzentrieren. Dieser Ansatz würde es erlauben, Expositionen zu beenden, sobald zusätzliche Informationen über schädliche Wirkungen bekannt werden. Neben persistenten und bioakkumulierenden Stoffen wurden auch eine Vielzahl an Arzneimitteln sowie aktuell zugelassene und bereits verbotene PSMs nachgewiesen. Diese Beispiele demonstrieren, dass chemische Exposition von Spitzenprädatoren komplex sind und nicht nur mit den Stoffeigenschaften zusammenhängen. Es zeigte sich, dass beispielsweise die Nahrungsökologie, die verwendeten Habitate (z.B. urban, landwirtschaftlich) sowie das Verwendungsmuster der jeweiligen Chemikalien eine wichtige Rolle für die Expositionen von Greifvögeln spielen. Auf der Grundlage der Ergebnisse dieser Dissertation wird empfohlen, dass Monitoringdaten, ökologische Faktoren (z. B. Fütterungsökologie) und der landschaftliche Kontext von Expositionen bei behördlichen Risikobewertungen besser berücksichtigt werden. Zusammen mit einer primären Fokussierung auf Persistenz und Bioakkumulation wird erwartet, dass diese Maßnahmen Greifvögel und andere Wildtierarten schützen, bevor sich negative Auswirkungen auf Individual- oder Populationsebene bemerkbar machen.

Summary

Environmental contaminants have caused substantial population declines of many predatory species during the 20th century. Especially raptors suffered from reproductive impairments and increased mortality due to the biomagnification of persistent organic pollutants such as dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs). These deleterious effects on raptors, in combination with adverse effects on human health, resulted in national and global bans of these substances. As a result, populations of many predator species began to recover from the 1980s onwards. Despite these advances, regulatory frameworks still have shortcomings that result in the environmental emissions of hazardous chemicals. Some of these chemical classes, like anticoagulant rodenticides (ARs), have been shown to threaten European raptor populations through secondary poisoning. ARs inhibit the synthesis of coagulation factors in the liver of vertebrates and are also used in Germany to control rodent populations. However, for other substances that are suspected of threatening raptors, such as plant protection products (PPPs) or medicinal products (MPs), only limited information is available in wildlife species.

As chemical legislations are harmonised across the member states of the European Union, monitoring the outcome of e.g. risk mitigation measures needs to be conducted at the same spatial scale. Therefore, the first part of this dissertation aimed to identify the most suitable species for pan-European biomonitoring of priority contaminants. Candidate species were shortlisted using a scoring scheme based on distribution and ecological criteria such as diet, habitat and migration (chapter 2). In contrast to other European countries, threats to birds of prey from environmental contaminants such as ARs are largely unknown in Germany. Therefore, the core topic of the dissertation dealt with the identification and characterisation of legacy and emerging chemical threats on a national scale. In the first step, the analysis focused on the livers of deceased birds as the liver allows for analyses of chemicals with different physicochemical properties (chapters 3 and 4). In the next step, blood from nestlings was analysed to increase the spatiotemporal resolution of contaminant signals (chapter 5). Chapters 3 and 5 investigated the distribution of priority substance groups such as ARs as well as selected PPPs and MPs in birds of prey of different feeding guilds. In contrast, chapter 4 focused on the identification of 2,441 legacy and emerging contaminants in white-tailed sea eagles (*Haliaeetus albicilla*) as an indicator species for the Baltic Sea region. For the analyses of livers (chapters 3 and 4), both liquid (LC) and gas chromatography (GC) coupled to mass spectrometry was

used. In contrast, the analyses of the blood focused on more polar, non-volatile LC amendable contaminants (chapter 5).

The results of chapter 2 demonstrated that the selection of candidate species for pan-European species can be reduced to only a few species. The common buzzard (*Buteo buteo*) and tawny owl (*Strix aluco*) were the most suitable sentinel species for most of the considered contaminants due to their wide-spread distribution, large habitat niche and residency. However, other species may be better sentinels for specific monitoring schemes, such as the golden eagle (*Aquila chrysaetos*) for lead (Pb) or the northern goshawk (*Accipiter gentilis*) for studies including far northern European regions. The applied trait-based approach for identifying raptor biomonitors has proven to be robust and can be extended to other continents and contaminants.

When focusing on the national monitoring of birds of prey from Germany, the results from the third chapter demonstrated that ARs pose the most severe threat among 30 PPPs and 7 MPs. Urban northern goshawks and red kites (*Milvus milvus*) showed ARs residues in >80% of the individuals, and concentrations frequently exceeded toxicity thresholds. The frequent detection of ARs in the northern goshawk as mainly avivorous (bird-eating) species indicates extensive food web contamination in urban areas. In contrast, the high detection rate of red kites as rodent-predating species is comparable to that in other European countries. It was shown that 38% of the mainly piscivorous (fish-eating) white-tailed sea eagles were also exposed to ARs at lower concentrations. In contrast, the purely piscivorous osprey showed no contaminant exposure. Due to the small sample size of ospreys, further studies are recommended to investigate the exposure pathway of ARs in white-tailed sea eagles. Among the MPs, ibuprofen was most frequently detected, with the highest detection rate in the livers of white-tailed sea eagles (24%). The large prescription volume and incomplete wastewater removal might be responsible for the observed exposures. Among the PPPs, only the neonicotinoid thiacloprid and the expired insecticide dimethoate (and its metabolite omethoate) were detected in two red kites each. The concentrations of dimethoate/omethoate were considered to be a result of deliberate poisoning. Together with acute AR poisoning in another red kite, deliberate poisoning is expected to threaten red kites in Germany. In addition to investigating chemical threats by three classes of priority contaminants, chapter 4 identified 85 legacy and emerging contaminants in the livers of white-tailed sea eagles. Most contaminants were MPs (including transformation products), even though they were not predicted to be persistent or bioaccumulative. Their frequent detection is expected to be influenced by the large representation of MPs among the target analytes (45%). Nevertheless, the results demonstrate that MPs enter aquatic food webs and

that removal rates in wastewater treatment plants seem to be insufficient. Legacy contaminants such as DDTs and PCBs were detected in all individuals but below toxicity thresholds. Other frequently detected contaminants were per- and polyfluoroalkyl substances (PFAS), commonly known as forever chemicals. Perfluorooctanesulfonic acid (PFOS) accounted for most of the PFAS contamination (96.8% of $\sum_{10}$PFAS) and showed the highest concentrations in the white-tailed sea eagles, together with DDTs and PCBs. The relatively high PFOS concentration of some individuals in the catchment area of the river Elbe indicates the presence of point pollution in northern Germany. The most frequently detected PPPs were spiroxamine (approved fungicide) and simazine (expired herbicide), which showed increasing concentrations in white-tailed sea eagles from agricultural landscapes.

The blood analysis from nestlings applied an extended LC method to chapter 3 by focusing on ARs, 90 PPPs and 7 MPs. Similar to chapter 3, red kites were particularly impacted by AR contamination (22.6%). In addition to red kites, AR residues were also detected in common buzzards (8.6%), while no residues were detected in Montagu's harriers (*Circus pygargus*), white-tailed sea eagles and ospreys. The ground breeding Montagu's harriers were sampled in cereal fields, which indicates that AR applications as PPPs do not seem to be a relevant exposure pathway in the sampling region anymore. However, the half-life of ARs in the blood is shorter than in the liver, which complicates their detection. The low half-life, in combination with the generally lower AR concentrations in white-tailed sea eagles, is expected to be responsible for non-detects in their blood. Ospreys did not show AR residues in their liver or blood, which indicates that the species is not at risk for exposure. In general, ARs residues were higher in terrestrial raptors from North-Rhine Westphalia compared to North-Eastern Germany, which was expected to be related to the increased biocidal application of ARs in regions of high population density and intensive livestock farming. The most frequently detected PPP in the blood of nestlings was the herbicide bromoxynil (14%). The median concentrations in Montagu's harrier were similar (red kite) or lower (common buzzard) compared to the other terrestrial tree-nesting raptors. Therefore, overlaps in their dietary niche are expected to be most influential for the observed exposure rather than direct exposures in cereal fields. Similar to ARs, bromoxynil concentrations in terrestrial raptors from North-Rhine Westphalia were higher compared to North-Eastern Germany, which might be related to the intense field agriculture in the region.

In summary, the results of this dissertation demonstrate that birds of prey are exposed to a large cocktail of chemicals across different regulations. In addition to the currently approved ARs,

banned persistent and bioaccumulative contaminants such as DDTs, PCBs and PFOS showed the highest concentrations. ARs have especially been shown to threaten birds of prey in urban areas and regions with intensive livestock farming. To reduce the impact of ARs on species that are particularly threatened, such as urban northern goshawks and red kites, additional sanitary measures in livestock farms and urban areas are recommended in combination with limiting the outdoor use of particularly toxic ARs. Due to the complexity of assessing toxic effects under field conditions, it is further recommended to primarily focus on persistence and bioaccumulation for protecting apex predators. This approach allows for the termination of exposures once additional information on adverse effects become apparent. In addition to persistent and bioaccumulating substances, many MPs and currently approved and expired PPPs have also been detected. These examples show that chemical exposures of apex predators are complex and do not solely rely on chemical properties. For example, the feeding ecology, the habitat uses (urban, agricultural), and the use pattern of the respective chemicals have been shown to play an important role for exposure. Based on the result of this dissertation, I recommended that monitoring data, ecological factors (e.g. feeding ecology) and the landscape context of exposures need to be better taken into account in regulatory risk assessments. Together with focusing on environmental persistence and bioaccumulation, these measures are expected to protect birds of prey and other wildlife species before adverse effects in individuals or populations manifest.

Chapter 1 – General introduction

1.1 Still impacted by the past - persistent organic pollutants and the beginning of ecotoxicological research.

Environmental chemical pollution has caused substantial population declines and local extinctions of many species during the 20th century and is considered to represent an underestimated threat to biodiversity (Groh et al. 2022; Köhler and Triebskorn 2013; Shore and Taggart 2019). Ecotoxicological research started with the observation of population declines of insectivorous farmland birds and broken eggshells of peregrine falcons (*Falco peregrinus*) during the 1950s (Carson 1962; Newton 2004; Ratcliffe 1958). The book *Silent Spring* by Rachel Carson brought the topic to a broader public interest and discussed a link between the observed avian population declines to the application of certain pesticides (Carson 1962). It soon became apparent that especially avivorous (bird-eating) raptors such as the peregrine falcon and Eurasian sparrowhawk (*Accipiter nisus*) were suffering from the decreased eggshell thickness and increased mortality (Ratcliffe 1967). Continuous research efforts led to the identification of organochlorine insecticides, particularly dichlorodiphenyltrichloroethane (DDT), as the major cause of the observed adverse effects (Blus et al. 1972; Ratcliffe 1970; Wiemeyer and Porter 1970). DDT was widely used after the second world war against arthropods in agriculture and forestry, as well as for preventing the spread of vector-borne diseases such as malaria. The major environmental problems of DDT and its metabolites were related to its persistence, reproductive toxicity and endocrine disruption (Padayachee et al. 2023). Especially higher trophic level species suffered from adverse effects due to biomagnification of DDT within food webs (Padayachee et al. 2023). Adverse effects were not restricted to avivorous trophic transfers as raptors feeding on the aquatic food web, such as the bald eagle (*Haliaeetus leucocephalus*) and white-tailed sea eagle (*Haliaeetus albicilla*), suffered from population declines during the 20th century as well (Grier 1982; Helander et al. 1982). Together with threats from industrial contaminants such as polychlorinated biphenyls (PCBs), it soon became apparent that many organohalogenated compounds share similar hazardous properties (Risebrough et al. 1968). As a consequence, many of these compounds were classified as persistent organic pollutants (POPs) and were banned during the 1970s and 1980s in the USA and many European countries (Padayachee et al. 2023). On a global scale, the United Nations Stockholm Convention on POPs initially banned 12 compounds (“Dirty Dozen”) in 2004 and continuously extends the list based on scientific evidence (UNEP 2001). The hazardous properties of POPs are usually associated with persistence, bioaccumulation,

toxicity (PBT), and the potential to undergo long-range transport (Boethling et al. 2009). As these compounds are hardly biodegradable, certain POPs still threaten apex predators through biomagnification today (e.g. Desforges et al. 2018; Williams et al. 2020). On a European scale, this is particularly well documented for regions that were heavily impacted by agricultural and industrial pollution, such as the Baltic Sea region (e.g. de Wit et al. 2020). As a consequence, particularly sensitive species such as the white-tailed sea eagle were included as sentinel species for anthropogenic pressures in current European environmental legislation such as the Marine Strategy Framework Directive (MSFD) (Zampoukas et al. 2014).

1.2 Current regulatory frameworks for phasing out hazardous chemicals in the European Union

Because of the deleterious effects of POPs on biodiversity and human health, the European Union (EU) defined cut-off values for PBT properties before registering or approving a chemical on the European market. The persistence is usually defined by the degradation half-live of a chemical (and known transformation products) in air, soil, water or sediment (Boethling et al. 2009). The tests for assessing B and T are usually based on controlled laboratory experiments using lower trophic level species such as algae, fish or daphnia as model organisms (Badry et al. 2022a; Treu et al. 2022). For apex predators, especially persistent and bioaccumulative substances have shown to represent a threat as these substances often magnify in food webs and thereby have a potential to exceed toxic thresholds (de Wit et al. 2020; Padayachee et al. 2023). The bioaccumulation potential of a chemical is, for example, determined by the partitioning coefficient between water and 1-octanol (test no. 123) (OECD 2022) or between fish and its surrounding media (bioconcentration) or diet (biomagnification) (test no. 305) (OECD 2012). Toxicity tests are usually also carried out on lower trophic level model organisms such as, e.g. northern bobwhite quail (*Colinus virginianus*) or Japanese quail (*Coturnix japonica*) in case of the avian toxicity test no. 223 (Moreau et al. 2022; OECD 2016). In general, such toxicity tests aim to derive a toxicity threshold value (e.g. half maximal effective concentration, EC_{50}) in a controlled laboratory environment but do not consider the ecological (e.g. different sensitivities of species and their ecosystem functions), management (e.g. application patterns of pesticides), and landscape context (e.g. land use and other co-occurring stressors) of chemical exposures (Moreau et al. 2022; Schäfer et al. 2019).

Prominent examples of legal frameworks that apply these endpoints and criteria are, e.g. the regulation on industrial chemicals (REACH - Registration, Evaluation, Authorisation and Restriction of Chemicals, Regulation EC 1907/2006), plant protection products (Regulation EC

1107/2009) or biocides (Regulation EU 528/2012) (Scholz et al. 2013). After determining hazard endpoints, a second step for approving a chemical usually requires a tiered environmental risk assessment, where a predicted environmental concentration (PEC) is supposed to remain below a predicted no-effect concentration (PNEC) to protect the environment from harmful effects (Scholz et al. 2013). However, there are many uncertainties in predicting a PEC and PNEC, which is why a safety factor is applied as a precautionary measure for field conditions. These advances in chemical legislations resulted in the restriction/ban of many chemicals with similar hazardous properties as the POPs mentioned above. Despite these advances, a recent study indicates that we are currently exceeding the planetary boundary for novel entities (i.e. new substances, new forms of existing substances and modified life forms), including chemical and anthropogenic mobilisation of naturally occurring elements (Persson et al. 2022). The following paragraph will address shortcomings in current chemicals legislations, which may have contributed to environmental emissions of hazardous chemicals and wildlife exposures.

1.2.1 Differences among chemical regulations – drawbacks of a fragmented approach

In general, information on (eco-)toxicological data, including hazard endpoints (e.g. PBT) of chemicals, are provided in Europe by the chemical manufacturer in a registration dossier, which represents the basis for marketing a chemical in the EU. Whereas plant protection products (PPPs) and biocides require an authorisation step, industrial chemicals regulated under REACH are marketed directly after registration. Industrial chemicals only require authorisation once a chemical is classified as substance of very high concern (e.g. PBT or carcinogenic, mutagenic or reproductive toxicity). A general issue related to the registration dossiers under REACH is that many dossiers are non-compliant and only up to 20% are checked for compliance by EU member states and EU agencies (Springer et al. 2015; van Dijk et al. 2021a). Currently, the sheer quantity of produced and imported chemicals outpaces the capacities of hazard and risk assessments. Thus, *in silico* tools become increasingly important for predicting hazardous properties (e.g. for estimating PBT properties) (Johnson et al. 2020; Treu et al. 2022). Data on bioaccumulation for chemicals regulated under REACH are only required for substances that are produced or imported in the European Economic Area at more than 100 tonnes (t) per year (European Commission 2006, Annex IX). For many chemicals, registration dossier information is often outdated as updates are only required for PPPs and biocides (after 10 years) but not for industrial chemicals (van Dijk et al. 2021a). As a consequence, many registration dossiers do not reflect on the latest scientific findings, which calls for closer collaboration between academia, regulators and policy (Topping et al. 2020; van Dijk et al. 2021a; Wang et al. 2021a).

In particular, chemicals tested prior to 2012 (and the updated OECD 305 guideline) or those tested using non-experimental studies are considered to underestimate the bioaccumulation potential as these studies only take into account the total concentration in water rather than the bioavailable fraction (Glüge et al. 2022). In general, the hazard and risk assessments focus on single substances, whereas the exposure to chemical mixtures under field conditions is currently not adequately addressed in chemicals legislations (Drakvik et al. 2020; Kortenkamp and Faust 2018; Treu et al. 2022). Providing information on chemical exposure under field conditions is therefore crucial for developing models that accurately predict chemical risks in ecosystems. On the other hand, the feedback of policy-relevant scientific questions to the scientific community is crucial, e.g. for selecting relevant target chemicals and appropriate sentinel species.

1.2.2 Recognising the need for action – chemical pollution as a driver of biodiversity loss

Currently, phasing out or substituting a hazardous chemical in the EU takes several years and is often accompanied by the replacement with structurally similar chemicals (van Dijk et al. 2021a). This process has been shown to lead to continuing environmental problems, and so-called regrettable substitutions as potential hazards of replacement products are often less studied (Maertens et al. 2021; Zimmerman and Anastas 2015). Furthermore, actions against environmental pollution usually become effective only after considerable damage has occurred, which is especially problematic for persistent compounds (Conrad et al. 2021). Such practices show an urgent need to make the chemical market safer and more sustainable for protecting the environment. Therefore, the Chemicals Strategy for Sustainability was implemented as part of the European Green Deal (European Commission 2020b). The European Green Deal represents a package of policies and initiatives that addresses chemical pollution in its environmental strategies and action plans (European Commission 2019). Aside from aiming to increase the sustainability of the European chemicals market, the European Commission also set out a Zero Pollution Ambition for a toxic-free environment along with specific action plans for reducing the impacts of environmental pollution (European Commission 2021). Such measures were proposed to include, e.g. the continuous monitoring of all environmental media, including selected organisms and humans (Conrad et al. 2021). Whereas there is a discussion on whether the term “toxic-free environment” is a scientific or rather political term (van Dijk et al. 2021b), it generally reflects the ambition of the European population, which considers pollution the most important environmental issue behind climate change (European Commission 2020a). Apart from the Chemicals Strategy for Sustainability and the Zero Pollution Ambition, the EU Biodiversity Strategy for 2030 specifically recognises that pollution is among the key drivers

for biodiversity loss and that greater efforts have to be made for reducing negative impacts caused by pesticides, pharmaceuticals and other harmful chemicals (European Commission 2020c).

1.3 Continuous wildlife exposure to hazardous chemicals under current regulatory frameworks

European environmental legislations generally focus on the chemical monitoring of a restricted number of known environmental contaminants in abiotic matrices or lower trophic-level species of the aquatic environment (Badry et al. 2022a). As a consequence, monitoring data from wildlife species are not routinely considered for identifying emerging contaminants and environmentally relevant chemical mixtures (Treu et al. 2022). There are numerous examples of chemicals that entered the environment and for which environmental concerns have been raised recently, which are generally referred to as contaminants of emerging concern (CECs) (Sauvé and Desrosiers 2014). CECs are often identified in the aquatic environment, as analytical methods for identifying CECs, such as suspect and non-target screening (NTS), were first developed for abiotic aquatic matrices (e.g. Schymanski et al. 2015). Recent research efforts led to the expansion of detected contaminants in biota (Barrett et al. 2021; Dürig et al. 2020; Liu et al. 2018). However, exposures to CECs in wildlife are still poorly characterised, especially for species of higher trophic levels (González-Rubio et al. 2020). The following parts will give four examples of substances (i.e. PPPs, biocides, industrial chemicals and medicinal products) that are or were registered under current European chemical legislations and caused substantial problems for wildlife species.

1.3.1 Plant protection products – toxicity of neonicotinoids

Due to the history of ecotoxicology and the detection of DDT, the focus of wildlife monitoring has traditionally been on PPPs. One of the most widely used classes of insecticides in recent years were the neonicotinoids, which have been marketed in the EU since 1991 (Auteri et al. 2017). In 2013, the European Commission started to restrict the use of three neonicotinoids and subsequently banned them in 2018 due to high toxicity for non-target invertebrates, in particular wild bees (Auteri et al. 2017; European Commission 2022). It also became apparent that avian wildlife species, such as farmland and gamebirds, were exposed to neonicotinoids (Lennon et al. 2020a; Lennon et al. 2020b; Millot et al. 2017). This is of particular interest since farmland bird populations are declining, and neonicotinoids were suspected to aggravate the declines of some species (Hallmann et al. 2014; Lennon et al. 2019; Millot et al. 2017). Yet, population level impacts are difficult to link to chemical exposures as standardised long-term wildlife

monitoring programs are lacking and precise information on use patterns of PPPs is generally not publicly available (Johnson et al. 2020).

1.3.2 Biocides – secondary poisoning by anticoagulant rodenticides

Anticoagulant rodenticides (ARs) are used in Germany as biocides to control rodent populations in urban areas, livestock farms, and sewer systems, whereas their approval as PPP expired (Regnery et al. 2019). Despite their classification as PBT compounds, ARs are currently still authorised, mainly due to the lack of suitable alternatives (Hohenberger et al. 2022). Adverse effects of ARs are caused by inhibiting the blood clotting system in vertebrates, which results in the delayed death of exposed individuals (Rattner et al. 2014b). The first-generation ARs (FGARs) require multiple feeds to cause death in exposed rodents and were continuously replaced in the 1970s by second-generation ARs due to increasing resistance in rodents (Thomas et al. 2011). Second-generation ARs (SGARs) are more persistent and potent (i.e. a single feeding event can be sufficient) than FGARs, which results in an increased risk for secondary poisoning (Rattner et al. 2014b). Research efforts have shown that ARs cause exposures numerous non-target exposure, such as to legally protected rodents (Geduhn et al. 2014), songbirds (Walther et al. 2021b) and fish (Kotthoff et al. 2018). Their wide-spread contamination in various food webs, together with their bioaccumulating properties, also resulted in secondary poisoning of predatory species such as red foxes (*Vulpes vulpes*) (Geduhn et al. 2015) and raptors (López-Perea and Mateo 2018).

1.3.3 Industrial chemicals regulated under REACH – global per- and polyfluoroalkyl substance contamination

Among the industrial compounds, per- and polyfluoroalkyl substances (PFAS), also publicly known as ‘forever chemicals’, cause the most severe environmental problems (Cousins et al. 2022). PFAS are for example used in firefighting foams, paints, outdoor clothing, or Teflon production due to their thermal stability and water-repellent properties (Glüge et al. 2020). Adverse effects were linked to, e.g. developmental toxicity, immunotoxicity and cancer (Briels et al. 2018; Sunderland et al. 2019). Depending on the definition, the group of PFAS comprises more than 4,700 substances from which only a fraction is currently regulated under REACH (Wang et al. 2021b). Among these substances, perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) were voluntarily phased out by their main producer in the early 2000s and subsequently included in the Stockholm Convention in 2009. Both PFOS and PFOA are classified as PBT substances and have, together with other PFAS, shown to be ubiquitously distributed in food webs around the world, including the Arctic and Antarctica (Gao et al. 2020;

Muir et al. 2019). However, monitoring data are currently only available for 40-50 non-volatile substances from the PFAS subgroup perfluoroalkyl acids (PFAA) due to the lack of chemical reference standards (De Silva et al. 2021). In biota, PFAAs are generally associated with protein-rich tissues such as the liver, blood or kidney by binding to serum albumin or fatty acid-binding proteins (Armitage et al. 2012; De Silva et al. 2021). Especially PFOS and long-chained perfluorinated carboxylic acids (PFCAs) ($\geq C_8$) have been shown to accumulate in food webs and reach particularly high concentrations in apex predators (Chen et al. 2021).

1.3.4 Medicinal products – incomplete wastewater removal and diclofenac toxicity for *Gyps* vultures

Among medicinal products (MPs), the environmental occurrence of antibiotics is associated with developments of antimicrobial resistance, which is considered to be critically important for the global public and animal health (WHO 2018). Emission sources for human medicinal products (HMP), commonly referred to as pharmaceuticals, differ from those of veterinary medicinal products (VMP). HMPs primarily enter freshwater via wastewater treatment plant effluents due to incomplete removal, whereas veterinary medicinal products (VMPs) enter terrestrial and aquatic compartments via manure fertilisation, agricultural run-off, or aquaculture (Arnold et al. 2014; Shore et al. 2014). As a consequence, MPs such as antibiotics, antidepressants or non-steroidal anti-inflammatory drugs (NSAIDs) were detected in fish and freshwater invertebrates in Europe (Boulard et al. 2020; Miller et al. 2019; Miller et al. 2021). Besides aquatic wildlife exposures, terrestrial exposures via livestock production and vulture feeding sites are known to pose a risk for scavenging species in Spain (Herrero-Villar et al. 2020). The detrimental effects related to foraging on treated livestock were first observed for *Gyps* vultures on the Indian subcontinent, where diclofenac (NSAID) caused population crashes due to renal failure and visceral gout in exposed individuals (Oaks et al. 2004). Despite this knowledge, diclofenac is currently registered for veterinary use in Spain, where it caused acute poisoning of a cinereous vulture (*Aegypius monachus*) nestling (Herrero-Villar et al. 2021). This example emphasises that little is known about the potential effects and environmental fate of MPs in non-mammalian wildlife species (Shore et al. 2014).

1.4 Birds of prey and chemical pollution – between monitoring for species conservation and being sentinels for contamination in food webs

Due to the described history of DDT and PCBs in raptors, biomonitoring initiatives in the 20th century therefore mainly focused on species conservation and led to the identification of population effects of persistent and bioaccumulative compounds (Helander et al. 2002; Roos et

al. 2001; Shore and Taggart 2019). These information were together with adverse effects on human health, important drivers for the development of global treaties on chemical pollution and early chemical legislations (UNEP 2001). It soon became apparent that certain predatory species can be reliable sentinels for the identification and spatiotemporal assessment of bioaccumulating substances in food webs (Desforges et al. 2022; García-Fernández et al. 2020). Especially raptors have proven to be suitable indicators for assessing the wider ecological health in food webs due to their high trophic level, relatively large home ranges and well-known ecology (Gómez-Ramírez et al. 2014; Movalli et al. 2019; Sergio et al. 2005). Today, the populations of many raptor species recovered, which allows for the development of biomonitoring studies over large spatial scales, including pan-European biomonitoring (Derlink et al. 2018; Ramello et al. 2022). Pan-European initiatives are crucial to assess, e.g. risk mitigation measures or to provide data on substances that are currently under assessment as chemical legislations are harmonised across the EU (Movalli et al. 2019; Treu et al. 2022). The potential of raptors to act as sentinels for chemical contamination in food webs resulted in the development of European research initiatives such as the European Raptor Biomonitoring Facility (ERBFacility) (Movalli et al. 2019) and the LIFE APEX project (Badry et al. 2022b; Treu et al. 2022)).

1.4.1 Birds of prey from Germany – known chemical threats

Similar to studies from other European countries and North America (e.g. Grier 1982; Helander et al. 1982; Ratcliffe 1967), DDT and PCBs were also linked to substantial population declines of raptor species in Germany (Denker et al. 2001; Scharenberg and Struwe-Juhl 2006; Wegner et al. 2005). A particular focus of ecotoxicological research has traditionally been on the peregrine falcon due to the described DDT-related population declines (Ratcliffe 1958; Ratcliffe 1967). In Germany, the peregrine falcon population in Baden-Württemberg declined by 80% during the 20th century, which was related to the application of DDT and associated eggshell thinning (Wegner et al. 2005). Another chemical stressor besides DDT and PCBs was methyl mercury (methyl Hg), which was e.g. used in seed treatments in the German Democratic Republic. (Schwarz et al. 2016; Wegner et al. 2005). Methyl Hg was, in combination with a prolonged use of DDT, linked to local extinctions of peregrine falcons in the German Democratic Republic (Wegner et al. 2005).

In general, POPs accumulated in almost all food webs, but population declines were most severe in avivorous and aquatic raptors in Germany by causing population crashes of peregrine falcons, sparrowhawks, ospreys (*Pandion haliaetus*) and white-tailed sea eagles (Denker et al. 2001;

Kannan et al. 2003; Scharenberg and Struwe-Juhl 2006; Weber et al. 2003). Sparrowhawks are specialised on avivorous prey (Götmark and Post 1996), whereas ospreys forage exclusively on piscivorous (fish-eating) food webs (Häkkinen 1978). In contrast, white-tailed sea eagles are not specialised in their diet but feed mainly on fish and waterfowl, with smaller proportion of (game) mammals (Nadjafzadeh et al. 2016). A negative effect on the shell-thickness of peregrine falcons could not be observed anymore in eggs between 2001-2009, which was linked to declining levels of the main DDT metabolite dichlorodiphenyldichloroethylene (DDE) and PCBs (Schwarz et al. 2016). A similar decline was observed in the eggs of white-tailed sea eagles from Schleswig-Holstein (Scharenberg and Struwe-Juhl 2006).

Apart from studies on eggs, feathers have proven to be reliable indicators for the internal concentration of certain contaminants (Jaspers et al. 2019). A study on feathers from the 1990s reported that especially white-tailed sea eagles and ospreys accumulated high Hg values compared to other raptors from Germany (Hahn et al. 1993). Sampling eggs or feathers is particularly valuable as a non-invasive sampling matrix for species that were close to (local) extinction. Today, populations of many raptors have recovered since the mid-1980s due to the ban of DDT in 1972 and PCBs in 1982 in Western Germany (Scharenberg and Struwe-Juhl 2006; Wegner et al. 2005). As a consequence, internal tissues from deceased raptors became available for research collections and natural history museums (Ramello et al. 2022). Among the internal tissues, the liver is the metabolic most competent organ and is particularly suitable for detecting contaminants over a large range of polarities, while eggs cover mainly lipophilic contaminants (Espín et al. 2016; Gkotsis et al. 2023).

Table 1 gives an overview of detected environmental contaminants in the livers of raptors from Germany. Until now, only a few raptor species have been analysed for a limited number of contaminants. In general, white-tailed sea eagles showed higher concentrations of toxic metals and legacy POPs compared to northern goshawks (*Accipiter gentilis*), a species that mainly forages on other birds and to a lesser extent on mammals (Tornberg and Reif 2007). In contrast to the other contaminants, lead (Pb) is only threatening raptors foraging on game species due to Pb-based hunting ammunition (Krone 2018). In Germany, this is especially relevant for white-tailed sea eagles and golden eagles (*Aquila chrysaetos*) as they are the only raptor species that are frequently foraging on larger game species. Apart from Pb, PFOS concentrations in white-tailed sea eagles significantly increased over time (Kannan et al. 2002), which demonstrates that the white-tailed sea eagle, as a mixed food web feeder, is exposed to a large variety of chemicals. Studies on contaminants other than legacy POPs, PFAS and toxic metals are limited

to a single study on ARs in a small number of barn owls (*Tyto alba*) (Table 1). This is particularly problematic since ARs are known to threaten raptors in Europe (López-Perea and Mateo 2018). For other classes of contaminants that are suspected to threaten wildlife, such as currently used PPPs or MPs (see 1.3, chapter 1), there is little information available on exposures in apex predators from Europe.

Table 1: Median concentration in µg g^{-1} of ∑PCBs, the main DDT metabolite DDE, ARs and toxic metals (lead (Pb), mercury (Hg)) in livers of German raptors. Five white-tailed sea eagles in Kenntner et al. (2001) originated from Austria. Values for ARs represent the percentage of individuals with detectable levels.

Species	N	Year	∑PCBs	DDE	PFOS	∑AR (%)	Pb	Hg	References
Northern Goshawk (*Accipiter gentilis*)	62 61*	1995 - 2001	1.26	1.99			0.13*	0.07*	(Kenntner et al. 2003)
White-tailed sea eagle (*Haliaeetus albicilla*)	24	1979 - 1998	6.5	6.4					(Kannan et al. 2003)
	36	1979 - 1998			0.03				(Kannan et al. 2002)
	57	1993 - 2000					0.18	0.38	(Kenntner et al. 2001)
Golden Eagle (*Aquila chrysaetos*)	3	2001					0.29	0.02	(Kenntner et al. 2007)
Barn owl (*Tyto alba*)	11	2011 - 2013				55%			(Geduhn et al. 2016)

1.5 Objectives of the thesis

The overall objective of this dissertation is to identify and characterise chemical threats for birds of prey from different feeding guilds in Germany. As European chemical legislation is harmonised across member states of the EU, this thesis also investigated the suitability of European raptors species to act as sentinel for contaminants on a continental scale. The results are expected to provide critical information on 1) chemicals known to pose threats to top predators, such as ARs, DDT and PCBs, as well as on 2) chemicals for which only limited information is available in wildlife species, such as currently used PPPs and MPs. Identifying chemical exposures is important for planning appropriate risk mitigation measures, status assessments in environmental legislations (e.g. MSFD) or for providing information on chemicals that are currently under assessment in chemical legislations. On a European perspective, this thesis aims to contribute to the establishment of a pan-European raptor biomonitoring scheme that is able to control the effectiveness of regulatory changes on a continental scale.

1.5.1 Specific objectives of the thesis

Chapter 2: "*Towards harmonisation of chemical monitoring using avian apex predators: Identification of key species for pan-European biomonitoring*"

European raptor biomonitoring schemes are currently using various raptor species (Derlink et al. 2018; Gómez-Ramírez et al. 2014), whereas a harmonised species selection for pan-European biomonitoring is missing. To address this gap, chapter 2 aims to identify the most suitable species or guild of species for a set of contaminants that were prioritised based on a literature review and expert opinion from an ERBFacility workshop in Thessaloniki, in 2019. The first hypothesis of chapter 2 was that the selection of sentinel species can be reduced to only a few common species based on the distribution and ecological criteria such as diet, habitat and migration. To test this, I reviewed the ecological traits of European raptor species (i.e. *Accipitriformes, Strigiformes*, *Falconiformes*) and applied a scoring system to traits that potentially maximise exposure to the contaminant of interest. Chapter 2 builds upon work by the ERBFacility network on existing raptor biomonitoring activities in Europe and the identification of the most suitable sample matrices for tracking pan-European contaminant trends (Espín et al. 2016; Gómez-Ramírez et al. 2014).

Chapter 2 specifically aims to answer the following questions:

- How do ecological criteria like distribution, diet, habitat, or migration influence the selection of sentinel species for those contaminants?
- Which species, or guild of species, are likely to be the most suitable sentinels for pan-European biomonitoring?

Chapter 3: "*Linking landscape composition and biological factors with exposure levels of rodenticides and agrochemicals in avian apex predators from Germany*"

On a European scale, ARs have especially been shown to pose a threat to various raptor species (see 1.3.2). However, there is currently only limited information on AR exposure in raptors from Germany (Chapter 1, Table 1). For other contaminant classes, such as currently used PPPs, there is generally limited information available for top predators, as many studies often focus on legacy pesticides for which exposure pathways differ. Apart from pesticides (i.e. ARs and PPPs), MPs are frequent contaminants of the aquatic environment, and certain MPs are a known threat to scavenging species in Spain (see 1.3.4). The objective of chapter 3 was to investigate the distribution of these contaminant classes (i.e. ARs, PPPs, MPs) in the livers of deceased birds of prey from different feeding guilds. The hypothesis of chapter 3 was that chemical exposure differs among terrestrial and aquatic feeding guilds based on the ecology of the species and the use patterns/emission sources of the contaminants. To test this, the study focused on terrestrial species feeding in agricultural landscapes, such as the red kite (*Milvus milvus*) and sparrowhawk to investigate exposure pathways of PPPs, ARs (livestock) and VMPs (manure fertilisation). Northern goshawks from urban areas were included due to the frequent biocidal applications of AR in cities. It was predicted that red kites accumulate ARs based on their feeding ecology as rodent predating species and reports from other European countries. Both in Germany occurring raptor species that utilise aquatic food-webs (white-tailed sea eagle, osprey) were included to cover aquatic exposure pathways of contaminants that were previously detected in fish from Germany, such as HMPs and ARs.

Chapter 3 specifically aims to answer the following questions:

- Are birds of prey from Germany exposed to ARs to a similar extent as birds of prey in other European countries? Are red kites particularly exposed to AR based on their feeding ecology?
- Does urban land use result in the exposure of a primarily avivorous species such as the northern goshawk?

- Are species feeding on aquatic food-webs (white-tailed sea eagles and osprey) exposed to ARs and HMPs?
- Are species foraging in agricultural landscapes, like red kites and sparrowhawks, exposed to PPPs and VMPs?
- How do landscape (urban, agriculture) and biological factors (e.g. age, nutrition condition, sex) influence exposures?

Chapter 4: "*Ecological and spatial variations of legacy and emerging contaminants in white-tailed sea eagles from Germany: Implications for prioritisation and future risk management*"

Currently, only limited information is available for CECs and chemical mixtures in apex predators, as established analytical procedures mainly focused on the target analysis of a limited number of contaminants (i.e. < 100). This represents a critical knowledge gap, as identifying chemical mixtures is essential for hazard and risk assessments. The objective of chapter 4 was to extend the current knowledge on chemical threats by analysing 2,441 legacy and emerging contaminants in livers. The chapter focused on the white-tailed sea eagle as a mixed food web feeder that combines multiple exposure routes. For the contaminants, chapter 4 hypothesised that white-tailed sea eagles are exposed to chemical mixtures consisting of persistent and bioaccumulative compounds such as POPs, PFAS and freshwater-specific contaminants such as HMPs. This is based on the hypothesis that the investigated white-tailed sea eagles predominantly forage on fish and waterfowl with a minor proportion of terrestrial diet. To test this, chapter 4 included the analysis of the stable isotope values of $\delta^{15}N$ and $\delta^{13}C$ and compared them with those of common prey species from the sampling region (Nadjafzadeh et al. 2016).

Chapter 4 specifically aims to answer the following questions:

- Does the analysis of stable isotopes ($\delta^{15}N$, $\delta^{13}C$) provide more detailed insights into the foraging behaviour of the investigated white-tailed sea eagles?
- What is the composition of chemical mixtures in white-tailed sea eagles, and how much do POPs still contribute to the contaminant burden?
- What is the influence of the trophic position ($\delta^{15}N$), habitat ($\delta^{13}C$) and landscape type on the most frequently identified contaminants?
- Is an *in silico* tool able to predict accumulating substances in white-tailed sea eagles, or are there potential mismatches between predicted PBT properties and observed exposures?

Chapter 5: "*Spatial variation of rodenticides and emerging contaminants in blood of raptor nestlings from Germany*"

Analysing blood from nestlings increases the spatiotemporal resolution as the life history of the individuals is known. Furthermore, an active monitoring approach might overcome a potential sampling bias when focusing on deceased birds. The analysis in the blood applied an extended analytical approach to chapter 3 by targeting the prioritised organic contaminant groups from chapters 2 and 3 in the blood of three terrestrial and two aquatic birds of prey. The selection of terrestrial species had a particular focus on the use of agricultural landscapes to investigate the exposure to chemicals that are applied within the surrounding of their breeding sites. It was hypothesised that the terrestrial birds of prey (red kite, common buzzard and Montagu's harriers (*Circus pygargus*)) accumulate ARs and PPPs based on their feeding ecology and habitat use. It was predicted that the terrestrial species would be more frequently exposed to ARs and PPPs in regions with intense field agriculture and livestock farming (i.e. North Rhine Westphalia) (Wallmann et al. 2020). Besides exposure to ARs, chapter 5 predicted that Montagu's harriers are particularly exposed to PPPs as ground-nesting species in cereal fields. White-tailed sea eagles and osprey were assumed to be exposed to HMPs based on their reported occurrence in fish. Exposures to ARs were expected to be less frequent compared to the terrestrial species.

Chapter 5 specifically aims to answer the following questions:

- Do nestlings show a similar contaminant pattern in blood compared to the livers of deceased juveniles and adults (chapter 3)?
- Are common buzzards and Montagu's harrier exposed to ARs to the same extent as red kites?
- Are Montagu's harriers particularly exposed to PPPs?
- Can a larger sample size of ospreys add further evidence on potential piscivorous exposures of white-tailed sea eagles from chapters 3?
- Are individuals from North Rhine-Westphalia more frequently exposed to agriculturally related contaminants compared to species from North-Eastern Germany?

Chapter 2: Towards harmonisation of chemical monitoring using avian apex predators: Identification of key species for pan-European biomonitoring

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Published in Science of The Total Environment (2020)
- https://doi.org/10.1016/j.scitotenv.2020.139198

Detailed author contributions:

A short-term scientific mission grant was awarded to AB by the ERBFacility to carry out the described work in the working group of RFS from 24/07/19 to 22/08/19 in Lancaster, UK. RFS had the initial idea for the manuscript. RFS, AB and OKro conceptualised the work based on the results of a workshop conducted by the ERBFacility network in Thessaloniki in 2019. All authors of the paper participated in the workshop and provided crucial information about the ecology and feasibility of pan-European biomonitoring. AB conducted the literature research and drafted the manuscript with input from all co-authors.

Science of the Total Environment 731 (2020) 139198

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Towards harmonisation of chemical monitoring using avian apex predators: Identification of key species for pan-European biomonitoring

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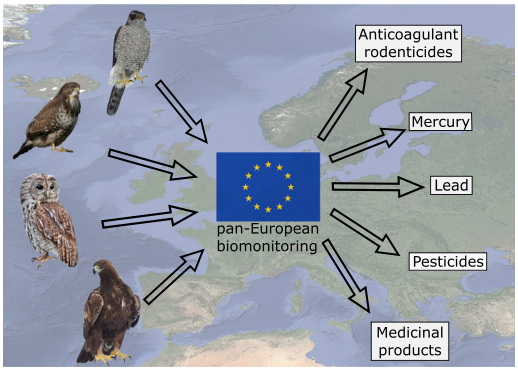
HIGHLIGHTS

- We identified key raptor and owl species for pan-European monitoring of pollutants.
- Selection was primarily on key ecological traits and distribution.
- Our focus was on Pb, Hg, rodenticides, pesticides and veterinary medicinal products.
- Common buzzard and tawny owl were the most suitable pan-European biomonitors.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 19 February 2020
Received in revised form 1 May 2020
Accepted 1 May 2020
Available online 7 May 2020

Editor: Adrian Covaci

Keywords:
Pan-European monitoring
Pollutants
Pesticides
Metals
Rodenticides
Raptors

ABSTRACT

Biomonitoring in raptors can be used to study long-term and large-scale changes in environmental pollution. In Europe, such monitoring is needed to assess environmental risks and outcomes of chemicals regulation, which is harmonised across the European Union. To be effective, the most appropriate sentinels need to be monitored. Our aim was to identify which European raptor species are the likely most appropriate biomonitors when pollutant quantification is based on analysing tissues. Our current study was restricted to terrestrial exposure pathways and considered four priority pollutant groups: toxic metals (lead and mercury), anticoagulant rodenticides, pesticides and medicinal products. We evaluated information on the distribution and key ecological traits (food web, foraging trait, diet, preferred habitat, and migratory behaviour) of European raptors to identify the most appropriate sentinel species. Common buzzard (*Buteo buteo*) and/or tawny owl (*Strix aluco*) proved the most suitable candidates for many of the pollutants considered. Moreover, they are abundant in Europe, enhancing the likelihood that samples can be collected. However, other species may be better sentinels for certain pollutants, such as the golden eagle (*Aquila chrysaetos*) for lead, the northern goshawk (*Accipiter gentilis*) for mercury across areas including Northern Europe, and vultures (where they occur in Europe) are likely best suited for monitoring non-steroidal anti-inflammatory drugs (NSAIDs). Overall, however, we argue the selection of candidate species

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https://doi.org/10.1016/j.scitotenv.2020.139198

for widescale monitoring of a range of pollutants can be reduced to very few raptor species. We recommend that the common buzzard and tawny owl should be the initial focus of any pan-European raptor monitoring. The lack of previous widespread monitoring using these species suggests that their utility as sentinels for environmnetal pollution has not been widely recognised. Finally, although the current study focussed on Europe, our trait-based approach for identifying raptor biomonitors can be applied to other continents and contaminants.

Contents

1. Birds of prey as sentinels for pollution monitoring

The monitoring of environmental pollutants in raptors has a long history (Cade et al., 1971; Helander et al., 1982; Ratcliffe, 1967). Such monitoring was often initiated to understand the risks from pollutants to individual species of high conservation value, but it is now recognised that it also can provide insights into wider ecological health and a warning of potential human exposure and effects on health (García-Fernández et al., 2020). There are a number of characteristics that make predatory birds particularly suitable as sentinels, especially for compounds that bioaccumulate or biomagnify through food webs. These include foraging through both terrestrial and aquatic food webs, occupation of high trophic position (typically raptors are apex predators), a long history of ecotoxicological research and associated understanding of contamination in various species, and, where appropriate, the potential to obtain non-destructive samples (feathers, carcasses from accidents, deserted eggs, blood) for analysis (Espín et al., 2016; Gómez-Ramírez et al., 2014).

Monitoring in raptors can reveal spatio-temporal trends in environmental contaminant concentrations (Gómez-Ramírez et al., 2019; López-Perea and Mateo, 2018; Walker et al., 2012). It can therefore be a key tool for evaluating the outcomes of regulation and other mitigation measures designed to reduce environmental contamination over large spatial scales (García-Fernández, 2020; Shore and Taggart, 2019). Monitoring at national or smaller spatial scales across Europe has involved the use of a variety of species (Gómez-Ramírez et al., 2014) and sample types (Espín et al., 2016). However, chemical regulation in much of Europe is now harmonised and delivered through European Union (EU) directives and regulations, such as the Biocidal Product Regulation (EU 528/2012), regulation on Plant Protection Products (EC 107/2009) and REACH - Registration, Evaluation, Authorisation and Restriction of Chemicals (EC 1907/2006). Recently, the European Parliament and the Council on Veterinary Medicinal Products (VMPs) also repealed the previous Directive 2001/82/EC and replaced it with a stronger/harmonised regulation (García-Fernández, 2020). Therefore, monitoring to detect the outcomes of legislation applied to large spatial scales (such as EU legislation) needs to be at the same scale. This imperative has led to initiatives to develop pan-European monitoring capability, such as EURAPMON; www.eurapmon.net and its follow-up programme, the European Raptor Biomonitoring Facility ERBFacility; www.erbfacility.eu (Movalli et al., 2019). However, a key challenge for large-scale monitoring is to determine which species, or guild of species, are likely to be the most suitable sentinels for monitoring contaminants and how species selection may vary depending upon the contaminants of interest. This is a critical knowledge gap.

The current study aimed to address this gap and evaluate the relative merits and disadvantages of different species for harmonised biomonitoring within and across large-spatial scales such as Europe. We shortlisted candidate species based on their European distribution and on ecological traits relevant to exposure to priority environmental pollutants. Our initial analysis indicated that the distribution across Europe of raptors that utilise aquatic food-webs was largely limited and it is arguable that non-raptor and non-avian species, such as the Eurasian otter (*Lutra lutra*), gull species and pinnipeds, may prove more suitable for large-scale biomonitoring of pollutant transfer through freshwater and marine systems. Therefore, the present work focuses on terrestrial exposures to priority pollutants. Our work builds on previous research into monitoring schemes that were, or currently are, operative within Europe (Gómez-Ramírez et al., 2014) and the practicalities of what sample types are suitable for pollution studies (Espín et al., 2016).

2. Prioritised environmental pollutants

We focussed on addressing which species may be most suitable for monitoring a sub-set of priority compounds. The choice of compounds was agreed at a European workshop of 30 experts that was hosted by the ERBFacility in February 2019. Pollutants were selected on the basis that they remain a current environmental risk across Europe, particularly to vertebrate wildlife, and are typically also subject to regulation. Pollutants groups were prioritised using a ranking exercise that was conducted independently by three breakout groups and the average rankings calculated (Table SI-1). The selected priority pollutants were two toxic metals (lead (Pb) and mercury (Hg)), anticoagulant rodenticides (ARs), pesticides as a general group and medicinal products (MPs), and in particular veterinary medicinal products (VMPs).

Lead is a toxic non-essential trace metal that occurs naturally in parts of the earth crust, but anthropogenic uses such as mining and metal production have resulted in a ubiquitous environmental distribution (Abadin et al., 2007). Lead has been recently identified as a substance of very high concern by the European Chemicals Agency (ECHA) due to its reproductive toxicity and is therefore subject to authorisation within REACH (ECHA, 2018). Certain uses (such as in gasoline) have already been regulated or banned. However, Pb is still frequently used in hunting ammunition and fishing weights (Stroud, 2015), although the use of Pb shot and ammunition for hunting varies between EU Member States depending on their national/regional legislation (Mateo and Kanstrup, 2019). It is the dietary ingestion of Pb shot and ammunition fragments that poses the most serious threat for predators (Krone, 2018; Nadjafzadeh et al., 2015; Pain et al., 2019). Species that are exclusively scavengers (obligate scavengers) as well as species that scavenge and actively hunt (facultative scavenger) are at particular risk because they frequently feed on game mammals and waterfowl (García-Fernández et al., 2005; Krone et al., 2009; Mateo, 2009). For example, Pb intoxication has been identified as an important mortality factor for vultures and facultative scavengers across Europe (Berny et al., 2015; Helander et al., 2009; Krone et al., 2009). However, foraging on gunshot-injured but still living mammals and waterfowl can also result in significant exposure risk for non-scavengers (Gil-Sánchez et al., 2018; Mateo et al., 1999).

Mercury is also a highly toxic non-essential trace metal. It is naturally emitted through volcanic activities, sea salt spray and soil particles (Nriagu, 1989) but is released in greater quantities by industrial activities such as coal-combustion, refuse incineration and metal production (Amos et al., 2013; Nriagu and Pacyna, 1988). Due to its high toxicity, Hg is currently included within Regulation (EU) 2017/852, which regulates the import and use of Hg containing products. In the atmosphere, Hg occurs mainly in its elemental form (Hg^0), whereas it is predominantly in its organic form methylmercury (MeHg), in soil, sediments and surface waters. Mercury can biomagnify in both aquatic and terrestrial food webs (Cristol et al., 2008; Douglas et al., 2012; Lavoie et al., 2013), and elevated concentrations are accumulated in birds of prey and other predators (Badry et al., 2019; Sun et al., 2019). Biomagnification with increasing trophic level means that Hg can reach toxic concentrations in apex predators (Lavoie et al., 2013). In terrestrial environments, raptors can accumulate sufficient Hg such that reproduction is impaired and behavioural abnormalities are manifest (Burger and Gochfeld, 1997; Whitney and Cristol, 2018).

Anticoagulant rodenticides are widely used biocides commonly applied in agricultural and urban settings to control populations of rats, mice and, in some countries, voles (Geduhn et al., 2014; López-Perea and Mateo, 2018). Their use as biocides is regulated under the EU Biocides Directive but ARs are also used (and regulated for) as Plant Protection Products (PPPs) in some countries (e.g. bromadiolone in Italy, France, Netherlands, Romania; Regnery et al., 2019). Eight ARs are currently registered for use in Europe. These are the older first generation ARs (FGARs) - warfarin, coumatetralyl and chlorophacinone – and five second generation ARs (SGARs): difenacoum, bromadiolone, brodifacoum, flocoumafen and difethialone (Regnery et al., 2019). SGARs were developed in the 1970s due to increasing resistance of rodents against FGARs (Buckle et al., 1994; Eason et al., 2002) but they all broadly have a common mode of action, which is inactivation of the vitamin K epoxide reductase in hepatocytes and a consequent failure to synthesize clotting factors like prothrombin (Rattner et al., 2014). Because the clotting system is highly conserved in evolutionary terms, ARs affect all vertebrates.

SGARs are formulated mainly as coated wheat baits, wax baits and as gels and may be deployed in bait boxes, in burrows or may be buried underground in rodent galleries; application can be made throughout the year or targeted when rodent pests are most abundant (López-Perea and Mateo, 2018). Non-target small mammal species also take bait and individuals within 15 m of bait stations have been shown to accumulate the highest SGAR residues, although individuals can range widely in agricultural landscapes (Geduhn et al., 2014; Tosh et al., 2012). Predators are thought to typically be exposed secondarily to ARs, mainly as a result of preying on rodents and/or scavenging (Elliott et al., 2014; López-Perea and Mateo, 2018).

Pesticides are a diverse group of chemicals that are commonly classed as PPPs when their insecticidal, herbicidal or fungicidal properties are used to protect agricultural crops. However, the term pesticide can also be used to refer to the same active ingredient when it is used for other purposes, such as biocide to treat ectoparasites on livestock. The acute mortality caused by legacy plant protection products, such as the organochlorine insecticidal seed dressings dieldrin, in combination with poor reproduction caused by dichlorodiphenyltrichloroethane (DDT)-mediated eggshell thinning, was one of the first examples of pesticides causing population declines in raptors and other species (Newton, 1986; Ratcliffe, 1967). Such pesticides have been widely banned at national and European levels because of their toxic effects on humans as well as wildlife, but significant residues of legacy organochlorines are still detectable in raptors today (Gómez-Ramírez et al., 2019). Pesticides used in agriculture to protect crops are regulated in the EU as Plant Protection Products (EC 1107/2009), and those sold as biocides are regulated as biocidal products (EU 528/2012). A risk assessment represents the first step of the authorization of pesticides in the EU and requires that a predicted environmental exposure concentration is below a concentration that is considered to cause an effect in non-target organisms (Schäfer et al., 2019). However, empirical data on bioaccumulation in wildlife systems and on exposure of apex predators are scarce and it is argued that biomonitoring could contribute valuable information on the accumulation of pesticides within food webs (Movalli et al., 2019).

Medicinal products are widespread environmental pollutants that have been associated with threats to non-target wildlife such as raptors (Shore et al., 2014). Within Europe, medicinal products are classified and regulated as human medicinal products (HMPs) (2001/83/EC), as VMPs (Regulation (EU) 2019/6) or both (aus der Beek et al., 2016; García-Fernández, 2020). Environmental risks have been associated with hormones, anti-parasitics, antibiotics and anti-inflammatories used as HMPs and VMPs and with analgesics and antidepressants used as HMPs (aus der Beek et al., 2016; Mateo et al., 2015). Medicinal products can enter the environment via landfills, livestock production and through application of sewage sludge as fertilizer (Arnold et al., 2014; Shore et al., 2014). Potential wildlife exposure pathways in wildlife include intake via diet and contaminated water and inhalation of dust in areas of intensive animal feeding operations (Shore et al., 2014). Even though the environmental half-lives of medicinal products are generally lower than those of many persistent organic pollutants (POPs), environmental emissions can exceed removal rates and so they are considered pseudo-persistent pollutants (Daughton and Ternes, 1999; Lazarus et al., 2015). Some medicinal products are predicted to accumulate along aquatic food chains (Connors et al., 2013; Lazarus et al., 2015), thereby potentially reaching toxic concentrations. The environmental life cycle for most medicinal products as well as their accumulation and metabolism in non-target wildlife species remains poorly understood (Shore et al., 2014), but these products can have devastating impacts, as demonstrated by the impact of diclofenac on *Gyps* vultures (Oaks et al., 2004).

3. Methods of selection of candidate species based on ecological traits

The 2019 ERBFacility workshop identified a putative “long-list” of candidate species (Table SI-2) that were considered suitable European species for monitoring the priority pollutants that are the focus of the present work.

The ERBFacility workshop also discussed what type of monitoring would be feasible if a pan-European monitoring programme was to be

established. The consensus was that, while active monitoring, for example sampling nestling blood, might offer a structured monitoring programme, it would be difficult to develop a sustainable programme with adequate geographical coverage. This is because such monitoring requires ethical permits, trained volunteer or professional personnel and is expensive. Although shed feathers or failed eggs could be collected from nests instead of blood, this would not overcome the likely geographical patchiness of sampling from nest sites and such samples, particularly feathers, are of limited use toxicologically. Espín et al. (2016) discussed in detail the advantages and disadvantages of different sample matrixes for contaminant monitoring in raptors and concluded that liver [and blood] were the most effective matrices for most analytes. Liver samples can be obtained from the carcasses of raptors found dead. Current monitoring schemes have demonstrated the feasibility of using interested members of the public to report and collect the carcasses of raptors that they find (Gómez-Ramírez et al., 2014; Jager et al., 1996; Naccari et al., 2009; Walker et al., 2008a); such collections can be across a broad geographical scale. The selection of candidate species for biomonitoring for the present study was therefore predicated on the assumption that pollutant characterisation would involve analysis of tissue samples obtained from the carcasses of birds that died from a variety of causes but particularly traffic accidents, other trauma and starvation (Jager et al., 1996; Naccari et al., 2009; Walker et al., 2008a).

After the conclusion of the ERBF workshop, we reduced the species long-list using an objective logical framework that first considered the geographical distribution of the species and then evaluated whether their trait characteristics were suitable for biomonitoring. Our first category, widespread distribution within Europe, was deemed the most important selection criterion given the aim for any biomonitoring was to track changes across Europe (Table SI-3). We considered Europe (here defined as EU countries together with Norway, Switzerland, United Kingdom (UK) and Iceland; Fig. 1) to consist of four regions (eastern, northern, southern and western Europe) based on the United Nations Geoscheme (United Nations Statistics Division, 1999). We classed a species as widely distributed if it was present in three or more countries in at least three of those four regions. Species distributions were taken from BirdLife International (2019). The requirement for widespread distribution reduced the species "long-list" down to 19 species that feed mainly on terrestrial species (Table SI-3). None of the raptors feeding on aquatic prey (Table SI-4) nor the vultures (Table SI-5) met the criteria for widespread distribution. The present work therefore subsequently focussed only on terrestrial exposure to our selected priority pollutants.

We then considered the main traits likely to influence exposure to our priority compounds; these were predominant feeding trait (scavenging, active hunting), diet, and type of habitat utilised (Table SI-3). Although we focused on terrestrial species, we also considered which was the predominant food web (terrestrial, freshwater, marine) when considering species that were mixed feeders as contaminant levels in birds of prey can be affected by their respective food webs (Eulaers et al., 2011; Jaspers et al., 2006). We extensively searched existing published information to describe the

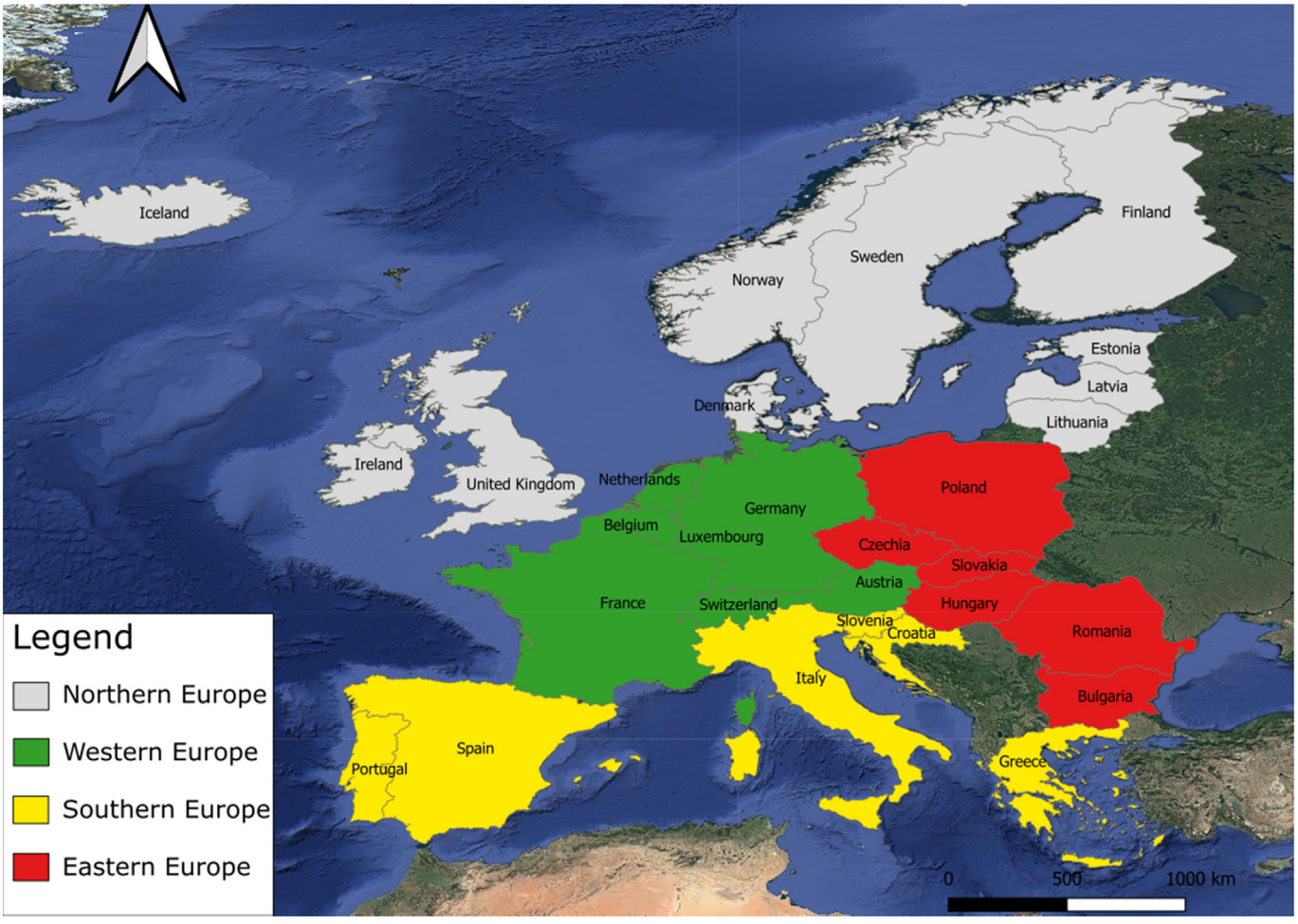

Fig. 1. Main regions of Europe based on the United Nations Geoscheme (United Nations Statistics Division, 1999). Considered countries include European Union countries together with Norway, Switzerland, UK and Iceland.

characteristics of each trait for every raptor in the reduced long-list. These are given in Table SI-3.

As pollutant characterisation was assumed to be based on tissue analysis, we included migration as a key trait. This was because exposure to and assimilation of a contaminant in a tissue could occur at location[s] distant from where the bird later died and was collected for analysis. This is particularly salient for contaminants that are only slowly metabolised in tissues, and potentially for contaminants accumulated in fat depots; body-lipids are remobilized during migration which can elevate liver concentrations of lipophilic compounds (Henriksen et al., 1996). Although migration may not affect residue magnitude for all contaminant classes/matrices (Elliott et al., 2007; Leat et al., 2019) and previous contaminant studies have involved migratory raptors, the origin of contaminant exposure can be difficult to interpret (Goutner et al., 2011; Lavoie et al., 2010). This adds uncertainty, compared to the use of non-migrants, when the aim is to use spatial and temporal variation in raptor contamination to inform chemicals management. This uncertainty may be particularly acute when using long-distant migrants as exposure may occur outside the jurisdiction of regulatory authorities, even when jurisdictions are continental in size. We categorised raptors as resident, partial-migrants and long-distance migrants (Table SI-3).

We classified different characteristics of each trait with respect to their suitability for pan-European monitoring of the compound of interest. Traits characteristics were categorised as advantageous (AD), limiting (LI) or excluding (EX). Advantageous characteristics were those likely to result in, and potentially maximise, exposure to the pollutant of interest. Residency and widespread distribution were also classified as advantageous. Limiting criteria were trait characteristics likely to lead to pollutant uptake through routes not considered the most important exposure pathway. Traits characteristics, such as partial migration, that somewhat compromised the spatial integrity of biomonitoring were also considered limiting, as was the absence of a species in three or more countries in one of the main regions of Europe. Exclusion criteria for pan-European biomonitoring were traits characteristics that were likely to markedly limit or prevent exposure. Long-term migration was also considered an excluding factor. We concluded that the species with the highest number of advantageous traits and no exclusion criteria were the most suitable for pan-European monitoring of the specific contaminant of interest. The trait categorisations for Pb, Hg, ARs, pesticides and MPs are given in Tables SI-7, SI-9, SI-12, SI-14 and SI-16, respectively.

We then examined how the trait characteristics described for each raptor species (Table SI-3) corresponded against our defined AD, LI and EXC criteria. In this way, we assigned an AD, LI or EXC category to each trait for each raptor. We then used this information to compile a short list of candidate species for each priority pollutant. Species were only included in these short-list on the basis that they had no excluding traits. The species short list for each priority pollutant, and their categorised trait characteristics, are given in Tables 1-5. There was typically more than one species in the short-list and the relative merits and demerits of short-listed species, in terms of their use as biomonitors, is the focal point of discussion in the current paper (Section 4). Where possible, this discussion reduced the short-list further to just one or two species that were argued to be the most suitable for biomonitoring at a pan-European scale. This included taking into account species abundance as a secondary or contextual criterion. The number of raptor carcasses found and submitted for contaminant analysis tends to be positively correlated with relative abundance (Newton et al., 1999).

After one or two species were identified as the most suitable candidates for pan-European monitoring, we conducted a web-based literature research, using specific key words and Boolean operators (Table SI-6), to ascertain whether it had been used for monitoring the contaminant of interest. Evidence of such monitoring provides some proof that generation of contaminant data in that species is actually possible.

4. Candidate species for biomonitoring of prioritised environmental pollutants within Europe

4.1. Trace metals

4.1.1. Lead (Pb)

After widespread geographical distribution, feeding ecology was considered to be the critical trait for selecting a sentinel for pan-European Pb monitoring. This was because predators and scavengers that feed on game species generally accumulate the highest Pb burdens and suffer incidents of Pb-related mortality (García-Fernández et al., 2005; Krone, 2018; Mateo et al., 2003). Scavengers and active predators of game species were therefore considered candidate species (Table 1). Of those, species that undertake partial migration were deemed less suitable for monitoring. This was because ability to examine spatial variation in exposure is likely to be important for Pb as regulations on hunting and use of Pb shot varies between countries and regions within Europe (Mateo and Kanstrup, 2019). Hence, the use of partial migrants as well as species feeding on migratory prey was considered limiting due to the uncertainty as to whether accumulated residues reflected local or pre-migration exposure. Habitat was considered a less important trait for selecting candidate species since foraging on game and waterfowl occurs across a broad range of different habitats (Table SI-7). By applying the aforementioned criteria, we compiled a short-list of just two candidate species, the common buzzard (*Buteo buteo*) and the golden eagle (*Aquila chrysaetos*) (Table 1).

The common buzzard is widely distributed across Europe, although it is a partial migrant in northern areas, as birds migrate to avoid unfavourable weather conditions (BirdLife International, 2019; Holte et al., 2017). Restricting sampling to birds found dead in the breeding season would largely avoid exposure biases resulting from migration as Pb tissue half-lives are relatively short (1–-3 months; Krone, 2018) and tissue residues in the breeding season can likely reflect exposure at that time. However, restricting sampling in this way might induce a temporal bias if exposure is maximal during the hunting season but this does not coincide with the buzzard breeding season. Furthermore, the common buzzard predominantly forages on non-game species, such as rodents, when such prey is highly abundant (Table SI-3 and references therein). This is likely to limit potential exposure to Pb-shot in injured prey and it is notable that liver Pb concentrations in common buzzard are generally lower than those in species, such as golden eagles, that are thought to forage more frequently and consistently on game species (Table SI-8). Nevertheless, the widespread distribution of common buzzards, together with their relative abundance (and associated high likelihood of carcass availability) are favourable characteristics and they have been used for measuring Pb contamination previously (Jager et al., 1996; Naccari et al., 2009; Walker et al., 2008a).

Golden eagles forage predominantly on terrestrial prey, mainly medium-sized mammals, including game species (Table SI-3). They scavenge carrion in the winter (Halley and Gjershaug, 1998) which makes them highly susceptible to Pb exposure and toxicosis (Ecke et al., 2017; Madry et al., 2015). Golden eagles are also non-migratory and territorial, which enhances their suitability for detecting regional differences in Pb exposure, although there can be long-range dispersal for sub-adults in Scandinavia and Estonia (Nebel et al., 2019). Golden eagles have been used previously for Pb monitoring studies (Ecke et al., 2017; Madry et al., 2015; Mateo et al., 2003) and have been widely used as a sentinel of environmental pollutants generally within Europe (Gómez-Ramírez et al., 2014), indicating that sampling of this species is feasible. However, golden eagles are not evenly distributed within Europe, mainly as a result of human persecution (BirdLife International, 2019; Watson and Whitfield, 2002), and are restricted to remote and wilderness habitats like montane/alpine regions in western Europe and forest landscapes

Table 1
Key traits of shortlisted candidate species for pan-European monitoring of Pb. A complete list of traits and species with associated references can be found in Table SI-3 and the assessment of the criteria as suitable for Pb monitoring is indicated in Table SI-7. Overall suitability is indicated for each criterion except for distribution where individual suitability is given in the superscript of each main region. AD = advantageous criterion, LI = limiting criterion for pan-European Pb monitoring.

Species	Distribution	Food web	Feeding trait	Diet	Migration
Common buzzard (*Buteo buteo*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Terrestrial → **AD**	• Active hunter • Facultative scavenger → **AD**	• Mainly small mammals • Insects • Birds • Reptiles → **LI**	• Partial migration in autumn and winter to southern Europe (depending on weather conditions) → **LI**
Golden eagle (*Aquila chrysaetos*)	• Eastern Europe^{AD} • Northern Europe^{AD} • Southern Europe^{AD} • Western Europe^{AD} (only alpine)	• Mainly terrestrial → **AD**	• Active hunter • Facultative scavenger (enhanced during autumn/-winter) • **AD**	• Mainly medium-sized (game-) mammals • Livestock and large game carcasses → **AD**	• Resident (but sub-adults might show dispersal in Northern Europe) → **AD**

in north-east Europe. This limits their suitability for pan-European monitoring.

Although primarily a species that feeds through aquatic food webs, the white-tailed sea eagle (*Haliaeetus albicilla*) also preys on and scavenges game species (Table SI-4). It has been widely used in ecotoxicological studies across Europe (Gómez-Ramírez et al., 2014) and, like golden eagles, suffer from Pb intoxication through ingestion of Pb ammunition in game species (Helander et al., 2009; Krone et al., 2009; Nadjafzadeh et al., 2013). White-tailed sea eagles are mainly distributed in northern and eastern Europe, but are absent in large parts of Europe (BirdLife International, 2019). Thus, they did not meet our selection criteria for widespread distribution and were not included per se in our candidiate short-list (Table 1). However, it could perhaps be used in combination with the golden eagle. This would have the benefit of increasing likely sample availability in areas where golden eagles are absent in western (Germany and non-alpine habitats in Austria), eastern (Czech Republic and parts in Poland and Hungary) and northern (Iceland) Europe (BirdLife International, 2019). However, neither species is present in southern parts of the UK, Ireland, Benelux and non-montane regions of France (BirdLife International, 2019).

One difficulty in using a combined golden eagle/white-tailed sea eagle approach for monitoring Pb is that exposure and accumulation is not necessarily directly comparable across the two species. White-tailed sea eagles are mixed food web feeders, predominantly forage on fish, and compared with golden eagles, take more avian game such as waterfowl (Tables SI-3 and SI-4). Liver Pb concentrations were found to be lower in white-tailed eagles than golden eagles from the same area in Norway (Table SI-8). Such inter-species differences in exposure might be minimised by only sampling those individuals that die in winter, when both species frequently scavenge game animals (Halley and Gjershaug, 1998; Nadjafzadeh et al., 2016). In addition, stable isotope signatures such as $\delta^{13}C$ and $\delta^{34}S$ which can be used to determine the likely habitat (aquatic vs. terrestrial) from which prey are taken (Eulaers et al., 2014; Kelly, 2000), could be used to screen samples so that only individuals feeding predominantly on terrestrial prey were included in any monitoring programme.

In summary, pan-European monitoring for Pb using raptors is likely best served using either the common buzzard or the golden eagle (alone or in combination with the white-tailed sea eagle). Use of either species has advantages and disadvantages that need to be weighed against the primary aims of the monitoring programme. For instance, use of the common buzzard may be most suitable where the primary aim is to track temporal changes in Pb contamination at a European scale. The high abundance of this species and its widespread distribution throughout Europe would help ensure the availability of adequate samples. However, use of the golden eagle would perhaps be better where the aim is to identify spatial differences in exposure or identify the likelihood of toxic effects – the foraging behaviour, territoriality and accumulation of high residues in golden eagles are all beneficial traits for such monitoring.

4.1.2. Mercury (Hg)

The main exposure route to Hg for vertebrate birds and mammals in aquatic and terrestrial food webs is dietary exposure (Kidd et al., 2012). We focused on the terrestrial exposure of Hg within this analysis and selected only species that predominantly feed on terrestrial food webs. We considered even partial migration and a preference for natural/montane habitats as exclusion criteria (Table SI-9). This was to ensure that monitoring could identify local anthropogenic emissions within countries, which can elevate Hg burdens in raptors (Badry et al., 2019). Since Hg has shown to biomagnify in food webs, correction of trophic level using $\delta^{15}N$ (Jardine et al., 2006; Kelly, 2000) may be needed to company residue analysis so as to untangle the effects on exposure of intra-species differences in foraging. By coupling these criteria to those for distribution and applying then to the species listed in Table SI-3, we compiled a candidate species shortlist of one raptor and four owl species: northern goshawk (*Accipiter gentilis*), tawny owl (*Strix aluco*), Eurasian eagle owl (*Bubo bubo*), barn owl (*Tyto alba*) and little owl (*Athene noctua*) (Table 2). Each of these species has traits that impact their suitability for pan-European monitoring of Hg in the terrestrial environment.

The northern goshawk forages mainly on avian prey, including other raptors, and on small mammals (Table SI-3). It generally favours forest as breeding habitat but hunts in farmland and has also started to breed in urban areas (Table SI-3). Northern goshawks are generally considered resident but some individuals, such as juveniles in Fennoscandia, disperse (Table SI-3). Nevertheless, due to their widespread distribution, sedentary behaviour and well-known ecology, northern goshawks are considered by others as suitable sentinels of environmental pollution in terrestrial ecosystems within Europe (Dolan et al., 2017; Eulaers et al., 2013; Martínez et al., 2012).

The tawny owl mainly forages on small mammals, in particular small rodents, as well as on birds and hunts over a wide-range of habitats including farmland, forest patches and urban areas (Table SI-3). They are widely distributed within Europe although absent in northern parts of Fennoscandia and Iceland (BirdLife International, 2019). Due to their territoriality, residency, abundance and the fact that non-destructive samples are easily obtained from individuals in nest boxes, they have been frequently used as sentinels for metal and trace element contamination, even at their most northern distribution range (Bustnes et al., 2013; Carneiro et al., 2015; García-Seoane et al., 2017).

The suitability of the other owl species for pan-European monitoring is more limited, largely because of restricted distribution or migration. The Eurasian eagle owl takes the largest prey (Comay and Dayan, 2018), mainly mammals but also birds including raptors (Lourenço et al., 2015). It inhabits forest patches and agricultural habitats across Europe (Table SI-3). However, its distribution is irregular and it is absent in the UK, Ireland, the Netherlands and Iceland as well as in parts of France, Poland and Hungary (BirdLife International, 2019). This limits its capacity to act as sentinel for pan-European monitoring. Nevertheless, this species has been used as a sentinel for regional pollution

Table 2
Key traits of shortlisted candidate species for pan-European monitoring of terrestrial Hg. A complete list of traits and species with associated references can be found in Table SI-3 and the assessment of the criteria as suitable for terrestrial Hg monitoring is indicated in Table SI-9. Overall suitability is indicated for each criterion except for distribution where individual suitability is given in the superscript of each main region. AD = advantageous criterion and LI = limiting criterion for pan-European Hg monitoring.

Species	Distribution	Habitat	Migration
Northern Goshawk (*Accipiter gentilis*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Ireland, Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Forest habitats • Forest patches • Rarely urban habitats → **AD**	• Resident (but juvenile dispersal might occur in Fennoscandia) → **AD**
Tawny owl (*Strix aluco*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Ireland, Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Wide-habitat niche • Urban habitats • Farmland with patched forest • Forest habitats → **AD**	• Resident → **AD**
Eurasian eagle owl (*Bubo bubo*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except UK, Ireland and Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Forest patches • Agricultural habitats • Open habitats → **AD**	• Resident → **AD**
Barn owl (*Tyto alba*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except Fennoscandia and Estonia) • Southern Europe^{AD} • Western Europe^{AD}	• Farmland habitats • Urban habitats → **AD**	• Resident → **AD**
Little owl (*Athene noctua*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except Fennoscandia, Ireland, Estonia) • Southern Europe^{AD} • Western Europe^{AD} (except alpine regions)	• Open farmland habitats → **AD**	• Resident → **AD**

studies (Gómez-Ramírez et al., 2019; Langford et al., 2013) and is known to bioaccumulate Hg (Broo and Odsjö, 1981; Espín et al., 2014). Barn owls predominantly feed on rodents in farmland habitats and are considered resident once they start breeding (Table SI-3). Although widely distributed, they are absent in Iceland and Fennoscandia, Estonia, alpine regions, and in parts of Romania and Bulgaria (BirdLife International, 2019). Finally, the little owl is more insectivorous than the other candidate owls (Comay and Dayan, 2018) but predominantly eats small mammals and birds (Table SI-3). The little owl is resident and prefers open agricultural landscapes, but, like the barn owl, is absent from Fennoscandia, Iceland, Estonia, alpine regions and Ireland (Table SI-3; BirdLife International, 2019).

Overall, the species listed in Table 2 generally meet key criteria for pan-European monitoring of Hg in the terrestrial environment. On the basis of selecting widespread species that do not migrate, tawny owl and northern goshawk may be the most suitable sentinels but there are two major advantages of the tawny owl. The first is that tawny owls occupy a large variety of different habitats, thereby facilitating assessment of habitat influences on Hg exposure. The second is that tawny owls are far more abundant with 535,000–939,000 breeding pairs in Europe compared with 166,000–220,000 for northern goshawks (BirdLife International, 2017). Northern goshawk might be the species of choice for monitoring particularly in areas of northern Fennoscandia due to its broader distribution in this region compared with that of tawny owls (BirdLife International, 2019). Interestingly however, although liver Hg concentrations were higher in northern goshawks than in tawny owls in Belgium, liver Hg concentrations in birds from Norway and Spain (Table SI-10) and feather Hg concentrations in individuals from Germany, Sweden and Spain were generally comparable in the two species (Table SI-11). Models for Hg deposition have reported highest deposition rates to be in central Europe and in localised regions in the UK (Lee et al., 2001). This is consistent with differences in Hg levels for both species for individuals from Germany, Belgium and UK compared with birds from Spain and Norway (Tables SI-10 and SI-11), which underlines their suitability for Hg biomonitoring. However, more studies using higher sampling numbers are needed to confirm this pattern, especially since local effects, such as the past use of alkyl-Hg in agriculture, might have resulted in elevated Hg levels in tawny owls from Sweden (Table SI-11).

4.2. Anticoagulant rodenticides (ARs)

A main factor associated with secondary exposure to ARs are a specialisation on rodent prey (López-Perea and Mateo, 2018), and so species that frequently forage on small mammals were shortlisted as the best candidate sentinel species. Facultative scavenging, because of increased likelihood of feeding on acutely poisoned prey was considered an advantageous trait and therefore obligate predation (species not known to scavenge) was considered a limiting factor. Use of habitats where ARs are commonly applied is associated with higher levels of exposure (López-Perea and Mateo, 2018) and so utilisation of anthropogenic land uses (habitats where ARs are most likely to be used) was also considered an advantageous trait. Limited distribution, lack of preference for mammalian prey, restricted habitat utilisation and partial migration were all considered traits that limited the suitability of the species for pan-European AR monitoring (Table SI-12). By applying these criteria, the list of all potential candidate species (Table SI-3) was reduced to the common buzzard, common kestrel, tawny owl, barn owl, Eurasian eagle owl, little owl and long-eared owl (Table 3). While all of these species have traits that make them suitable for pan-European monitoring of ARs, they also each have traits that limit their usefulness.

Although a generalist, the common buzzard predominantly forages on rodents when they are abundant and also scavenges rodents and other small mammals (Table SI-3 and references therein). These characteristics predispose this species to ingest sub-lethal AR concentrations in live prey and likely higher residues in poisoned rodents (López-Perea and Mateo, 2018). Common buzzards have been used in Europe to monitor both rodenticide exposure and poisoning (Coeurdassier et al., 2014; López-Perea and Mateo, 2018; Shore et al., 2006) but their partial migration in northern Europe limits their suitability for spatially-resolved pan-European monitoring of AR exposure. Although, the red kite (*Milvus milvus*), another scavenger, is particularly at risk of secondary AR exposure and

Table 3
Key traits of shortlisted candidate species for pan-European monitoring of ARs. A complete list of traits and species with associated references can be found in Table SI-3 and the assessment of the criteria as suitable for monitoring ARs is indicated in Table SI-12. Overall suitability is indicated for each criterion except for distribution where individual suitability is given in the superscript of each main region. AD = advantageous criterion, LI = limiting criterion for pan-European AR monitoring.

Species	Distribution	Foraging trait	Diet	Habitat	Migration
Tawny owl (*Strix aluco*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Ireland, Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Small mammals Insects • Small birds → **AD**	• Wide-habitat niche • Urban habitats • Farmland with patched forest → **AD**	• Resident → **AD**
Common buzzard (*Buteo buteo*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter • Facultative scavenger → **AD**	• Mainly small mammals • Insects, Reptiles, Birds → **AD**	• Agricultural habitats • Forest mosaics • Rarely urban habitats → **AD**	• Partial migration → **LI**
Common kestrel (*Falco tinnunculus*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Mainly rodents • Avian prey • Invertebrates → **AD**	• Agricultural habitats • Urban habitats → **AD**	• Partial migration (mainly to SE but also to northern Africa) → **LI**
Eurasian eagle owl (*Bubo bubo*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except UK, Ireland and Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Mainly mammals • Avian prey → **AD**	• Forest patches • Agricultural habitats • Open habitats → **AD**	• Resident → **AD**
Barn owl (*Tyto alba*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except Fennoscandia and Estonia) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Mainly rodents → **AD**	• Farmland habitats • Urban habitats → **AD**	• Resident → **AD**
Little owl (*Athene noctua*)	• Eastern Europe^{AD} • Northern Europe^{LI} (except Fennoscandia, Ireland, Estonia) • Southern Europe^{AD} • Western Europe^{AD} (except alpine regions)	• Active hunter → **LI**	• Small mammals • Invertebrates → **AD**	→ Open farmland habitats → **AD**	→ Resident → **AD**
Long-eared owl (*Asio otus*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Mainly small mammals • Birds → **AD**	• Forest patches • Agroforestry → **AD**	• Partial migration in Fennoscandia → **LI**

poisoning (Berny and Gaillet, 2008; Coeurdassier et al., 2012; Molenaar et al., 2017; Walker et al., 2018), it was not included as a candidate species for pan European monitoring because it is mostly absent in northern Europe and is migratory.

The common kestrel preys largely on small mammals but is not thought to scavenge extensively (Table SI-3), has a wide European distribution across agricultural and urban landscapes where ARs are widely used, and is known to be exposed to ARs (López-Perea and Mateo, 2018). Common kestrels are therefore likely to be generally suitable for monitoring exposure to ARs but they partially migrate to southern Europe (Holte et al., 2016), numbers are declining (BirdLife International, 2017) and they are less abundant than common buzzards (estimated European population of 409,000–603,000 pairs compared with 814,000-1,390,000 pairs of common buzzards; Birdlife International, 2017).

Of the owls, the tawny owl and barn owl have both been used for short and long-term monitoring of AR exposure in Europe (Geduhn et al., 2016; López-Perea and Mateo, 2018; Shore et al., 2019). They are abundant and often killed in traffic collisions, so carcasses are readily available for collection and subsequent analysis (Walker et al., 2008b). The barn owl however is more restricted than the tawny owl in habitat use, tending to be found primarily in agricultural landscapes, and is absent from parts of Europe. The Eurasian eagle owl and little owl can also be exposed to ARs (López-Perea and Mateo, 2018), but like the barn owl, both species are absent from areas of Europe (Table 3). The long-eared owl is similar to the barn owl in that it is a rodent specialist but is restricted in its habitat use, favouring agroforestry habitats (Table SI-3); it has been less widely monitored for ARs across European countries compared with, for example, common buzzards or tawny owls (López-Perea and Mateo, 2018).

On the basis of our proscribed methodology, the likely best candidate species for AR exposure monitoring at a European scale were the common buzzard and the tawny owl (Table 3). Another factor that may be important is whether sample mass for chemical analyses is a critical factor – the average mass of livers in non-starved individuals found dead in the UK between 2002 and 2019 were greater in common buzzard than tawny owls (mean ± SD of 16.9 ± 5.0 g (n = 284) vs 10.7 ± 2.9 g (n = 392); *Shore-pers. comm.*). Although common buzzards, as facultative scavengers, might be expected to accumulate higher liver AR residues than tawny owls, average residues in the two species, where measured, appear to be broadly similar (Table SI-13). Thus, facultative scavenging per se may in fact not be a more advantageous trait than active hunting when selecting a sentinel for monitoring AR exposure at a European scale. Furthermore, the partial migration of common buzzards in central and northern Europe (Table SI-3) is likely to be a significant issue if a key aim of monitoring is to examine spatial variation in exposure. This cannot be overcome, as suggested for Pb, by restricting carcass selection to the breeding season because liver half-lives can be months for some ARs (Vandenbroucke et al., 2008), longer than for Pb. Although the tawny owl may not be as widely or heavily exposed to ARs as some other species in Europe (López-Perea and Mateo, 2018; Walker et al., 2008b), its traits of feeding widely on rodents, residency and utilisation of multiple habitats, coupled with widespread distribution, abundance and availability/accessibility of carcasses, make it the most suitable species for monitoring pan-European spatio-temporal trends in AR exposure.

4.3. Pesticides

There are a large number of legacy and current-use pesticides that may potentially be of interest for pan-European monitoring. This diversity makes it difficult to select a single or small number of sentinel species that are best suited for monitoring this group of compounds as a whole. The current work focusses on selecting candidate species to evaluate outcomes of chemical, including PPP, regulation. However, raptors are unlikely to be first choice sentinels for monitoring trends in pesticides that do not bioaccumulate/biomagnify through food webs, as widespread significant exposure at high trophic levels is unlikely. However, birds of prey have been widely used to monitor environmental trends in legacy pesticides, such as organochlorine insecticides (Helander et al., 1982; Newton, 1986; Ratcliffe, 1967).

Exposure to pesticides is mainly related to foraging within agricultural settings such as farmlands, agroforestry and orchards. Active foraging is also likely to be an advantageous trait over facultative scavenging since exposure in scavengers may include individuals subject to deliberate and illegal persecution through the use of poison baits (Table SI-14). Although information on such persecution is important for forensic and toxico-surveillance studies, it is outside the scope of the current study. Finally, we also selected species that predominantly feed on rodents. Although feeding on avian prey is not a trait that prevents or limits bioaccumulation of pesticides (Herzke et al., 2002; Jaspers et al., 2006; Newton, 1986), feeding on relatively sedentary rodents and invertebrates means that exposure of prey and predator will broadly be co-located. The presence of birds migrating along the African-Eurasian flyway in the diet of sedentary raptors in Europe can introduce some uncertainty in the origin of contaminants. This can be avoided if the monitored raptors feed on sedentary prey. We used these traits and our European distribution as selection criteria to reduce the candidate species list for pesticide monitoring to common buzzard, common kestrel, Eurasian eagle owl, barn owl, little owl, long-eared owl and tawny owl. With the exception of favouring active hunting over facultative scavenging, the selection of species was the same as for ARs, reflecting that exposure to both pesticides and ARs is effectively largely influenced by the same ecological traits.

Given the shortlist of species was the same for pesticides as for ARs, we used the same logic as for ARs to eliminate Eurasian eagle owl, barn owl and little owl on the grounds of irregular species distribution, and common buzzard, common kestrel and long-eared owl because of partial migration. This left the tawny owl as the only species that met all the outlined criteria necessary for a sentinel suited for assessing spatio-temporal trends in exposure to pesticides (Table 4).

Although our selection criteria identified the tawny owl as potentially the most suitable raptor for biomonitoring PPPs, selection of a single species is problematic. This is because of the diversity of PPPs compounds and their varied environmental behaviour. Even if just bioaccumulative compounds such as the legacy organochlorine insecticides are considered, the tawny owl was used to monitor these compounds (for example; Table SI-15) but so were a wide range of other raptor species, and eggs were often analysed as well as tissues (Blus, 2011; Elliott and Bishop, 2011). As far as we are aware, there has been no over-arching evaluation of the relative sensitivities of different raptor species for monitoring temporal and spatial trends in OC insecticides. Such an analysis may provide a clearer picture of which raptor species may prove the most effective for monitoring trends of bioaccumulative pesticides. In terms of more current pesticides such as neonicotinoids, we found few studies that reported residues in raptors (Byholm et al., 2018; Taliansky-Chamudis et al., 2017). This likely reflects the move towards preventing registration of PPPs with high bioaccumulation potential and lower-trophic species may prove more useful sentinels for tracking changes in wildlife exposure (Bonneris et al., 2019; Bro et al., 2015). However, raptors that nest on the ground in agricultural habitats, such as Montagu's harrier (*Circus pygargus*) and western marsh harrier (*Circus aeruginosus*), may be useful indicators of risk from direct exposure (Cardador et al., 2012; Espín et al., 2018). Both are long-distance migrants but analysis of blood from nestlings or addled eggs might still provide important information for regional exposure within agricultural areas.

4.4. Medicinal products (MPs)

Terrestrial environmental emissions of MPs have been related to losses from human and animal manure fertilizers in arable and pasture areas, from livestock/poultry production units and from landfills (Arnold et al., 2014; Sarmah et al., 2006; Shore et al., 2014). Scavenging on treated livestock and other medicated animals, as exemplified by the effects of non-steroidal anti-inflammatory drugs (NSAIDs) on Asian vultures (Oaks et al., 2004), is also a key direct point of entry of VMPs into wildlife food webs (Blanco et al., 2017; Cuthbert et al., 2014; Margalida et al., 2014). Facultative scavenging and utilisation of agricultural habitats were therefore regarded as key traits facilitating exposure to MPs but, unlike with previous contaminant groups, long-distance and partial migration were not considered reasons to exclude species as candidates for pan-European monitoring (Table SI-16). This is because MPs typically have short half-lives in tissues of hours to days (Hutchinson et al., 2014) and so detection of residues in carcasses is likely to reflect recent exposure. Using these criteria, candidate species for monitoring MPs at a pan-European scale included common buzzard, common kestrel, Eurasian eagle owl, barn owl, little owl, long-eared owl and tawny owl. This is the same short-list that was derived for anticoagulant rodenticides (Table 3) and pesticides.

Of these species, the common buzzard meets the highest number of advantageous criteria for pan-European monitoring of MPs (Table 5). It is potentially exposed to MPs, particularly VMPs, through multiple routes because it actively forages in agricultural settings and is a facultative scavenger of livestock carcasses (Table 5). Other species that similarly scavenge include the red kite and also the black kite (*Milvus migrans*) which forages near freshwater habitats as well as dump sites (Table SI-3). However, both red and black kites are mainly absent in Fennoscandia (BirdLife International, 2019). Thus, these species may be suitable for monitoring MPs over large spatial ranges but their absence from the northern Europe region excluded them from the shortlist of candidate pan-European biomonitors of MPs.

Table 4
Candidate species for pan-European monitoring of pesticides. A complete list of traits and species with associated references can be found in Table SI-3 and the assessment of the criteria as suitable for monitoring pesticides is indicated in Table SI-14. Overall suitability is indicated for each criterion except for distribution where individual suitability is given in the superscript of each main region. AD = advantageous criterion and LI = limiting criterion for pan-European pesticide monitoring.

Species	Distribution	Foraging trait	Habitat	Migration
Tawny owl (*Strix aluco*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Ireland, Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **AD**	• Wide-habitat niche • Urban habitats • Farmland with patched forest • Forest habitats → **AD**	• Resident → **AD**

Table 5
Candidate species for pan-European monitoring of MPs. A complete list of traits and species with associated references can be found in Table SI-3 and the assessment of the criteria as suitable for monitoring of MPs is indicated in Table SI-16. Overall suitability is indicated for each criterion except for distribution where individual suitability is given in the superscript of each main region. AD = advantageous criterion and LI = limiting criterion for pan-European MP monitoring.

Species	Distribution	Foraging trait	Habitat	Migration
Common buzzard (*Buteo buteo*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter • Facultative scavenger → **AD**	• Agricultural habitats • Forest mosaics • Rarely urban habitats → **AD**	• Partial migration in autumn and winter to southern Europe (depending on weather conditions) → **AD**
Common kestrel (*Falco tinnunculus*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Agricultural habitats • Urban habitats → **AD**	• Partial migration (mainly to SE but also to northern Africa) → **AD**
Tawny owl (*Strix aluco*)	• Eastern Europe^{AD} • Northern Europe^{AD} (except Ireland, Iceland) • Southern Europe^{AD} • Western Europe^{AD}	• Active hunter → **LI**	• Wide-habitat niche • Urban habitats • Farmland with patched forest → **AD**	• Resident → **AD**

Of the non-scavenging species, tawny owls and common kestrels had a similar number of favourable traits for MP monitoring as did the common buzzard, if exposure from scavenging livestock carcasses was not a focal interest (Table 5). However tawny owls may be preferred because of their greater abundance and the current stability of their numbers (BirdLife International, 2017). Other non-scavengers such as the Eurasian eagle owl, barn owl, little owl, and long-eared owl had similar favourable traits to tawny owls for monitoring MP but, as with other compounds, were excluded as pan-European biomonitors because of their limited species distribution. Further non-scavenging species like Montagu's harrier and western marsh harrier both breed in agricultural habitats and might therefore be directly exposed to MPs from manure fertilization (Table SI-3). However, as discussed previously for pesticides, major limitations for using harriers include their absence in most parts of northern Europe. Furthermore, their abundance is low in comparison with species such as the common buzzard (BirdLife International, 2017).

According to our proscribed methodology, the common buzzard appears to be the key sentinel species meeting the highest number of advantageous criteria, although tawny owl and common kestrel may also be suitable if exposure from scavenging was not a focal interest. However, we found no studies that reported MP residues in these species. This might be associated with low detection rates due to rapid metabolism of residues in tissues, although our knowledge of metabolic pathways in non-mammalian species is poor (Hutchinson et al., 2014), and may also reflect that screening of feathers for rapidly-metabolised pharmaceuticals (Whitlock et al., 2019), may not be commonplace. Furthermore, many wildlife studies on MPs have focussed on NSAIDs and concentrated on those species most at risk.

NSAIDs are poorly metabolised within their target organisms (Cuthbert et al., 2014; Sarmah et al., 2006) and this leads to direct exposure in scavengers that forage on dead livestock and other medicated species (Margalida et al., 2017). Monitoring of NSAIDs in vultures in Europe is of prime interest because exposure to these compounds, principally diclofenac, has led to massive population declines in *Gyps* vulture populations elsewhere (Margalida et al., 2014; Oaks et al., 2004). Such monitoring provides important information that underpins and informs risk management. There are four vulture species resident within Europe, namely the bearded vulture (*Gypaetus barbatus*), cinereous vulture (*Aegypius monachus*), Egyptian vulture (*Neophron pernopterus*) and Eurasian griffon vulture (*Gyps fulvus*). All four forage on livestock within montane regions, and this is likely to be their main route of exposure to NSAIDs and to VMPs generally (Cuthbert et al., 2014), although the Egyptian vulture also frequently feeds on landfills (Table SI-5) which can contain HMPs. These vulture species do not have widespread European distributions and are mainly restricted to montane/alpine regions (Table SI-5), and so are not suitable monitors for pan-European monitoring of MPs. However, monitoring of NSAIDs in vultures across all the areas of Europe where they occur is merited for conservation and risk management purposes.

5. Conclusions

Our study has focussed on biomonitoring the European terrestrial environment for a set of priority pollutant groups through measurement of residues in tissues obtained from the carcasses of raptors found dead. Traits that we argue may be key are widespread distribution across the monitoring area, feeding ecology and habitat selection. Overall, for the geographical region, compound groups and monitoring techniques that we considered, the common buzzard and tawny owl were amongst, if not the most, suitable species. Both are abundant and widely distributed across Europe (BirdLife International, 2017). Although used in contaminant studies in Europe (Gómez-Ramírez et al., 2014), they are by no means the most intensively monitored species. While choice of one over the other of these two species may depend upon how important scavenging is considered as an exposure pathway and whether partial migration (common buzzard) is likely to compromise the aims of any programme, the lack of widespread contaminant monitoring in these two species suggests that their utility as sentinels for environmnetal pollutaion is not generally recognised. Furthermore, although we focussed here on monitoring across Europe, the trait-based approach that we used to identify the most suitable species could be easily applied to other continents and contaminants. Such analyses may equally reveal species in those regions that have been under-appreciated as biomonitors of pollution.

Our study, not surprisingly, does not suggest that a single species is ideal for monitoring exposure to all different groups of priority pollutants. For example, we concluded that the golden eagle, perhaps in combination with the white-tailed sea eagle, may be better than common buzzard for monitoring exposure to, and particularly toxic effects from, Pb in ammunition. However, such combined monitoring is potentially complex as confounding factors include interspecific differences in pharmacokinetics or seasonal variation in scavenging. We also suggest that when northern Fenno-Scandinavian habitats may be an important component of biomonitoring, the northern goshawk could be a better monitor than tawny owl for terrestrial Hg, reflecting the lack of tawny owls in those northern areas. However, there are always likely to be trade-offs in terms of balancing completeness of spatial coverage against likely widespread availability of carcasses for monitoring. Even when a single species appears the most suitable biomonitoring

candidate, there may be significant intra-specific variation in contaminant exposure because individuals have different diets (Palma et al., 2005). Such effects may be marked when individuals feed at different trophic levels (Badry et al., 2019; Elliott et al., 2009). Stable isotopes values of nitrogen ($\delta^{15}N$), carbon ($\delta^{13}C$) and sulphur ($\delta^{34}S$) can be used as proxies to control for dietary plasticity and trophic position in raptors (Eulaers et al., 2014; Eulaers et al., 2013) and we recommend that they are routinely measured along with the contaminants. This would help refine interpretation of apparent spatial and temporal trends in contaminants, particularly if accompanied by information on the isotopic signatures of common prey species.

In conclusion, the present study suggests that the selection of candidate species for continental-scale monitoring of exposure to a range of contaminants can be reduced to very few raptor species. This may be true for many regions of the world, not just Europe, and a trait-based evaluation (as used here) of the suitability of raptors as biomonitors across other continents may prove worthwhile. In our study, the common buzzard and tawny owl appear to be the two most suitable species for a range of contaminant groups. A logical conclusion from our study is that, if common buzzard and tawny owl are both broadly suitable for monitoring pan-European spatio-temporal trends in exposure, then any such trends will be similar in both species. We are not aware of datasets which we can use to test this prediction or assess the relative power of monitoring in both species to detect such trends. This is a key data-gap. Pilot monitoring studies involving harmonised sampling across Europe in these two species are merited.

Funding

A short-term scientific mission was awarded to Alexander Badry by the European Raptor Biomonitoring Facility, COST Action (CA16224) to support his work. This study has also been supported by the LIFE project LIFE APEX (LIFE17 ENV/SK/000355) which supported the costs of the senior author (RFS) in developing this work.

Declaration of competing interest

The authors declare no conflicts of interest.

Acknowledgements

All authors gratefully acknoweldge the inputs of all the participants at the European Raptor Biomonitoring Facility workshop held in Thessaloniki, 2019. We also thank Lisa Giese for the support with the graphical abstract.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.139198.

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Chapter 3: Linking landscape composition and biological factors with exposure levels of rodenticides and agrochemicals in avian apex predators from Germany

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Published in Environmental Research (2021)
- https://doi.org/10.1016/j.envres.2020.110602

Detailed author contributions:

OKro, AB and GT conceptualised the work. OKro was responsible for the project administration, funding acquisition and conducted the necropsies. The chemical analysis was conducted in collaboration with the Julius Kühn-Institut in Berlin, where AB conducted his work in the laboratory of DS. AB was responsible for conducting recovery tests, sample preparation, extraction, and data evaluation. DS established the analytical methodologies and supervised the analysis and data evaluation. The manuscript was drafted by AB with input from all co-authors. AB conducted the statistical analysis and visualisations.

Environmental Research 193 (2021) 110602

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Linking landscape composition and biological factors with exposure levels of rodenticides and agrochemicals in avian apex predators from Germany

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ARTICLE INFO

Keywords:
Raptors
Agriculture
Rodenticides
Medicinal products
Pesticides

ABSTRACT

Intensification of agricultural practices has resulted in a substantial decline of Europe's farmland bird populations. Together with increasing urbanisation, chemical pollution arising from these land uses is a recognised threat to wildlife. Raptors are known to be particularly sensitive to pollutants that biomagnify and are thus frequently used sentinels for pollution in food webs. The current study focussed on anticoagulant rodenticides (ARs) but also considered selected medicinal products (MPs) and frequently used plant protection products (PPPs). We analysed livers of raptor species from agricultural and urban habitats in Germany, namely red kites (MIML; *Milvus milvus*), northern goshawks (ACGE; *Accipiter gentilis*) and Eurasian sparrowhawks (ACNI; *Accipiter nisus*) as well as white-tailed sea eagles (HAAL; *Haliaeetus albicilla*) and ospreys (PAHA; *Pandion haliaetus*) to account for potential aquatic exposures. Landscape composition was quantified using geographic information systems. The highest detection of ARs occurred in ACGE (81.3%; n = 48), closely followed by MIML (80.5%; n = 41), HAAL (38.3%; n = 60) and ACNI (13%; n = 23), whereas no ARs were found in PAHA (n = 13). Generalized linear models demonstrated (1) an increased probability for adults to be exposed to ARs with increasing urbanisation, and (2) that species-specific traits were responsible for the extent of exposure. For MPs, we found ibuprofen in 14.9% and fluoroquinolones in 2.3% in individuals that were found dead. Among 30 investigated PPPs, dimethoate (and its metabolite omethoate) and thiacloprid were detected in two MIML each. We assumed that the levels of dimethoate were a consequence of deliberate poisoning. AR and insecticide poisoning were considered to represent a threat to red kites and may ultimately contribute to reported decreased survival rates. Overall, our study suggests that urban raptors are at greatest risk for AR exposure and that exposures may not be limited to terrestrial food webs.

1. Introduction

Intensification of agricultural practices resulted in a substantial decline of Europe's farmland bird populations during the past 50 years (Busch et al., 2020; Donald et al., 2001; Emmerson et al., 2016). Besides factors such as declined landscape heterogeneity and habitat fragmentation, the increased use of agriculturally related chemicals was identified as a driver of population declines (Emmerson et al., 2016; Tscharntke et al., 2005). Exposure to agriculturally related chemicals has been shown to negatively impact populations of many wildlife species including raptors (Köhler and Triebskorn, 2013; Shore and Taggart, 2019). However, the application of pesticides is not restricted to agricultural habitats as anticoagulant rodenticides (ARs) are frequently used in urban areas to control rodent populations (López-Perea and Mateo, 2018). Certain pesticides have been classified as being persistent, bioaccumulative, or toxic (PBT) and raptors have shown to be particularly sensitive to compounds that bioaccumulate or biomagnify (Gómez-Ramírez et al., 2019; Shore and Taggart, 2019). Raptors are typically apex predators of high conservation value that are frequently used sentinels for contamination in food webs (Gómez-Ramírez et al., 2014). The current study focusses on chemical pollution arising from agricultural intensification and urbanisation such as ARs, medicinal products (MPs) and plant protection products (PPPs), which were identified as current threats for raptors in Europe (Badry et al., 2020).

Many ARs are classified as PBT substances and are divided into first-

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https://doi.org/10.1016/j.envres.2020.110602
Received 18 September 2020; Received in revised form 3 December 2020; Accepted 4 December 2020
Available online 8 December 2020

generation ARs (FGARs) and second-generation ARs (SGARs) (Elliott et al., 2016; Regnery et al., 2019a). SGARs are more persistent in animal tissues than FGARs and have been developed as more acute toxic substances due to increasing resistance of rodents against FGARs (Eason et al., 2002; Rattner et al., 2014b). Both FGARs and SGARs inhibit the synthesis of clotting factors in the liver, which represents a risk for many wildlife species as the clotting system is highly conserved among vertebrates (Eason et al., 2002; Rattner et al., 2014b). Non-target wildlife species such as raptors are indirectly exposed to ARs due to the delayed death of poisoned rodents taken alive as well as through scavenging on carcasses (López-Perea and Mateo, 2018). Besides agricultural and urban applications, ARs are frequently used in sewage systems, which has resulted in fish exposures in Germany (Kotthoff et al., 2018; Regnery et al., 2019b). Due to their global use, high toxicity to vertebrate wildlife and potential to bioaccumulate in food webs, the current study had a large focus on AR exposure in avian top predators.

Other agriculturally related substance classes that have negatively impacted avian top predators in the past include MPs and PPPs. MPs are increasingly used as a result of an ageing human population and intensification of food production (Arnold et al., 2014; Shore et al., 2014). Environmental emissions of human medicinal products (HMPs) are associated with liquid waste effluents from domestic or hospital sewage whereas veterinary medicinal products (VMPs) enter the environment through livestock production and manure fertilisation (Arnold et al., 2014; Kümmerer, 2009; Shore et al., 2014). Even though risks for mammalian consumption are well characterised for MPs, much less data is available on birds (Shore et al., 2014). This can lead to fatal consequences as exemplified for the metabolism of the non-steroidal anti-inflammatory drug (NSAID) diclofenac in Gyps vultures (Oaks et al., 2004).

PPPs refer to pesticides i.e. insecticides, herbicides or fungicides that are used to protect agricultural crops. Persistent and bioaccumulative PPPs have been shown to negatively affect raptors (Helander et al., 1982; Ratcliffe, 1967) and residues of persistent PPPs in agricultural habitats are still detectable in raptors after their ban (Gómez-Ramírez et al., 2019). Besides chronic exposures, threats to raptors include deliberate pesticide abuses and wildlife poisoning (Berny et al., 2015; Coeurdassier et al., 2014). Even though currently applied PPPs are tested for PBT properties, usually under laboratory conditions, current legislation is lacking information on the ecological and landscape context (Schäfer et al., 2019). As a result, data on the actual exposure levels of currently registered PPPs to wildlife including apex predators is scarce.

The present study focuses on the analysis of livers from raptors that died in Germany, where agricultural intensification has shown to negatively impact farmland bird populations (Busch et al., 2020). We specifically focused on the red kite (MIML; *Milvus milvus*), a species of high conservation value for Germany as more than 50% of all worldwide breeding pairs live there (Heuck et al., 2013). Red kites are facultative scavengers in agricultural habitats and show a decline in survival, which was suggested to be related to agricultural intensification and pesticide poisonings (Katzenberger et al., 2019). Moreover, we included the northern goshawk (ACGE; *Accipiter gentilis*), a species that has recently established stable populations in urban areas such as Berlin as well as the Eurasian sparrowhawk (ACNI; *Accipiter nisus*) sampled in predominantly agricultural habitats to investigate AR exposure risks associated with avivorous trophic pathways (Vyas, 2017; Walker et al., 2015). Two aquatic species, namely the white-tailed sea eagle (HAAL; *Haliaeetus albicilla*), a facultative scavenger feeding on fish, waterbirds and game carcasses, as well as the osprey (PAHA; *Pandion haliaetus*), a migratory species feeding exclusively on fish were included as previous studies suggested potential AR exposure risks for fish-eating predators in Germany (Regnery et al., 2020a). Including species feeding on aquatic food webs further allows to account for agricultural runoffs and incomplete wastewater removals.

Monitoring and determining factors that influence exposures is crucial for understanding population declines and to inform chemicals management. Therefore, the current study specifically aims (i) to assess exposures of the investigated environmental pollutants among the different species and associated feeding guilds and, where applicable, to evaluate concentrations regarding toxicity thresholds, (ii) to model the influence of landscape composition and (iii) to model the influence of biometric and individual-level factors on the probability and extent of exposure.

2. Methods

2.1. Sampling and study areas

The study included a total of 186 birds of prey that died in Germany between 1996 and 2018. Most birds were found as carcasses and a few alive, which died within 24 h in veterinary clinics. Carcasses were frozen at −20 °C and thawed at room temperature for necropsy. A complete veterinary and parasitological investigation was conducted for all individuals (Krone, 2000). Most individuals in the study were apparently healthy and died from collisions or intraspecific fights but we also included individuals that died from poisonings or infections (Table SI-1). During necropsy, a liver aliquot of 1–1.5 g was derived from 42 red kites (1996–2019), 48 northern goshawks (1998–2018), 23 sparrowhawks (1996–2012), 60 white-tailed sea eagles (2004–2015) and 13 ospreys (2003–2016). We defined two age classes, five categories for the cause of death (similar to López-Perea et al., 2019) and three groups of nutrition condition based on the measurement/presence of subcutaneous fat tissue, fat in the body cavity and in the coronary sulcus (Table SI-1). Most samples (n = 149) originated from (sub-)adults with a minor proportion of juveniles (n = 36). GPS coordinates were manually assigned to samples that had only a written description of the location where a carcass was found. The majority of birds originated from the north of Germany (Fig. 1).

2.2. Selection of analytes

All currently registered ARs were analysed (brodifacoum, bromadiolone, chlorophacinone, coumatetralyl, difenacoum, difethialone, flocoumafen and warfarin). For MPs and PPPs, individual substances within the prioritised pollutant classes were selected based on the sales figures (BVL, 2017; Wallmann et al., 2018), the fate and behaviour, the general toxicity of the substances (Lewis et al., 2016) as well as the financial framework available for the realisation of the study. These criteria resulted in the selection of three fluoroquinolone antibiotics (ciprofloxacin, enrofloxacin and marbofloxacin), one sulfonamide antibiotic (sulfamethazine) as well as one pyrethroid (permethrin) and two NSAIDs (diclofenac and ibuprofen). For PPPs, eight herbicides, nine insecticides (+one metabolite) and 12 fungicides were selected for analysis (Table SI-2).

2.3. Sample extraction and analysis

The frozen liver aliquots were stored at −80 °C after arrival at the analytical laboratory and were thawed before analysis. The sample treatment is presented step by step in Table SI-3 (Geduhn et al., 2014). The liver tissues (0.3–1 g) were weighed in polypropylene tubes, spiked with a surrogate mixture for ongoing validation of analytical performance and subsequently homogenized in methanol/water (2:1) using an Ultra Turrax. After centrifugation, a saturated sodium chloride solution was added to the aliquots of the supernatant. The mixture was subsequently transferred to a diatomaceous earth column (ChemElut, Agilent) and completely absorbed. After 15 min, the analytes were eluted with dichloromethane. Aliquots were reduced to dryness and resuspended in internal standards for LC-MS/MS (methanol/water (1:1); Tables SI-4, SI-5and GC-MS/MS (acetonitrile; Tables SI-6, SI-7). The separation of analytes by LC was performed using four different methods: two

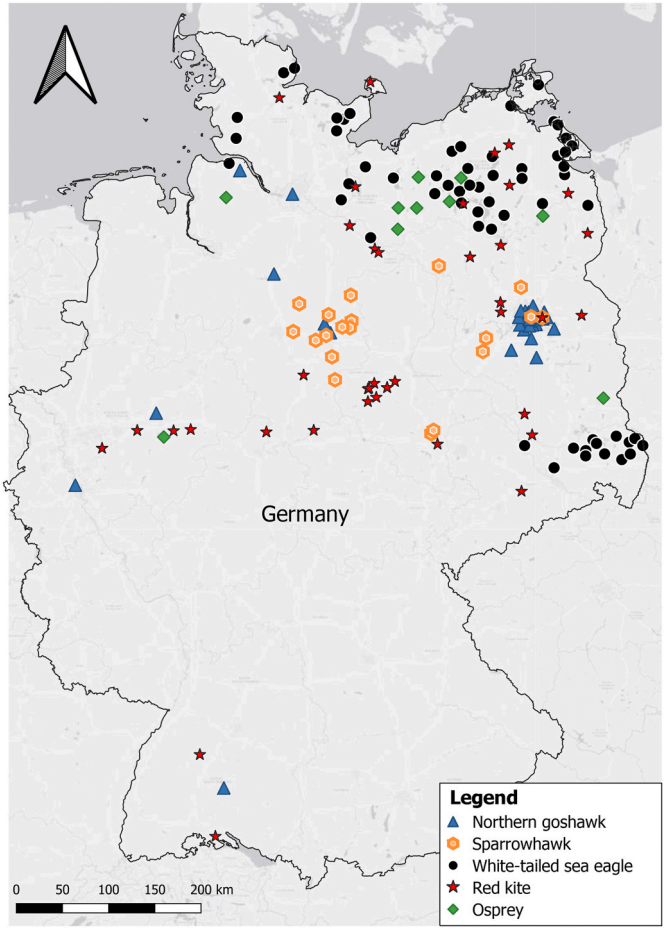

Fig. 1. Sampling locations of investigated birds of prey within Germany. Blue triangles to northern goshawks (ACGE), orange hexagons to sparrowhawks (ACNI), black dots refer to white-tailed sea eagles (HAAL), red stars to red kites (MIML) and green squares to ospreys (PAHA). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

reversed-phase columns, each with two different gradient programmes (Table SI-4). The measurement of analytes was performed with a QTRAP-Triple Quad Linear Ion Trap 6500+ (SCIEX) in electrospray ionisation mode. The identification and quantification of analytes were done with precursor – product ion – transition (Table SI-5). We used the linear ion trap mode with dynamic fill time to confirm the identity of a substance. A substance was accepted when its enhanced product ion spectra in the sample (with intensity > 500 cps) matched more than 80% of those in the matrix standards in the same sequence. The GC separation of the semi-volatile substances was done on a column with low polarity (Table SI-6). The qualification and quantification of the substances (pyrethroids) were carried out in two runs by electron impact ionisation mode and negative chemical ionisation mode of a TSQ Quantum GC XLS (Thermo Scientific). Two ion transitions were extracted in the selected reaction monitoring mode for each substance. A substance was confirmed when the ion ratio of the two ion transitions of the sample was within ±30% of the average of the reference standards in the same sequence. All analytes in all samples (LC and GC) were quantified against a matrix-matched standard and the criterion for the acceptance of the calibration curve was the correlation coefficient ($r^2 > 0.99$). The validation of the analytical procedure was checked by recovery tests using blank chicken liver. Sample preparation and extraction did not cause interferences in the blank liver samples. The reporting limit refers to the lowest calibration level with a signal to noise ratio >6:1 and relative standard deviation < 20% in the sequence (Table SI-2). The measured concentrations of the analytes were neither surrogate nor recovery corrected.

2.4. Statistical analysis

We conducted all statistical analysis in R version 3.6.3 (R Core Team, 2020) and set the threshold for the level of significance to $p = 0.05$. Graphical visualisations were generated using the Rpackage "ggplot2" (Wickham, 2016) and Inkscape 0.92.4.

2.4.1. Extraction of environmental variables

All land cover types defined by the Corine Land Cover 2018 (artificial structures, agricultural areas, forest and semi-natural areas, water bodies and wetlands; EEA, 2018) were extracted within circular buffer zones of 5 (i.e. 78 km^2) and 10 km (i.e. 314 km^2) around the location where a bird of prey was found to approximate potentially used foraging habitats (Badry et al., 2019). The contribution of the five land cover classes in the 10 km buffer zone is given in Tables SI–8. Artificial structures were used as a proxy for urbanisation since they mainly refer to urban-like features such as industrial units and urban fabrics (Kosztra et al., 2017). All land cover variables were extracted using QuantumGIS software version 3.10.2 (QGIS Development Team, 2020). To fit inter-dependent land cover data into statistical models, we summarise the information in a single variable by extracting the axis from either a principal component analysis (PCA) using the R-package "FactoMineR" (Lê et al., 2008), or from a detrended correspondence analysis (DCA) using the R-package "vegan" (Oksanen et al., 2013). Both methods used to create a synthetic variable from the land cover data resulted in similar results and effectively separated anthropogenic land cover types (artificial (urban) and agricultural areas) from non-anthropogenic land cover types (Figure SI-1) irrespective of the radius of the buffer zone selected. We selected the 10 km radius to minimise the risk of bias and relied on the PCA to approximate anthropogenic areas.

2.4.2. Anticoagulant rodenticides (ARs)

First, we built a generalized linear model (GLM) with logit link including all individuals for fitting exposure probability using the presence/absence of ARs as binary response (0/1) of a binomial distribution. Fixed factors included anthropogenic areas identified by PCA (Figure SI-1); sex (to observe potential differences in exposure for males and females); age class ("adult" and "juvenile"); year of death as well as the cause of death ("trauma": unspecific trauma and traffic collisions; "Pb-poisoning"; "other poisonings": such as insecticide poisonings; "infection"; "unclear", and "other": such as intraspecific fight, starvation or predation; Table SI-1). Nine individuals had missing information for one of the fixed factors and were thus excluded by the GLM resulting in n = 176. Values below the reporting limit (Table SI-2) were given a value of zero.

We then built a second GLM with gamma distribution and log link including only AR-positive individuals using untransformed ∑AR-residue concentration [ng g^{-1}] as the response. Fixed factors in this GLM included anthropogenic areas; species ("ACGE", "MIML", "HAAL", "ACNI"); year of death and nutrition condition ("bad", "moderate", "good"; Table SI-1) to observe potential mobilisation of lipid-soluble pollutants that may decrease residue concentrations in starved birds. For the analysis, all contaminant concentrations were tested visually for influential outliers. One red kite (Bra305) had an unusual high brodifacoum concentration (4853.47 ng g^{-1}), which was considered to be a consequence of deliberate poisoning, and thus excluded from statistical analysis. Four individuals with missing information for one of the fixed factors were excluded from the GLM resulting in n = 94.

All model assumptions (linearity of the predictor, independence of errors and expected dispersion) were checked (Figures SI-2, 3) by simulating data from the fitted model and comparing the residuals of the model fitted on such simulated values to the residuals of the model fitted on the observed data using the R-package "DHARMa" (Hartig, 2020).

We assessed collinearity among the investigated fixed factors by computing Generalized Variance Inflation Factors ($GVIFs^{1/(2*Df)}$), where Df refers to the number of coefficients in a subset (Fox and Monette, 1992). Only variables showing $GVIFs^{1/(2*Df)} < 2$ were included in the model (Zuur et al., 2010). The overall significance of all fixed effect structures was checked using a likelihood ratio test by comparing the fitted model to that of a model fitted without the fixed factors of interest. Model predictions, predictor effect plots and confidence intervals were visualised using the R-package "effects" (Fox and Weisberg, 2018, 2019).

2.4.3. Medicinal products (MPs)

For the analysis of MPs, we only included individuals that were found dead to ensure that birds had been environmentally exposed to MPs and to exclude deliberate treatments prior to death. This approach reduced the samples size to 87 birds (ACGE = 15, MIML = 19, HAAL = 42, ACNI = 3, PAHA = 8; Table SI-1). Statistical modelling was not possible due to low detection rates.

3. Results

3.1. Anticoagulant rodenticides (ARs)

3.1.1. Exposure among species

Overall, one or more ARs were found in 98 (53%) of the investigated samples (Fig. 2A). Exposure to a single AR was found in 41 samples (22.2%), whereas 57 (30.8%) had combinations of more than one AR (two: 33; three: 18; four: 3; five: 2; six: 1; Fig. 2B). The detection rate of ARs was highest in northern goshawks (81.3%), closely followed by red kites (80.5%), white-tailed sea eagles (38.3%) and sparrowhawks (13%). Exposure of ARs among individuals of the respective species is given in Figure SI-4. The most frequently detected AR was difenacoum with an overall detection rate of 34.6% followed by brodifacoum (31.9%), bromadiolone (19.5%), difethialone (9.7%), coumatetralyl (4.3%) and flocoumafen (2.2%) (Table SI-9). Except for coumatetralyl in northern goshawks, no FGARs (chlorophacinone and warfarin) were detected in any of the samples.

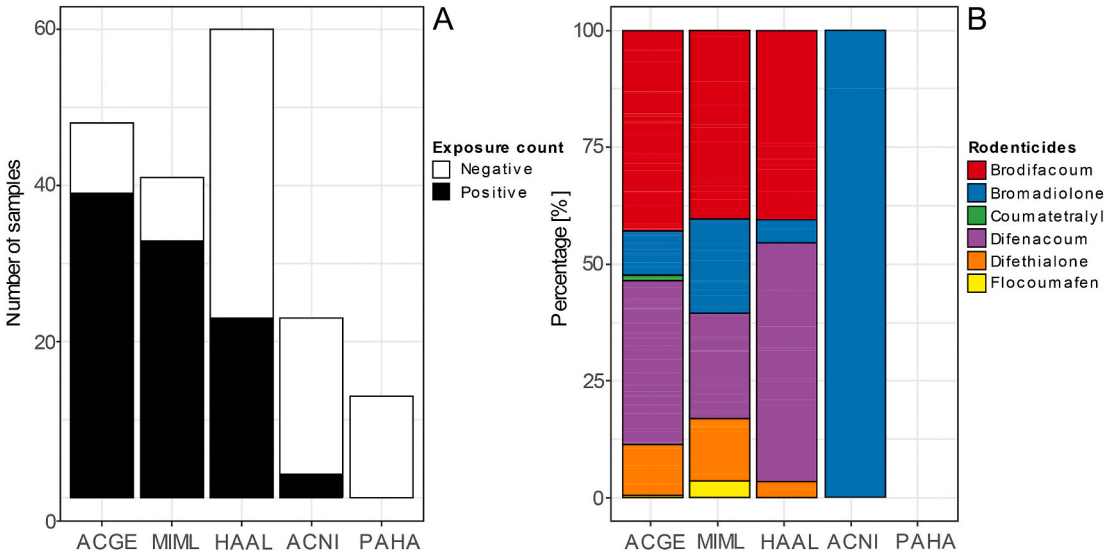

Fig. 2. **A**: Exposure count of ΣARs per species (0/1) and **B**: Percentage of AR concentrations per species. ACGE: *Accipiter gentilis* (n = 48); MIML: *Milvus milvus* (n = 41); HAAL: *Haliaeetus albicilla* (n = 60); ACNI: *Accipiter nisus* (n = 23); PAHA: *Pandion haliaetus* (n = 13). One MIML (Bra305) was excluded due to deliberate poisoning.

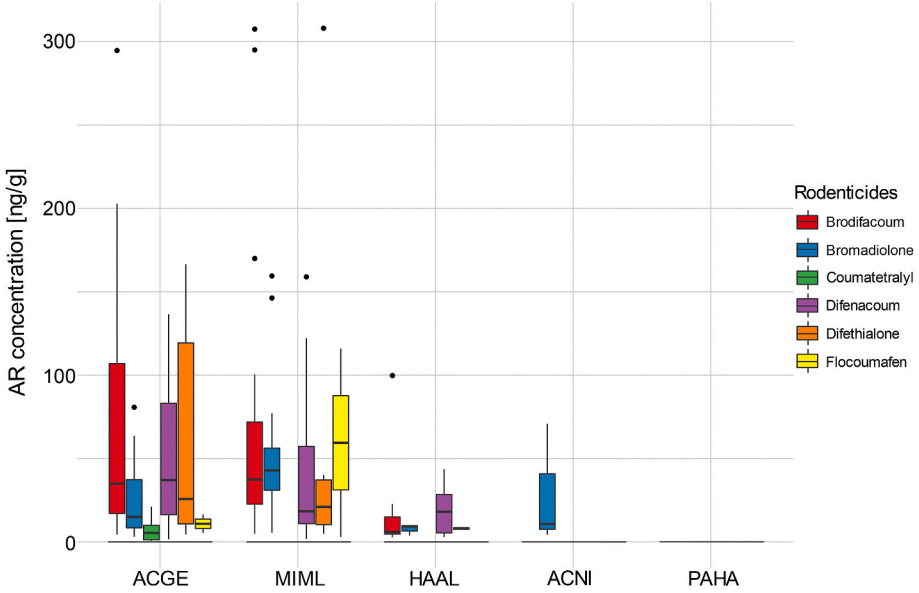

Fig. 3. Box plots of detected ARs among the different species. The lower and upper hinges of the box correspond to the 25th and 75th percentile. The upper whisker extends from the hinge to the largest value no further than 1.5*IQR from the hinge. The lower whisker extends from the hinge to the smallest value at most 1.5*IQR of the hinge. Data points beyond are plotted individually by black dots. ACGE: *Accipiter gentilis*, MIML: *Milvus milvus*; HAAL: *Haliaeetus albicilla*; ACNI: *Accipiter nisus*; PAHA: *Pandion haliaetus*. One MIML (Bra305; brodifacoum: 4853.47 ng g^{-1}; difenacoum: 69.41 ng g^{-1}) was excluded due to deliberate poisoning.

The highest detection rate of difenacoum was found in northern goshawks with 66.7% (median wet weight concentrations (interquartile range; IQR): 37.03 (66.79) ng g^{-1}; Fig. 3) followed by red kites with 46.3% (18.35 (46.46) ng g^{-1}) and white-tailed sea eagles with 21.7% (18.04 (23.08) ng g^{-1}). The detection rate of brodifacoum was in the same order as difenacoum with northern goshawks being most frequently exposed (34.9 (89.85) ng g^{-1}; 60.4%), followed by red kites (37.38 (49.15) ng g^{-1}; 46.3%) and white-tailed sea eagles (5.85 (10.23) ng g^{-1}; 18.3%). Bromadiolone was detected in 37.5% of northern goshawks (15.01 (28.87) ng g^{-1}), again followed by red kites (42.88 (25.26) ng g^{-1}; 29.3%) and was the only AR detected in sparrowhawks (10.71 (33.29) ng g^{-1}; 13%). Furthermore, 5% of the white-tailed sea eagles were exposed to bromadiolone (9.28 (3.17) ng g^{-1}). Difethialone showed the highest detection rate in red kites (20.99 (26.78) ng g^{-1}; 19.5%) followed by northern goshawks (25.73 (108.52) ng g^{-1}; 16.7%) and white-tailed sea eagles (8.03 (0.89) ng g^{-1}; 3.3%). Coumatetralyl was detected only in northern goshawks (5.37 (8.65) ng g^{-1}; 16.7%), whereas flocoumafen was detected in both, red kites (59.44 (56.49) ng g^{-1}; 4.9%) and northern goshawks (10.87 (5.58) ng g^{-1}; 4.2%). No ARs residues were detected in ospreys (Figs. 2 and 3).

3.1.2. Variation in the presence and absence of AR residues

The estimates of Table 1 refer to changes in log(odds) of AR exposure when a continuous fixed factor increases by one unit (and all other fixed effects are at a fixed value). When returning to the original scale for interpretation purposes, exponentiation of fixed factors results in a multiplicative effect on the response (odd ratios; Table 1). For each factor, one level needs to be chosen as reference so that parameter estimates are shown in reference to the intercept. Selecting a reference category is the default contrast used by R to express parameter values. It does not influence the model fit. Parameter estimates relative to each other are presented by predictor effect plots in Figure SI-6. The presence of AR residues increased with the contribution of artificial areas as shown by the negative relationship between the log odds of AR exposure and the first PCA axis (anthropogenic areas) which can be interpreted as a measure of urbanisation ($p < 0.01$; Table 1; Figure SI-1). Age class revealed that adults are 3.42 times more likely to have AR residuals compared to juveniles ($p = 0.01$; Table 1). Year of death tended to have a weak positive effect ($p = 0.07$) on the presence of ARs, whereas no effect was observed for sex ($p = 0.86$). Birds of prey that died from unclear reasons tended to have an increased odd for being exposed to ARs compared to birds of prey that died from trauma ($p = 0.06$). A similar trend was observed for birds of prey that died from infection ($p = 0.18$; Table 1). Poisonings as well as other causes of death did not show an effect on the presence of AR residues.

Table 1
Estimates (changes in log(odds) and odd ratios) of the fixed effects on the presence and absence of ARs in livers of northern goshawks (n = 45), red kites (n = 39), white-tailed sea eagles (n = 60), sparrowhawks (n = 22) and ospreys (n = 10). The reference category for cause of death was set to trauma, for age class to juvenile and for sex to female.

Presence/absence of ARs	Estimates (odd ratios)	Estimates (log odds)	Std. Error	z value	Pr (>|z|)
Anthropogenic areas	0.58	−0.55	0.19	−2.87	<0.01
Age class - adult	3.42	1.23	0.48	2.55	0.01
Sex -male	1.06	0.06	0.32	0.17	0.86
Year of death	1.05	0.05	0.03	1.8	0.07
Cause of death - infection	2.44	0.89	0.67	1.34	0.18
Cause of death - other	1.17	0.15	0.48	0.32	0.75
Cause of death – Pb-poisoning	1.34	0.29	0.57	0.52	0.6
Cause of death – other-poisonings	2.25	0.81	0.9	0.9	0.37
Cause of death - unclear	2.51	0.92	0.48	1.91	0.06

Table 2
Estimates of the fixed effects on AR concentration in livers of northern goshawks (n = 38), red kites (n = 31), white-tailed sea eagles (n = 22) and sparrowhawks (n = 3) with detected residues. The reference category for species was set to HAAL and for nutrition condition to moderate.

ΣAR concentration [ng g^{-1}]	Estimates (multiplicators)	Estimates (log scale)	Std. Error	t value	Pr (>|t|)
Anthropogenic areas	0.9	−0.11	0.15	−0.73	0.47
Species – ACGE	4.77	1.56	0.4	3.9	<0.01
Species - ACNI	1.88	0.63	0.69	0.92	0.36
Species – MIML	5.09	1.63	0.29	5.62	<0.01
Year of death	1.03	0.03	0.02	1.67	0.1
Nutrition condition - bad	1.05	0.05	0.32	0.14	0.89
Nutrition condition - good	1.11	0.1	0.28	0.37	0.71

3.1.3. Variation of AR concentrations in AR-positive birds of prey

Similar to the GLM described above, the estimates of the gamma GLM are on the log scale and assumed to be additive in their effect on the response (ΣAR concentration [ng g^{-1}]; Figure SI-5). All model predictions are visualised relative to each other in Figure SI-7. In contrast to the binomial model including all individuals, the current model revealed no effect of anthropogenic areas on the concentration of ΣARs in AR-positive individuals (Table 2). However, concentrations of northern goshawks were 4.77 times higher and those of red kites 5.09 times higher than those of white-tailed sea eagles ($p < 0.01$; Table 2). ΣAR concentrations in sparrowhawks were similar to those of white-tailed sea eagles ($p = 0.36$) but interpretation warrants caution due to a low number of AR-positive sparrowhawks (n = 3). Year of death tended to increase with increasing ΣAR concentrations ($p = 0.1$; Table 2). Good and bad nutrition condition did not significantly affect ΣAR concentrations compared to moderate nutrition condition.

3.2. Medicinal products (MPs)

Among all investigated MPs, we detected the NSAID ibuprofen, two fluoroquinolone antibiotics (enrofloxacin and its metabolite ciprofloxacin) and permethrin in individuals that were found dead (Fig. 4; Table SI-10). Ibuprofen was detected in 14.9% of all samples with white-tailed sea eagles (33.6 (53.05) ng g^{-1}; 23.8%) showing the highest detection rate followed by northern goshawks (18.55 (3.73) ng g^{-1}; 13.3%). Furthermore, one red kite (NRW42; 55.45 ng g^{-1}) had residues of ibuprofen whereas no residues were detected in sparrowhawks and ospreys (Fig. 4). Both fluoroquinolones were detected in two individuals (2.3%) with one red kite being exposed to both antibiotics (NRW42; enrofloxacin: 1655.35 ng g^{-1}; ciprofloxacin: 135.34 ng g^{-1}), one northern goshawk only to enrofloxacin (B97; 21.12 ng g^{-1}) and one white-tailed sea eagle only to ciprofloxacin (MV327; 257.3 ng g^{-1}). Additionally, permethrin was found in one northern goshawk from Berlin (B194; 35 ng g^{-1}; Fig. 4).Marbofloxacin, diclofenac, and sulfamethazin were not detected.

3.3. Plant protection products (PPPs)

Among all 30 investigated PPPs, dimethoate, omethoate and thiacloprid were detected in red kites (Figure SI-8; Table SI-11). Dimethoate (21042.21 (10682.33) ng g^{-1}) and its metabolite omethoate (4077.85 (3649.86) ng g^{-1}) were detected in the same two individuals whereas thiacloprid (99.95 (46.43) ng g^{-1}) was found in two different individuals.

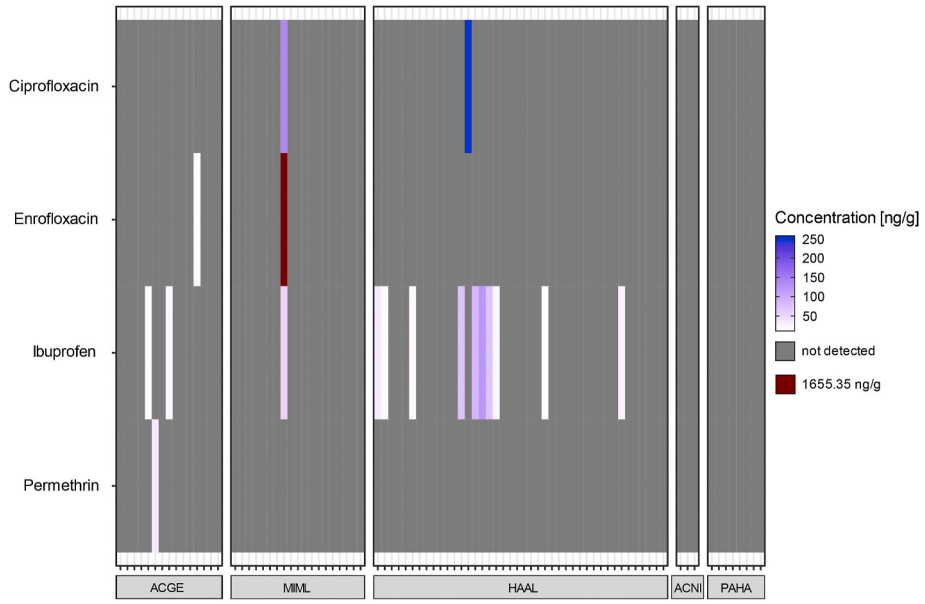

Fig. 4. Heat map of detected MPs among individuals that were found dead. ACGE: *Accipiter gentilis* (n = 15); ACNI: *Accipiter nisus* (n = 3); HAAL: *Haliaeetus albicilla* (n = 42); MIML: *Milvus milvus* (n = 19); PAHA: *Pandion haliaetus* (n = 8). Not detected = concentration below reporting limit (Table SI-2). Summary statistics are given in Table SI-10.

4. Discussion

4.1. Anticoagulant rodenticides (ARs)

4.1.1. Concentrations among feeding guilds

AR poisoning represents an important cause of death for raptors even when no misuses were reported to authorities (Coeurdassier et al., 2014). Species that facultatively scavenge or that are feeding specifically on small mammals have shown to be at highest risk (López-Perea and Mateo, 2018). Surprisingly, the northern goshawk was the most highly exposed species in the current study. The northern goshawk is characterised as a forest inhabiting species that mainly preys on other birds and to a lesser degree on mammals, depending on latitude and availability (Kenward, 2006). However, individuals of the present study originated from Berlin, where northern goshawks have established stable populations in recent years. Despite not being specialised on mammalian prey, the current study demonstrates high ARs exposures for avivorous predators in urban habitats. Thresholds related to acute toxic effects from ARs such as coagulopathy and haemorrhage have been associated with liver concentrations exceeding 100 ng g^{-1} and 200 ng g^{-1} wet weight (Berny et al., 1997; Rattner et al., 2014a; Thomas et al., 2011). When applying the acute toxicity threshold of >200 ng g^{-1} ΣSGAR, nine individuals (18.8%) exceeded this level, while these were not identified as being poisoned during necropsy. During necropsy, a special emphasis was put on pathological indications of AR poisoning such as generalized hemorrhages, subcutaneous bleedings and un-coagulated blood in large vessels or the heart. However, the decomposition of the carcasses often makes it impossible to find clear indications of AR poisoning. Few studies with small sample sizes exist on AR residues in northern goshawks in Europe (López-Perea and Mateo, 2018), demonstrating that northern goshawks have generally not been considered for AR poisoning. Interestingly, a study investigating potential prey species detected high AR exposures of passerine birds from Germany, which was linked to AR applications in local bait boxes (Walther et al., 2021). The high exposure of northern goshawks and accessibility of bait boxes by prey species calls for further investigations of northern goshawks in urban habitats. The observed lower concentration in sparrowhawks, a species that is specialised on avian prey, indicates that the quality of habitat might be most influential for AR exposure as sparrowhawks from the current study originated predominantly from agricultural and forest habitats. Previous studies demonstrated that sparrowhawks have comparable exposure rates to raptors that forage on mammals but concentrations were generally lower (Hughes et al., 2013; Ruiz-Suárez et al., 2014; Walker et al., 2015). Nevertheless, the potential that ARs are transferred in avian trophic pathways in combination with the use of habitats where AR are frequently applied is considered to pose a threat to avivorous raptors.

In contrast to species foraging on the avian trophic pathways, facultative scavengers such as the red kite are known to be at high risk for ARs poisoning as they frequently forage on (dead) mammals in agricultural habitats (Coeurdassier et al., 2012; Heuck et al., 2013; López-Perea and Mateo, 2018). The results of the current study confirm the high risk for AR poisoning of red kites in Germany, where more than 50% of the breeding population lives. The detection frequency of ARs in the current study is comparable to red kites from the UK (1994–2018, 80.4%, n = 214; Hughes et al., 2013; Walker et al., 2019; Walker et al., 2008) and Spain (2005–2016, 80.1%, n = 21; López-Perea et al., 2019; Sánchez-Barbudo et al., 2012), whereas in France they seem to be lower (1992–2011, 61%, n = 95; Berny and Gaillet, 2008; Coeurdassier et al., 2014). Six individuals (14.3%) exceeded the applied threshold of >200 ng g^{-1} ΣSGAR, which was, except for one individual, not associated with AR-poisoning during necropsy. In particular, the high levels of brodifacoum in red kites are considered to be a threat for scavengers as prolonged effects that increase in toxicity with subsequent exposure were reported (Rattner et al., 2020). The results of the current study add evidence that AR exposure contributes to reported declined survival rates of red kites in Germany (Katzenberger et al., 2019). However, further measures such as the observation of blood clotting in rehabilitation centres for raptors that are known to be at high risk for AR poisoning are recommended to further investigate the impact of chronic AR exposures on survival rates (Hindmarch et al., 2019).

Besides AR exposure in species foraging on terrestrial prey, the white-tailed sea eagle showed a considerable exposure to ARs as well. White-tailed sea eagles are mixed food web feeders that predominantly forage on fish but also on water birds, game species and carrion (Nadjafzadeh et al., 2016). Besides exposure routes from scavenging on poisoned prey, aquatic AR residues might also be taken up from the aquatic food web since ARs were detected in fish from Germany

(Kotthoff et al., 2018; Regnery et al., 2019b, 2020a). Almost 80% of the municipalities in Germany indicated in a nation-wide survey that they were using ARs in sewage systems in 2017 (Regnery et al., 2020b), which was suggested to result in aquatic trophic transfers (Regnery et al., 2020a). AR residues were previously detected in a white-tailed sea eagle from Scotland (Hughes et al., 2013) whereas no AR residues were detected in sea eagles from Finland (Koivisto et al., 2018). AR concentrations in the current study were lower compared to species feeding dominantly on terrestrial prey, which could be a result of the feeding ecology and the use of rather pristine habitats in the north of Germany. However, further studies including stable isotope analyses are needed to determine the sources of contaminants since no ARs were detected in ospreys, a species that is known to exclusively prey on fish (Häkkinen, 1978). Even though samples sizes for ospreys were comparably small, the results indicate that the primary source of ARs for white-tailed sea eagles might be carcasses of smaller mammals.

4.1.2. Modelling exposure probability and influence on residue concentrations

Exposure to ARs is expected to occur at a very local scale where baiting stations are placed. Previous studies reported exposures to small mammals less than 100 m around baiting stations (Geduhn et al., 2014; Tosh et al., 2012). This can lead to a high risk for secondary poisoning in the direct surrounding of baiting stations. In the current study, secondary exposures increased with increasing urban habitat, which might be related to an enhanced use of ARs on public and private property rather than on the countryside. Similar observations were made for predators (including raptors) in Spain where the presence of SGARs was related to urban area and human population density rather than agricultural activity (López-Perea et al., 2019). Furthermore, associations between AR occurrence and urban areas were reported for red foxes (*Vulpes vulpes*) in Germany (Geduhn et al., 2015) as well as for urban wild boars (*Sus scrofa*) in Spain, where AR occurrence was positively related to human population and anthropization (Alabau et al., 2020). Other factors that have shown to be important determinants for AR residue occurrence were related to cattle and pig farm density (Geduhn et al., 2015; López-Perea et al., 2019), which might represent a risk for raptors in the north-western parts of Germany where animal farming is most frequent.

Although the degree of urban land cover was linked to the AR exposure probability in the current study, it was not related to the extent of exposure. This indicates that habitat composition, i.e. patterns of anthropogenic land use, may determine the probability of AR exposure, whereas species-specific ecological factors such as feeding ecology seem to be the main drivers for the extent of exposure. Due to the high risk of AR exposure in urban habitats, we recommend further studies on trophic magnification (e.g. songbirds, rodents, wild boars, foxes, raptors) in urban terrestrial food webs as done for legacy pollutants in Canada (Fremlin et al., 2020).

The higher risk of adults to be exposed to ARs compared to juveniles is expected to be attributed to the larger number of exposure events over time, which may ultimately lead to accumulation of compounds that reach detectable levels at a certain point. Similar observations were made for sparrowhawks in the UK (Walker et al., 2015) as well as for brodifacoum in raptors from Denmark (Christensen et al., 2012). However, red kites showed similar exposures of adults and juvenile birds in the UK (Walker et al., 2019), which is in line with a previous study reporting high exposures of juvenile red kites (Hughes et al., 2013). This emphasizes the susceptibility of red kites to be exposed to toxic AR concentrations.

Similar to our study, Christensen et al. (2012) and López-Perea et al. (2019) found no significant influence of cause of death on AR residues in various raptors from Denmark and Spain. ΣAR residues in the present study tended to be higher in raptors that died from unclear reasons compared to raptors that died from trauma, which indicates that AR poisoning often remains unnoticed during necropsy. The same trend was observed for raptors that died from infections. Interactions between infectious diseases and AR exposure were previously reported for voles (Vidal et al., 2009) but associations between chronic AR exposure and effects in wildlife species remain poorly characterised (Rattner et al., 2014b), which complicates the evaluation to which degree AR exposure contributes to the respective cause of death.

Sex did not influence the probability of AR exposure, which is in line with previous research (Christensen et al., 2012; Walker et al., 2015). Both the risk for AR exposure as well as the exposure extent tended to increase during the sampling period, which might be related to the intrinsic properties of AR as being persistent and bioaccumulative (Rattner et al., 2014b). Furthermore, ARs such as brodifacoum and difenacoum were expected to have an increased potential to partition and accumulate in fatty tissues as indicated by their octanol-water partition coefficient (log Kow $>$ 4). We therefore expected higher AR concentrations in individuals with good nutritional status and associated lipid-rich livers, which was not observed in the current study. This indicates that other factors such as the binding affinity of ARs to the active side of the vitamin K epoxide reductase (Rattner et al., 2014b) might be more influential for the accumulation in livers.

4.2. Medicinal products (MPs)

The NSAID ibuprofen (HMP) was the most frequently detected MP in the current study followed by the fluoroquinolone antibiotics, enrofloxacin (VMP) and its metabolite ciprofloxacin (HMP). Between 2002 and 2012, consumption of ibuprofen increased from 250 to 975 tonnes (t) per year making it one of the most sold HMPs in Germany (Küster and Adler, 2014). Ibuprofen has shown to be frequently detected (57%) in wastewater treatment plant effluents across Europe (Loos et al., 2013) as well as in surface waters in Germany (Bergmann et al., 2011). The highest detection rate of ibuprofen was found in white-tailed sea eagles, indicating that feeding on the aquatic food web may be responsible for exposures to ibuprofen. This is supported by the detection of ibuprofen in otters (*Lutra lutra*) from the UK as otters feed predominantly on fish (Richards et al., 2011). However, no ibuprofen residues were detected in ospreys, which might be related to the small sample size and varying impacts of wastewater treatment plant effluents at local foraging habitats, but further studies are needed to verify this assumption. Sorption of ibuprofen to sewage sludge is lower compared to e.g. diclofenac (Bergmann et al., 2011; Ternes et al., 2004) indicating that sewage sludge fertilisation did not represent a major exposure source. Furthermore, foraging on treated livestock can be excluded as a potential exposure source as ibuprofen is not registered as VMP. However, terrestrial exposures might still have occurred through agricultural applications of contaminated wastewater as ibuprofen had one of the highest environmental risk scores in wastewater samples intended for agricultural reuse (Alygizakis et al., 2020). Thus, the detection of ibuprofen in two northern goshawks might be attributed to exposures through agricultural wastewater reuse.

Sales of antibiotics for veterinary use has been registered in Germany since 2011 and fluoroquinolones have, in contrast to other antibiotics, constant sales of ~10 t per year (Wallmann et al., 2018). Fluoroquinolones are known to alter the normal microbiome and cause adverse effects on the embryonic development of birds (Hruba et al., 2019). The absorption of fluoroquinolones in organisms is driven by lipophilicity (Cabrera Pérez et al., 2002) and the liver represents a target tissue for metabolization after enrofloxacin administration (EMA, 2002). Enrofloxacin was previously detected in the plasma of griffon vulture nestlings (*Gyps fulvus*) in Spain, which was suggested to be related to foraging on livestock prior to sampling as the half-live in bird tissues are short (<10 h) (Cox et al., 2004; Gómez-Ramírez et al., 2020). Furthermore, all investigated fluoroquinolones were detected in the plasma of griffon vulture nestlings, which was suggested to be associated with scavenging on livestock as well (Blanco et al., 2016). Marbofloxacin was not detected by the current study, which might reflect the

lack of readily available livestock carcasses in Germany, different antibiotic use patterns as well as matrix specific differences. Exposure of one white-tailed sea eagle to ciprofloxacin but not enrofloxacin might be related to aquatic exposures as ciprofloxacin was detected in 90% of wastewater treatment effluents across Europe (Loos et al., 2013). However, transformations of enrofloxacin to ciprofloxacin are known to occur in mammals (Martinez et al., 2006) but correlations between both are not always observed in raptors (Gómez-Ramírez et al., 2020). Furthermore, ciprofloxacin sorbs to solids (Golet et al., 2003) and shows considerable concentrations in sewage sludge from Germany (max. 3500 μg g^{-1}; Bergmann et al., 2011), which indicates that sewage sludge fertilisation may contribute to environmental exposures. In contrast to ciprofloxacin, enrofloxacin is used as VMP and exposures might rather be related to manure fertilisation as enrofloxacin (max. 8300 μg l^{-1}) shows considerably higher concentrations in manure from Germany than ciprofloxacin (max. 28 μg l^{-1}; Bergmann et al., 2011).

As Germany prohibits the provision of livestock carcasses to scavengers, we assume that the detection of certain MPs in raptors in the present study might be explained by (i) the wide dispersive use in large quantities of MPs in both humans and livestock, and by (ii) the insufficient elimination capacity of wastewater treatment plants (Van Doorslaer et al., 2014). The latter potentially leads to high concentrations in water and sewage sludge intended for agricultural reuse. However, it cannot be ruled out that carcasses of treated companion and farm animals are available to scavengers. The fact that we found concentrations of both fluoroquinolones in one red kite at similar concentrations to pigs under treatment (5 mg kg^{-1}, 1 day post-dose; Garcia et al., 2005) might most likely be explained by the recent uptake of treated prey items as red kites frequently patrol dunghills on farms and settlements in the search of small carcasses. Alternatively, the red kite might have been treated, set free and later collided with a wind power plant, as the bird died from trauma next to a wind park. However, birds treated in captivity are normally marked with a ring prior to release and reported to the ringing centre to provide this type of information. Nevertheless, based on the frequency of detection and the exclusion of species treated in veterinary clinics, the results indicate that environmental exposures of raptors to ibuprofen and fluoroquinolone antibiotics prevails.

4.3. Plant protection products (PPPs)

The concentrations of the organophosphate insecticide dimethoate and its main metabolite omethoate in two red kites (Bra391, SH77; Tables SI–1) were a consequence of deliberate poisoning, which was confirmed as the cause of the death for the latter through the analysis of gut and gizzard content. Poisonings of raptors foraging in agricultural areas (such as the red kite) were reported as a frequent cause of death in Europe (Berny and Gaillet, 2008; Molenaar et al., 2017). As a consequence, poisonings of red kites in their winter grounds in Spain have shown to negatively impact the number of breeding pairs which even resulted in local extinctions (Mateo-Tomás et al., 2020). Together with AR poisonings, the current study adds evidence that poisonings represent a threat for red kites, which is expected to contribute declined survival rates in Germany (Katzenberger et al., 2019).

Both red kites with thiacloprid residues were found dead in agricultural habitats (NS57, S70; Table SI-8) where neonicotinoid (NNs) were commonly used as insecticidal seed dressings. The potential of NNs for persistency and bioaccumulation is low due to rapid metabolization and clearance (<24 h) in bird livers (Bean et al., 2019). Interestingly, NS57 was found dead in October (2009) and S70 in March (2015), which coincides with the timeframes at which sowing of winter and spring cereals occurs. During these timeframes, suspected NN poisoning of seed-eating farmland birds has shown to be most frequent (Millot et al., 2017). This is supported by a recent study showing that farmland birds have significantly higher concentrations of the NN clothianidin after sowing in autumn (Lennon et al., 2020). Therefore, facultative scavengers such as the red kite might be at risk for exposures shortly after NN application through foraging on acutely poisoned prey. Previous studies on NNs detected imidacloprid and thiacloprid in blood of European honey buzzards (*Pernis apivorus*) from Norway (Byholm et al., 2018) and imidacloprid in blood of an eagle owl nestling (*Bubo bubo*) from Spain (Taliansky-Chamudis et al., 2017). The authorisation of thiacloprid in the European Union was withdrawn in August 2020 due to its classification as being toxic for reproduction category 1 B as well as due to toxic groundwater exposures of metabolites (EC, 2019). Due to its low potential for bioaccumulation, persistency and potential rapid excretion from bird tissues, a long-term threat for raptors after its period of grace in the European Union (03/02/2021) is considered to be unlikely.

5. Conclusion

Our study demonstrates that AR contamination poses a threat to raptors in Germany. Whereas the use of urban habitats seems to determine exposure probability to ARs, species-specific traits such as scavenging on smaller carcasses seem to explain the extent of exposure. The observed link between AR exposure probability and degree of urban land cover calls for further studies investigating terrestrial trophic transfers and associated risks in urban ecosystems. Among the investigated species, northern goshawks from urban habitats and red kites in general were at greatest risk for AR poisoning as levels exceeded thresholds associated with adverse effects. Together with deliberate insecticide poisoning, AR poisoning is considered to represent a threat to red kites and might ultimately contribute to decreasing survival rates in Germany. The detection of ARs in white-tailed sea eagles suggests that AR exposure might not be limited to terrestrial food webs but further studies including dietary proxies are needed to identify exposure sources. For MPs, the detection of ibuprofen and fluoroquinolone antibiotics suggests that their wide dispersive use in large quantities in combination with manure fertilization and incomplete wastewater removal results in environmental emissions. Most analysed and currently used PPPs were not detected, indicating that widespread contamination in the study region is unlikely. However, rapid metabolization of some PPPs in biological tissues indicates that other sample matrices such as blood from nestlings might be more adequate to assess spatiotemporal exposure scenarios in future. Taken together, the results of the current study demonstrate that ARs exposure represents a threat for facultative scavengers as well as for raptors living in urban habitats.

Funding

This work was supported by a grant through the World Wide Fund For Nature, Germany.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank Susanne Auls for her assistance during necropsy, Alexandre Courtiol and Heribert Hofer for giving critical advice as well as Martina Hoffmann, Ramazan Koç, Christine Reichmann and Ina Stachewicz-Voigt for their support during residue analysis. We furthermore thank Lisa Giese and Nikolai Kraneis (https://nikolai-kraneis.com) for providing species illustrations for the graphical abstract.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.110602.

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Chapter 4: Ecological and spatial variations of legacy and emerging contaminants in white-tailed sea eagles from Germany: Implications for prioritisation and future risk management

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Published in Environment International (2022)
- https://doi.org/10.1016/j.envint.2021.106934

Detailed author contributions:

OKro, AB and GT conceptualised the work. OKro was responsible for the project administration, funding acquisition and conducted the necropsies. The chemical analysis was conducted in collaboration with the University of Athens, where GG, MCN, NA, and NST were responsible for the chemical analysis and data treatment. AB completed an analytical training for the applied methodologies in the laboratory of NST at the University of Athens (13/01/2020-24/01/2020). AB was responsible for the sample preparation for the stable isotope analysis in the laboratory of CCV who supervised the analysis. AB drafted the manuscript except for some parts of the introduction, 2.7, 4.4 (GT), and 2.3, 2.4, 2.5 (GG, MCN, NA). All co-authors provided input on the manuscript. AB was responsible for the statistical analysis and visualisations, and GT conducted the risk assessment.

Environment International 158 (2022) 106934

Contents lists available at ScienceDirect

Environment International

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ARTICLE INFO

Handling Editor: Olga Kalantzi

Keywords:
Baltic Sea
Birds of prey
Chemicals of emerging concern
Persistent organic pollutants
Stable isotopes
JANUS tool

ABSTRACT

The increasing use of chemicals in the European Union (EU) has resulted in environmental emissions and wildlife exposures. For approving a chemical within the EU, producers need to conduct an environmental risk assessment, which typically relies on data generated under laboratory conditions without considering the ecological and landscape context. To address this gap and add information on emerging contaminants and chemical mixtures, we analysed 30 livers of white-tailed sea eagles (*Haliaeetus albicilla*) from northern Germany with high resolution-mass spectrometry coupled to liquid and gas chromatography for the identification of >2400 contaminants. We then modelled the influence of trophic position ($\delta^{15}N$), habitat ($\delta^{13}C$) and landscape on chemical residues and screened for persistent, bioaccumulative and toxic (PBT) properties using an *in silico* model to unravel mismatches between predicted PBT properties and observed exposures. Despite having generally low PBT scores, most detected contaminants were medicinal products with oxfendazole and salicylamide being most frequent. Chemicals of the Stockholm Convention such as *4,4′*-DDE and PCBs were present in all samples below toxicity thresholds. Among PFAS, especially PFOS showed elevated concentrations compared to other studies. In contrast, PFCA levels were low and increased with $\delta^{15}N$, which indicated an increase with preying on piscivorous species. Among plant protection products, spiroxamine and simazine were frequently detected with increasing concentrations in agricultural landscapes. The *in silico* model has proven to be reliable for predicting PBT properties for most chemicals. However, chemical exposures in apex predators are complex and do not solely rely on intrinsic chemical properties but also on other factors such as ecology and landscape. We therefore recommend that ecological contexts, mixture toxicities, and chemical monitoring data should be more frequently considered in regulatory risk assessments, e.g. in a weight of evidence approach, to trigger risk management measures before adverse effects in individuals or populations start to manifest.

1. Introduction

The use of an increasing number of chemicals over the last century has resulted in environmental emissions and wildlife exposures (Chiaia-Hernández et al., 2020; González-Rubio et al., 2020a). The global chemicals production (excluding pharmaceuticals) are expected to double by 2030, with the European Union (EU) being the second biggest producer accounting for ~17% of the global sales (EC, 2020). Among the currently produced chemicals, >70% are classified as hazardous to human health and ~30% as hazardous to the environment (EUROSTAT, 2020). In the EU, producers and importers are responsible for conducting health and environmental risk assessments and compile the information in dossiers with guidance from different regulatory frameworks, depending on their intended use. These comprise e.g. industrial

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https://doi.org/10.1016/j.envint.2021.106934
Received 18 June 2021; Received in revised form 20 September 2021; Accepted 10 October 2021
Available online 15 October 2021

chemicals (REACH - Registration, Evaluation, Authorisation and Restriction of Chemicals, EC 1907/2006), plant protection products (EC 1107/2009), and medicinal products (veterinary medicinal products (VMP): Regulation (EU) 2019/6; human medicinal products (HMP): Directive 2001/83/EC). A first step for registering or approving a chemical requires a hazard identification, including the assessment of persistence, bioaccumulation, and toxicity (PBT properties). A second step requires a risk assessment, where the predicted environmental concentration (PEC) is supposed to remain below the so-called predicted no-effect concentration (PNEC). However, (eco)toxicological data and information on exposure scenarios of the registered substances are often missing (EEA, 2019). This is emphasized in a study that demonstrated that 58% of the registration dossiers for REACH chemicals with tonnages above 1000 tons (t) per year were non-compliant (Springer et al., 2015). Both hazard and risk assessments are usually based on data generated under laboratory conditions, typically lacking information on the ecological, landscape and management context (Schäfer et al., 2019). This has resulted in inaccurate predictions of environmental exposures (Knäbel et al., 2014; Knäbel et al., 2012). As a consequence, the term chemicals of emerging concern (CECs) has been established for a wide range of contaminants and transformation products (TPs) that entered the environment recently (Dulio and Slobodnik, 2009).

Besides regulations on a nationwide or continental scale such as REACH, treaties like the Stockholm Convention have been established on a worldwide scale to restrict the use of persistent organic pollutants (POPs). POPs are classified as PBT or very persistent and very bioaccumulative (vPvB) substances that result in long-lasting environmental exposures, have the potential for long-range transport as well as for toxic effects in biota (de Wit et al., 2020; Sonne et al., 2020). Whereas many POPs are biomagnified in food webs even after mitigation measures were established (e.g. de Wit et al., 2020), much less information is available on the behaviour of CECs and complex chemical mixtures, as established analytical procedures mainly focussed on the target analysis of a limited number of contaminants (i.e. < 100) without considering metabolites and TPs. This represents a critical knowledge gap as identifying chemical mixtures is essential for conducting hazard and risk assessments. Recent developments in analytical techniques resulted in wide-scope target screening techniques based on high resolution-mass spectrometry (HR-MS) coupled to both liquid (LC) and gas chromatography (GC) that allow for the simultaneous quantification of a large set of chemicals (i.e. >2400) within each sample (Alygizakis et al., 2020; Gago-Ferrero et al., 2020).

Most studies on CECs focussed on abiotic matrices such as water or sediment (Chiaia-Hernández et al., 2020; Diamanti et al., 2020), whereas information on the occurrence of CECs in biota, in particular apex predators is scarce (González-Rubio et al., 2020a). An important means for wildlife biomonitoring is the selection of sentinel species for which suitability is expected to depend on ecological traits such as migratory behaviour, diet and habitat preference (Badry et al., 2020). This becomes especially important when a species forages on both the aquatic and the terrestrial food web or feeds on different trophic levels. An efficient way to control for dietary plasticity is the use of stable isotopes of nitrogen ($^{15}N/^{14}N$) and carbon ($^{13}C/^{12}C$) (Elliott et al., 2009; Eulaers et al., 2013). Nitrogen isotopes are commonly used as proxies for estimating the trophic position of animals since consumers get enriched with ^{15}N in relation to ^{14}N by ~2 to 3.4 ‰ compared to their prey (Vanderklift and Ponsard, 2003), whereas the stable isotope of carbon can be used to distinguish different carbon sources of terrestrial and aquatic environments (Kelly, 2000).

In the present study, we focussed on the white-tailed sea eagle (*Haliaeetus albicilla*; hereafter HAAL), a mixed food web feeder that forages mostly on fish but also on water birds, carrion and game species depending on season and availability (Nadjafzadeh et al., 2016). In northern Germany, HAALs inhabit mainly inland and coastal habitats of the Baltic Sea region. The Baltic Sea region is influenced by industrial and agricultural pollution, where apex predators including HAALs have suffered from population declines during the 20th century (de Wit et al., 2020; Helander et al., 2002; Sonne et al., 2020). As a consequence, HAALs have been included as an indicator species for biodiversity and anthropogenic pressures in the EU Marine Strategy Framework Directive for the Baltic Sea environment (Zampoukas et al., 2014).

With this study, we specifically aim to (i) characterise the food web of German HAALs by using stable isotope values of $\delta^{15}N$ and $\delta^{13}C$, (ii) to determine >2400 POPs and CECs via wide-scope target screening (iii) to compare contaminant concentrations with those detected in other HAAL subpopulations (iv) to determine the influence of trophic position, habitat and land cover on POPs and CECs and (v) to predict PBT properties based on a (quantitative) structure–activity relationship ((Q)SAR) model to unravel potential mismatches between predicted PBT properties and observed exposures.

2. Methods

2.1. Study area and sampling

The study included 30 liver samples from HAALs that were found dead between 2015 and 2018 in the north of Germany (Fig. 1). One exception represents MV542, which died within 24 h of being kept in captivity. Carcasses were frozen at −20 °C and thawed at room temperature for necropsy. During necropsy, a liver aliquot of 10–20 g (wet weight, ww) was taken and stored at −20 °C. Prior to shipment to the analytical laboratory, the liver samples were stored at −80 °C and subsequently lyophilised. Most birds were found as adults (≥5 years, n = 23) including one sub-adult (4 years) with a minor proportion of immature birds (2–3 years; n = 6) (Table SI-1). Most birds were of good nutritional status (n = 19) based on the measurement/presence of subcutaneous fat tissue, fat in the body cavity and in the coronary sulcus (moderate: n = 8; bad: n = 3) (Table SI-1). GPS coordinates were manually assigned to samples that had only a written description of the location where a carcass was found (Fig. 1).

2.2. Stable isotope analysis

As a first step, 0.5 mg sub-samples of dried, lyophilised and homogenised HAAL livers were weighed into tin cups and combusted in a Flash Elemental Analyser (Thermo Finnigan, Bremen, Germany). Further analyses of resultant N_2 and CO_2 gases were performed using an elemental analyser (Flash EA, Thermo Fisher, Bremen, Germany) connected in sequence via a Conflo (Thermo Fisher, Bremen, Germany) to a Delta V Advantage isotope ratio mass spectrometer (Thermo Fisher, Bremen, Germany). The isotope ratios were reported as δ-values and expressed as relative difference per mil [‰] according to the following equation, shortened according to Coplen (2011): $\delta X = R_{sample} = R_{standard} - 1$, where X is ^{13}C or ^{15}N, R_{sample} is the corresponding ratio $^{13}C/^{12}C$ or $^{15}N/^{14}N$, and $R_{standard}$ refers to the ratio of the international references Pee Dee Belemnite (V-PDB) for carbon and atmospheric N_2 (AIR) for nitrogen. The $\delta^{13}C$ and $\delta^{15}N$ values of the protein laboratory standards were −24.0‰ and 4.4‰, respectively, for tyrosine and −30.3‰ and 11.0‰, respectively, for leucine. The precision of repeated measurements of laboratory standards was better than 0.04‰ (1 standard deviation, sd) for carbon and 0.04‰ (1 sd) for nitrogen.

2.3. Chemical analysis

Simultaneous extraction of contaminants with different physicochemical properties from lyophilised and homogenised HAAL livers was carried out using generic sample preparation protocols (Androulakakis et al., 2021; Gkotsis et al., 2019). An Accelerated Solvent Extraction (ASE) and Solid Phase Extraction (SPE) were employed prior to the analysis by LC-/GC-HR-MS. Two generic sample preparation methods per sample were performed. More polar, less volatile, and thermally unstable compounds were extracted by the method-specific for LC-

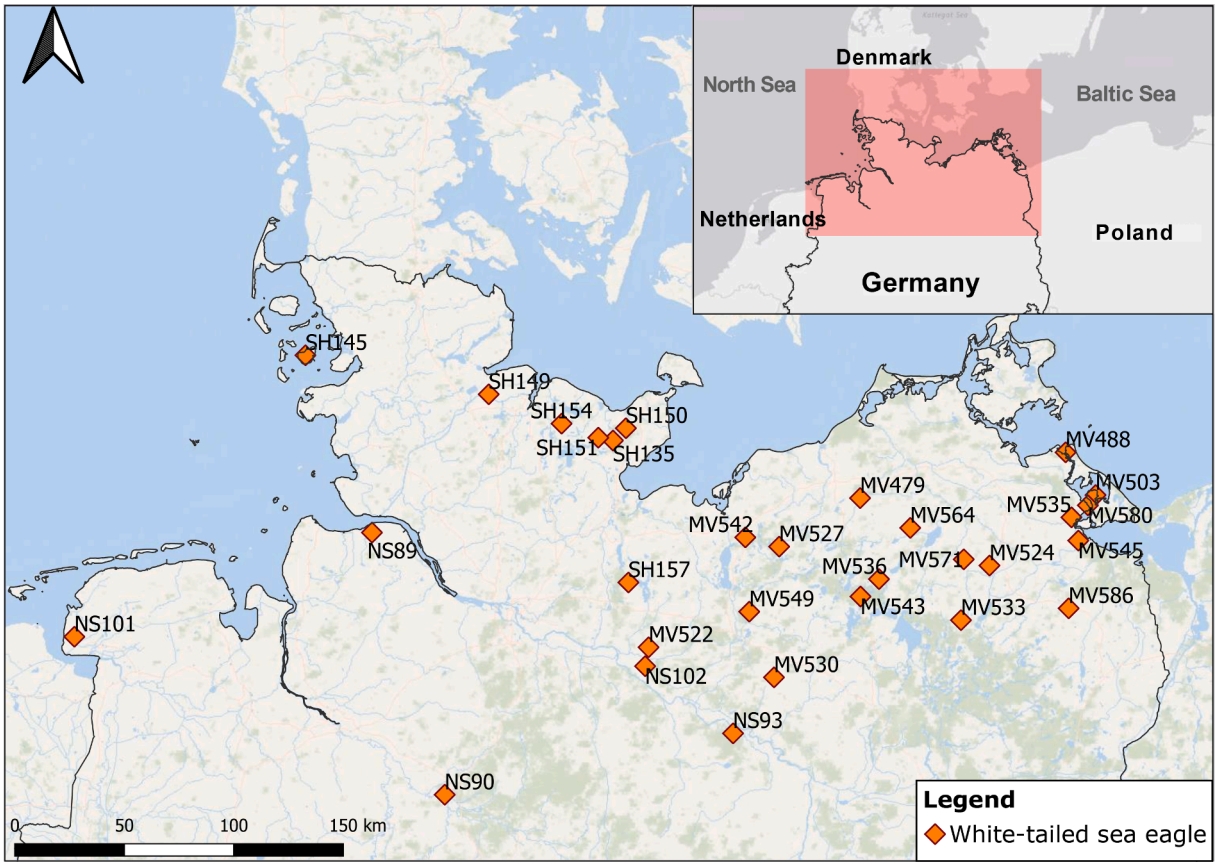

Fig. 1. Sampling locations of white-tailed sea eagles (HAAL) in the north of Germany. Letters indicate the federal state followed by continuous enumeration: MV = Mecklenburg-Western Pomerania, NS: Lower Saxony, SH: Schleswig-Holstein.

amenable compounds, whereas a different sample preparation method was followed for the extraction of more volatile and thermostable GC-amenable compounds. Detailed information on the extraction of LC- and GC-amenable compounds can be found in the supplementary information (SI-1.1/1.2).

2.4. Instrumental analysis

The analysis for LC-amendable compounds was conducted using Ultra High Performance Liquid Chromatography (UHPLC) apparatus with an HPG-3400 pump (Dionex UltiMate 3000 RSLC, Thermo Fisher Scientific) and Acclaim TM RSLC 120 C18 column (100 × 2.1 mm, 2.2 µm; Thermo Fisher Scientific). The gradient elution program for the LC system is given in Table SI-3. The system is coupled to a Hybrid Quadrupole Time of Flight Mass Analyzer (QTOF-MS) (Maxis Impact, Bruker Daltonics) with an electrospray ionization interface (ESI) operated in both positive and negative mode. Two scan modes were used: 1st run in Data Independent mode comprised a broadband Collision Induced Dissociation (bbCID) acquisition mode (acquisition of full scan MS spectra (4 eV) and MS/MS (25 eV) spectra in a single run). The second mode in data dependent mode consisted of a full scan MS spectra and MS/MS spectra of the 5 most abundant ions per MS scan in a single run.

The GC-APCI-QToF system consisted of a Bruker 450 GC coupled to the same MS as the LC system. GC was operated in splitless injection mode and the splitless purge valve was activated 1 min after injection. The injection volume was 1 µL. A Restek Rxi-5Sil MS column of 30 m (0.25 mm i.d. × 0.25 µm film thickness) was used with Helium as carrier gas in a constant flow of 1.5 mL min^{-1}. The GC oven was programmed as follow: 55 °C initial hold for 3 min, increase at a rate of 15 °C min^{-1} to 180 °C, then increase with a step of 6.5 °C min^{-1} to 280 °C and hold for 5 min followed by an increase of 10 °C min^{-1} to 300 °C and hold for 5.28 min. The temperature of splitless injector port, GC–MS transfer line and MS source were maintained at 280, 290 and 250 °C, respectively. The QToF mass spectrometer was equipped with an atmospheric pressure chemical ionization (APCI) source operated in positive ionization mode. The operating parameters of APCI interface were: capillary voltage, 5000 V; corona voltage, 2000 V; endplate offset, 500 V; nebulizer, 3.5 bar; drying gas, 1.5 L min^{-1}. The QTOF MS system operated in the same two different acquisition modes as described above for LC.

2.5. Data treatment

Target screening was performed using in-house developed databases of 2441 contaminants (the LC target list (https://zenodo.org/record/3723478) is available as S21 UATHTARGETS in Suspect List Exchange (https://www.norman-network.com/nds/SLE/) and the GC target list (https://doi.org/10.5281/zenodo.3753372) is available in the following link: https://zenodo.org/record/3753372. The target lists included: 1099 MPs (&TPs), 762 legacy and modern PPPs (&TPs), 313 drugs of abuse (&TPs), 232 legacy and modern industrial chemicals, and 35 contaminants from various other categories. The data treatment was performed using TASQ Client 2.1 and DataAnalysis 5.1 (Bruker Daltonics, Bremen, Germany) software. The detection was based on specific screening parameters [mass accuracy < 2 mDa, retention time shift ±0.2 min, isotopic fitting <100 mSigma (only for confirmation of positive findings), whereas the presence of adduct and fragment ions confirmed the analytes]. The Screening Detection Limit (SDL) was calculated from spiked samples; specifically, it refers to the lowest concentration level for which the identification of 95% of the target analytes was reliable (Gago-Ferrero et al., 2020). In the in-house developed method, the SDL was established as the concentration at which the thresholds of (i) retention time and (ii) mass accuracy of the

precursor ion were satisfied (SI-1.3). The SDL was not compound-specific, but a generic reporting value derived after method validation (Gago-Ferrero et al., 2020). Further, thorough compound-specific validation was performed for quantification purposes of the compounds detected with the screening method. Compound-specific limit of detection (LOD) and limit of quantification (LOQ) values were calculated after the treatment and analysis of samples spiked with the detected compounds and structure-related isotope-labelled compounds. Both LOD and LOQ as well as the analytical techniques (LC vs. GC) used for the determination of the detected contaminants are given in Table SI-4.

For quantification, a representative mix of isotopically labelled reference standards (IS) covering a wide range of classes, polarities, and other physicochemical properties was added to every sample before extraction for quality control/assurance reasons (tracing and correcting potential sample preparations and instrumental analysis variations) as commonly suggested in HRMS screening studies (Kruve et al., 2021; Ng et al., 2020). The quantification of the detected analytes was based on the standard addition method (spiked matrix curve of 5 concentration levels), which achieves reliable and accurate quantification in cases of high matrix effects. In selected cases when the internal standard was available, a combination of the standard addition method and the isotopic dilution was used. The equation for quantification is provided in the supplementary information (SI-1.3).

2.6. Statistical analysis

We conducted all statistical analyses in R version 3.6.3 (R Core Team, 2020) and set the level of significance to $p < 0.05$. Heat maps were generated using the R-package ggplot2 (Wickham et al., 2016) and Inkscape 0.92.4. The sampling map was created using QuantumGIS software version 3.10.2 (QGIS Development Team, 2020). Concentrations ranging between LOD and LOQ were substituted with LOQ/2 in accordance with Directive 2009/90/EC. Concentrations below LOD were given a value of zero for modelling. Isotopic values of the HAALs were normally distributed (Shapiro-Wilk test, $p > 0.05$) and given as mean ± 2*Standard Error (SE). Concentrations of contaminants are given as median with interquartile range (IQR) as most contaminant concentrations were not normally distributed (Shapiro-Wilk test, $p < 0.05$). Summary statistics (median, IQR) refer to samples with detectable residues.

2.6.1. Extraction and transformation of land cover variables

We selected a buffer radius of 5 km (~78.5 km^2) for the quantification of land cover variables from the Corine land cover data set (EEA, 2018) as the recommended 3 km buffer zones for wind parks has shown to not be sufficient for HAALs in the Mecklenburg Lake District (Krone and Treu, 2018). The contribution of land cover class for each individual is given in Table SI-6. We applied a detrended correspondence analysis (DCA) using the R-package "vegan" (Oksanen et al., 2020) and extracted the scores of the first axis to create a single synthetic variable encompassing information from the different land cover classes while removing collinearity between them (Dormann et al., 2013). The DCA separated agricultural inland areas (negative scores) from mainly water bodies and wetlands (positive scores) on the first axis (Figure SI-5).

2.6.2. Generalised linear modelling (GLM)

For the statistical modelling of individual substances, we only considered those with ≥ 80% detection frequency (excluding nornicotine as potential sources remain difficult to assess in the current study). For polychlorinated biphenyls (PCBs), the sum of the six indicator PCB congeners ($\sum_6$PCB 28, 52, 101, 138, 153 and 180) was used as the response variable of the model as it comprises about half of the amount of total non-dioxin-like PCBs (NDL-PCBs) present in feed and food according to Regulation (EU) No 277/2012. For approximating DDT exposure, *4,4′*-DDD and *4,4′*-DDE were summed to $\sum_2$DDT. For per- and polyfluoroalkyl substances (PFAS), we used the sum of perfluorosulfonic acids ($\sum_4$PFSAs: C_6-C_8: PFHxS, PFHpS. PFOS linear&branched) and the sum of perfluorinated carboxylic acids ($\sum_6$PFCAs: C_8–C_{13}: PFOA, PFNA, PFDeA, PFUnA, PFDoA, PFTrD) as the responses (similar to Sun et al. (2020b)). For PPPs, we used spiroxamine and simazine and for MPs, we used oxfendazole as the response. Full compound names and CAS numbers of all detected chemicals are given in Table SI-5.

For modelling, we tested the effect of $\delta^{15}N$ as proxy for the trophic position (Fig. 2), $\delta^{13}C$ as proxy for the food web (Fig. 2), and DCA1 land cover scores (Figure SI-5) separately on the respective responses. We only considered univariate models due to the small sample size (n = 30), which limits the statistical power of our analysis and can lead to an increase of false positives due to multiple testing. Therefore, we adjusted (adj) *p*-values by controlling the expected proportion of false discoveries amongst the rejected hypotheses (false discovery rate) using the approach from Benjamini and Hochberg (1995), which is more powerful than that of the traditional Bonferroni correction (Benjamini and Hochberg, 1995). Additionally, we simulated data for our model system (n = 30; 7 responses referring to chemical (groups) with detection frequency ≥80%, and 3 univariate fixed effects) assuming either a gamma or a gaussian distribution of the response to assess the risk of false positives in our particular setting. Model assumptions (linearity of the predictor, independence of errors and expected dispersion) were checked by simulating data from the fitted model and comparing the residuals of the model fitted on such simulated values to the residuals of the model fitted on the observed data using the R-package "DHARMa" (Hartig, 2020). A $\log_e(x + 1)$ transformation was applied to simazine to normalise the distribution. Predictor effect plots and confidence intervals were depicted in the scale of the linear predictor using the R-package "effects" (Fox and Weisberg, 2019; Fox and Weisberg, 2018).

2.7. Screening for PBT properties

All chemicals detected in the study were assessed by the JANUS tool (https://www.vegahub.eu/portfolio-item/janus/) for PBT properties (Table SI-5). The JANUS software is based on a battery of (Q)SAR models integrated with a specific workflow for each endpoint (UBA, 2016). The final predictions are combined in a PB and PBT score, which allows to rank and prioritize the list of detected target compounds. A score of 0–0.3 means that the compound is predicted to not meet the PB/PBT criteria, a score of 0.3–0.6 means that no conclusion can be drawn, while a score above 0.6 indicates that PB/PBT properties are likely to be met (Pizzo et al., 2016; UBA, 2016).

3. Results

3.1. Stable isotope analysis

The stable isotope values of livers from 30 HAALs are plotted together with those of muscle tissue from common prey species from the study area (taken from Nadjafzadeh et al. (2016)) in Fig. 2. Summary statistics as well as Latin species names are given in Table SI-7. The stable isotope values of HAALs ($\delta^{15}N$: 12.4 ± 0.7‰; $\delta^{13}C$: −24.7 ± 0.5‰) are positioned within the isotopic range of selected prey species, yet closer to freshwater fish and piscivorous birds than to ungulates. In particular, omnivorous fish species such as common rudd showed values close to those of the investigated HAALs, whereas predatory species such as European perch and northern pike showed enriched $\delta^{15}N$ values. Similar observations were made for aquatic birds, where piscivorous species (great cormorant and great crested grebe) had enriched $\delta^{15}N$ values compared to omnivorous (black-headed gull, mallard, Eurasian coot) and herbivorous species (geese: *Anser* sp.). Among the terrestrial game mammals, only carnivorous/omnivorous species such as racoon dog and red fox showed overlapping stable isotope values with some HAAL individuals, whereas ungulates had considerably lower $\delta^{15}N$ values.

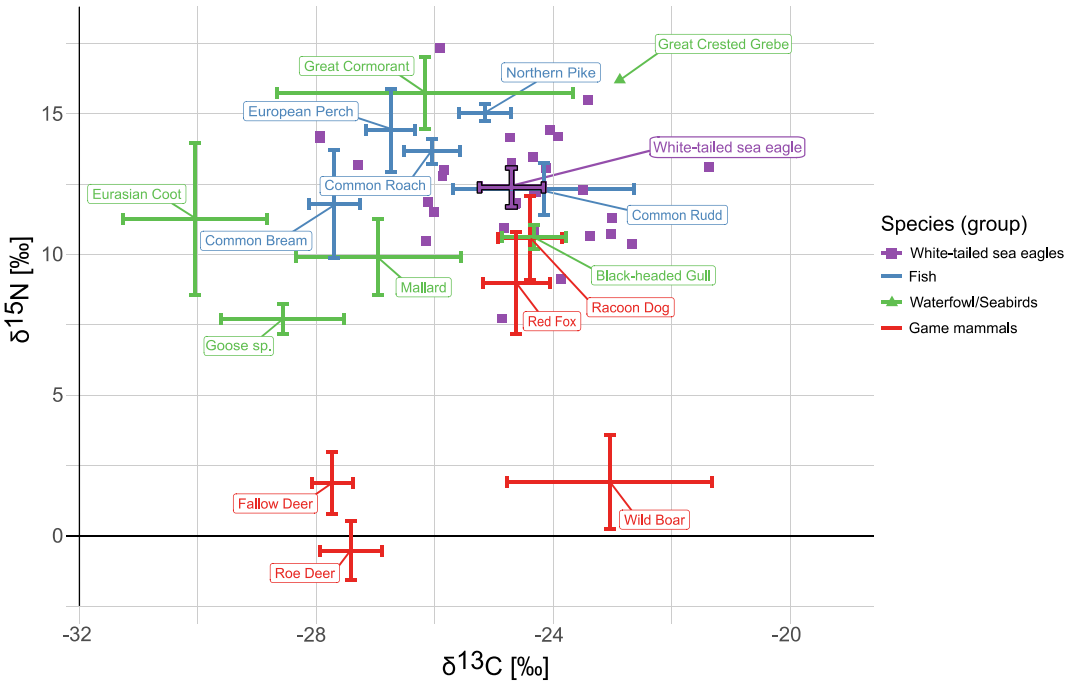

Fig. 2. Stable isotope values of $\delta^{15}N$ and $\delta^{13}C$ (cross: mean ± 2.0 * SE) for livers of white-tailed sea eagles (HAAL, n = 30, this study) and muscles of common prey species (taken from Nadjafzadeh et al., 2016). European perch (n = 5), northern pike (n = 6), common bream (n = 6), common roach (n = 6), common rudd (n = 6), great cormorant (n = 6), great crested grebe (n = 1), black-headed gull (n = 6), mallard (n = 5), Eurasian coot (n = 6), goose sp. (n = 7), red fox (n = 6), racoon dog (n = 6), wild boar (n = 6), fallow deer (n = 6), roe deer (n = 6). Summary statistics and Latin species names are given in Table SI-7. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.2. *Wide-scope target screening*

In total, we detected 85 chemicals of which 27.1% were medicinal products (MPs) including TPs followed by POPs regulated under the Stockholm Convention (23.5%) and plant protection products (PPPs) (20%). Industrial chemicals regulated under REACH accounted for 17.6% of the identified compounds. Furthermore, 7.1% were stimulants and 4.7% belonged to chemicals regulated under various other legislations. Non-detected compounds of the target list were below the method SDL of 1.83 ng g^{-1} ww. Seven individuals were previously analysed by a multi-target method (Badry et al., 2021) for a subset of the 2441 target compounds analysed in this study (Table SI-15/16). Reported concentrations (median, IQR) in both studies refer to individuals with detected residues. A comparison of both analytical methods indicates that rodenticides such as brodifacoum may need compound-specific extraction and analysis protocols as concentrations were detected only in the individual with the previously highest residue. A comparison between the results of both methods can be found in the supplementary information (SI 2.1 and Table SI-15/16).

3.2.1. *Chemicals of the Stockholm Convention*

Among the chemicals regulated under the Stockholm Convention, PCB138 (median ww concentration (IQR): 238 (384) ng g^{-1}) and PCB180 (113 (321) ng g^{-1}) as well as *4,4′*-DDE (169 (159) ng g^{-1}) and *4,4′*-DDD (2.18 (5.41) ng g^{-1}) were detected in all individuals (Fig. 3; Table SI-8). For the investigated PCBs the order of detection is as follows: PCB138/180: 100% > PCB101: 93% (6.91 (13.0) ng g^{-1}) > PCB153: 80% (90.1 (217) ng g^{-1}) > PCB28: 53% (0.6 (1.53) ng g^{-1}) > PCB52: 43% (0.52 (5.17) ng g^{-1}) > PCB209: 17% (1.76 (12.0) ng g^{-1}). PFOS as well as PFOA are included in the Stockholm Convention as well but are presented together with other PFAS to allow for comparisons among chemicals of the same group. For the other POPs, dicofol was detected in 70% (0.77 (1.1) ng g^{-1}) and its metabolite 4,4′-dichlorobenzophenone in 60% (0.51 (1.25) ng g^{-1}) of the individuals followed by β-hexachlorocyclohexane (β-HCH) in 33% (4.35 (13.2) ng g^{-1}), heptachlor epoxide in 17% (0.87 (1.44) ng g^{-1}) and pentachlorobenzene in 10% (0.24 (0.21) ng g^{-1}). Hexachlorobenzene (44.9 (25.7) ng g^{-1}), *cis*-chlordane (4.4 (1.95) ng g^{-1}) and *trans*-chlordane (11.9 (1.3) ng g^{-1}) were detected in two individuals each. None of the tested univariate models ($\delta^{13}C$, $\delta^{15}N$ and DCA1 land cover scores) significantly (adj $p < 0.05$) explained the variation of $\sum_6$PCB and $\sum_2$DDT (Table 1).

3.2.2. *Industrial chemicals regulated under REACH*

Except for PFAS, eight industrial compounds regulated under REACH were detected in the HAAL livers. The synthetic musk galaxolide was detected in 30% (11.3 (15.4) ng g^{-1}) of the individuals followed by tributylamine in 20% (2.71 (all LOQ/2) ng g^{-1}) and phenanthrene in 20% (1.74 (2.65) ng g^{-1}). Furthermore, benzenesulfonamide (10.7 (all LOQ/2) ng g^{-1}) and didecyldimethylammonium (8.4 (all LOQ/2) ng g^{-1}) were detected in two individuals and 2-OH-benzothiazole (9.59 ng g^{-1} (LOQ/2)), methylparaben (7.95 ng g^{-1}), and lauric isopropanolamide (1.6 ng g^{-1} (LOQ/2)) were detected in one individual (Table SI-9).

3.2.2.1. Per- and polyfluoroalkyl substances (PFAS). Linear and branched PFOS isomers were the most frequently detected PFSAs and PFASs (100%) with higher concentration of the linear isomer 480 (518) ng g^{-1} vs. the branched isomer: 8.41 (12.7) ng g^{-1} (Fig. 4A, Table SI-10). The other PFSAs were detected in fewer individuals with PFHpS in 30% (0.22 (0.29) ng g^{-1}) and PFHxS in 23% (0.05 (0.12) ng g^{-1}) of the individuals at lower concentrations. The order of detected PFCAs is as follows: PFDeA: 97% (1.78 (2.5) ng g^{-1}) > PFNA: 90% (3.97 (2.23) ng g^{-1}) > PFUnA: 60% (1.98 (1.57) ng g^{-1}) > PFOA: 23% (0.67 ng g^{-1} (all LOQ/2)) > PFDoA: 20% (0.6 ng g^{-1} (LOQ/2)) and PFTrDA: 20% (0.68 (1.38) ng g^{-1}). Linear PFOS concentrations made up 98.2% of $\sum_4$PFSA concentrations (Fig. 4B) and 96.8% of $\sum_{10}$PFAS concentrations. Among $\sum_6$PFCA concentrations, PFNA contributed to 47.2% followed by PFDeA (32.5%) and PFUnA (13.7%) (Fig. 4C). For $\sum_6$PFCA, concentrations significantly increased with $\delta^{15}N$ (1.38 times higher per ‰; adj $p < 0.01$; Fig. 4D), whereas no significant relationships were observed

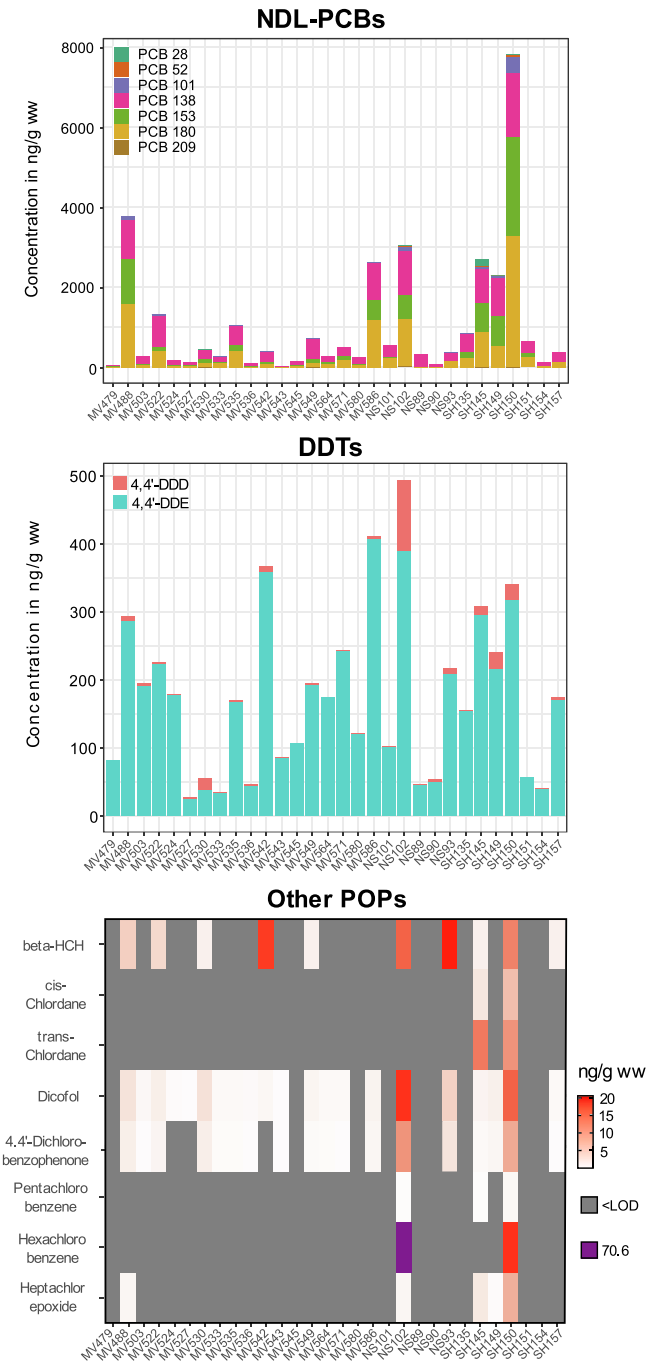

Fig. 3. Detection of non-dioxin-like PCBs and *4,4′*-DDD/*4,4′*-DDE in white-tailed sea eagles (HAAL, n = 30) given as bar charts. Other persistent organic pollutants (POPs) of the Stockholm Convention are visualised as heat map. Grey tiles in the heat map refer to samples below the limit of detection (LOD). Summary statistics are given in Table SI-8. Model estimates of all univariate models are given in Table 1. None of the univariate models significantly (adj $p < 0.05$) explained the variation of $\sum_6$PCB and $\sum_2$DDT.

for $\sum_4$PFSA (Table 1).

3.2.3. Plant protection products (PPPs)

The majority of detected PPPs was approved in Germany during the sampling period (2015–2018). Spiroxamine was detected in all individuals (3.03 (1.79) ng g^{-1}) followed by napropamide in 17% (1.75 ng g^{-1} (all LOQ/2)) and pymetrozine in 13% (7.71 (5.33) ng g^{-1}) of the individuals (Figure-5A). Bromoxynil, dimethachlor metabolites ESA-&OXA, dichlorobenzamide (parent compounds: fluopicolide/dichlobenil), metalaxyl, myclobutanil, propamocarb and pyrethrin I were detected in three or fewer individuals (Table SI-11). Besides the approved PPPs, five non-authorised PPPs were detected with simazine in 93% (4.67 (4.21) ng g^{-1}) of the individuals showing the highest detection rate followed by the metabolites ethiofencarb-sulfone in 33% (2.85 (2.52) ng g^{-1}) and alachlor-OXA in 30% (15.54 ng g^{-1} (LOQ/2)). Carbofuran, dikegulac and propachlor were detected in two individuals each with carbofuran showing the highest concentrations (1334 (1143) ng g^{-1}). For spiroxamine and simazine, concentrations significantly decreased with DCA1 land cover scores (adj $p < 0.05$; Fig. 5 B&C), which can be interpreted as a proxy for agricultural land cover within the 5 km buffer zone (Figure SI-5).

3.2.4. Medicinal products (MPs)

MV542 was excluded from the analysis of MPs due to potential deliberate treatments. Oxfendazole (VMP) was detected in all individuals (40.6 (9.2) ng g^{-1}) followed by salicylamide (HMP) in 72% (36.5 (33.8) ng g^{-1}) and meptazinol (HMP) in 55% (25.3 (27.0) ng g^{-1}) of the individuals (Fig. 6, Table SI-12). Residues of O-desmethylnor-tramadol were detected in 59% (19.0 (25.2) ng g^{-1}) along with other tramadol metabolites (O-desmethyldinor-tramadol, N-bisdesmethyl-tramadol, nor tramadol) and its parent compound (tramadol: HMP/VMP), which were were found at lower concentrations and detection rates. The venlafaxine (HMP) metabolite D L-N N didesmethyl-venlafaxine was detected in 38% of the individuals (5.38 (4.45) ng g^{-1}), whereas D L-N O didesmethyl-venlafaxine was detected in 10% of the individuals (7.77 (3.73) ng g^{-1}). The metabolite N-desmethyl-tapentadol (HMP) was detected in 17% (17.2 (9.08) ng g^{-1}) of the individuals. Other MPs were detected in three or fewer individuals. None of the fixed effects significantly explained the variation observed for oxfendazole (Table 1).

3.2.5. Stimulants and others

Residues of tobacco-related substances such as nor-nicotine were detected in 83% (194 (129) ng g^{-1}) of the individuals followed by nicotine in 20% (92.6 (26.2) ng g^{-1}), hydroxy cotinine in 7% (388 (34.6) ng g^{-1}) and cotinine (58.9 ng g^{-1}) in one individual. In general, metabolites showed higher concentrations and detection rates compared to their parent compounds (Table SI-13). We furthermore detected the drug of abuse methamphetamine in three individuals (6.49 ng g^{-1} (all LOQ/2)). Detection rates and concentrations of chemicals from various origins such as the artificial sweetener aspartame, which was detected in 40% (14.8 (22.3) ng g^{-1}) of the individuals or the biocide 1,2-benziso-thiazolinone (13.3 ng g^{-1}; one individual) are given in Table SI-14.

3.3. Estimated PBT scores

Estimated PBT scores are given for better accessibility as separate Excel file in the supplementary information (Table SI-5). High estimated P, B, and/or T scores (>0.6) were most frequently observed for chemicals regulated under the Stockholm Convention. Among the chemicals regulated under REACH, especially PFAS had high P and/or B scores. Furthermore, 2-OH-benzothiazol had high P and galaxolide high B and T scores. Among the approved PPPs, bromoxynil, myclobutanil, napropamide, pymetrozine and spiroxamine were predicted P candidates similar to the expired PPPs alachlor-OXA, propachlor, and simazine. None of the PPPs had B or T scores > 0.6, which is in line with results for the MPs. In contrast to PPPs most MPs also had a P score < 0.6. Among the MPs with P score > 0.6 were the HMPs pindolol, desethylhydroxy-chloroquine and the VMPs oxfendazole, sulfadoxine as well as lidocaine and lidocaine-N-oxide (HMP/VMP). Except for hydroxy-cotinine (P > 0.6), all detected stimulants (and other compounds) had P, B and T scores < 0.6 (Table SI-5).

Table 1
Estimates of the univariate models on contaminant concentrations in livers of white-tailed sea eagles (HAAL, n = 30; medicinal products: n = 29). *p*-values were adjusted due to multiple testing by controlling the false discovery rate. Associations with negative DCA1 scores can be interpreted as a proxy for agricultural land cover and associations with positive DCA1 scores as a proxy for aquatic land cover (Figure SI-5).

	Estimates (multiplicators)	Estimates (log scale)	Std. Error	t value	Adjusted p-values
$\sum_6$PCB concentration [ng g^{-1}] gamma (log link)					
$\delta^{13}C$	1.10	0.10	0.19	0.52	0.98
$\delta^{15}N$	1.24	0.21	0.14	1.52	0.33
Land cover (DCA1 scores)	1.13	0.12	0.77	0.15	0.88
$\sum_2$DDT concentration [ng g^{-1}] gamma (log link)					
$\delta^{13}C$	1.07	0.07	0.09	0.78	0.98
$\delta^{15}N$	1.05	0.05	0.07	0.78	0.78
Land cover (DCA1 scores)	1.07	0.07	0.35	0.20	0.88
$\sum_4$PFSAs concentration [ng g^{-1}] gamma (log link)					
$\delta^{13}C$	1.01	0.01	0.12	0.09	0.99
$\delta^{15}N$	1.15	0.14	0.09	1.62	0.33
Land cover (DCA1 scores)	0.83	−0.18	0.46	−0.39	0.88
$\sum_6$PFCAs concentration [ng g^{-1}] gamma (log link)					
$\delta^{13}C$	1.05	0.05	0.10	0.50	0.98
$\delta^{15}N$	1.38	0.32	0.07	4.36	$p < 0.01$
Land cover (DCA1 scores)	1.32	0.28	0.42	0.66	0.88
Spiroxamine [ng g^{-1}] gamma (log link)					
$\delta^{13}C$	0.93	−0.07	0.04	−1.59	0.86
$\delta^{15}N$	1.02	0.02	0.04	0.46	0.90
Land cover (DCA1 scores)	0.65	−0.44	0.16	−2.75	$p < 0.05$
		Estimate (ng g^{-1})	**Std. Error**	**t value**	**Adjusted p-values**
Log$_e$(Simazine + 1) gaussian (identity link)					
$\delta^{13}C$		0.00	0.09	−0.01	0.99
$\delta^{15}N$		−0.01	0.07	−0.08	0.93
Land cover (DCA1 scores)		−0.80	0.31	−2.62	$p < 0.05$
Oxfendazole [ng g^{-1}] gaussian (identity link)					
$\delta^{13}C$		−0.48	1.22	−0.39	0.98
$\delta^{15}N$		0.10	0.94	0.11	0.93
Land cover (DCA1 scores)		−2.25	4.74	−0.48	0.88

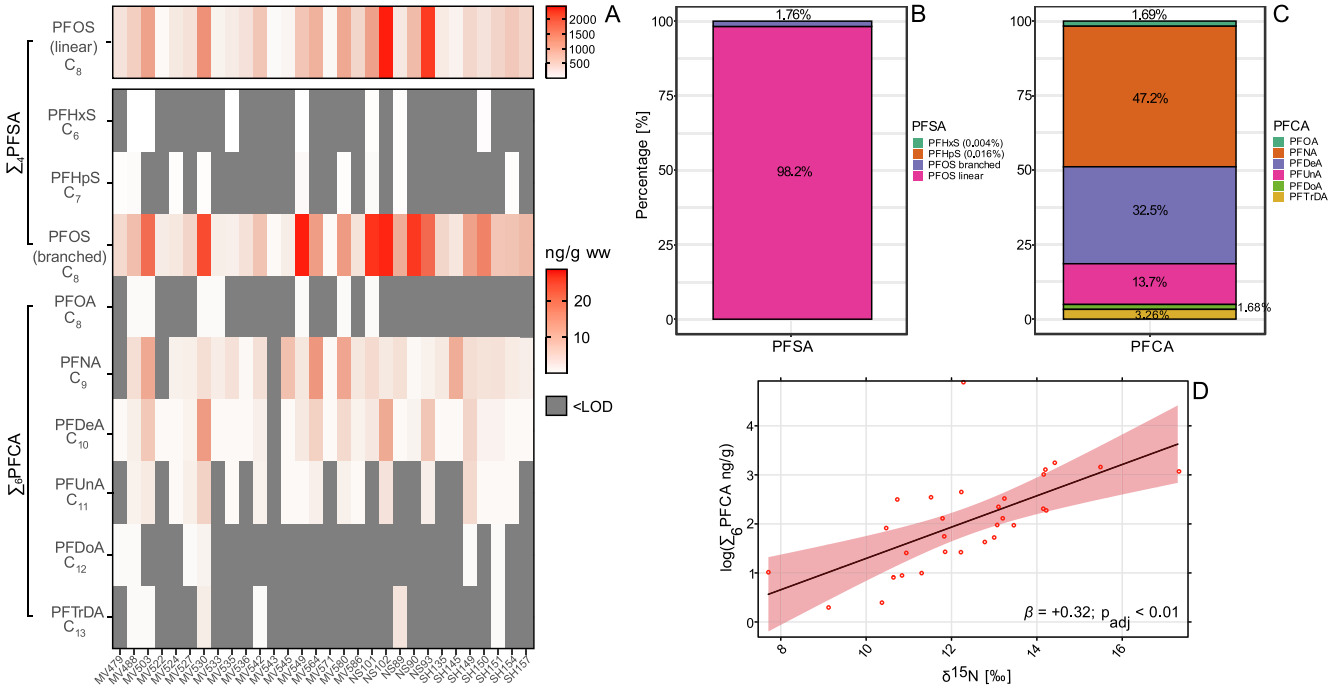

Fig. 4. Detection of PFSAs and PFCAs in white-tailed sea eagles (HAAL, n = 30) given as heat map (A). Grey tiles refer to samples below the limit of detection (LOD). Summary statistics are given in Table SI-10. Percentage of individual PFSA (B) and PFCA (C) concentrations are given as stacked bar plots. The significant effect (adj $p < 0.01$) of $\delta^{15}N$ on $\sum_6$PFCA is given as predictor effect plot with regression line, residuals (dots), and 95% confidence interval (D). Model estimates of all univariate models are given in Table 1.

4. Discussion

Whereas raptors played a critical role in developing awareness of chemical pollution and policy, they have so far played a much smaller role in research on CECs. Recent research efforts have led to the detection of novel CECs in European raptors (recently reviewed by González-

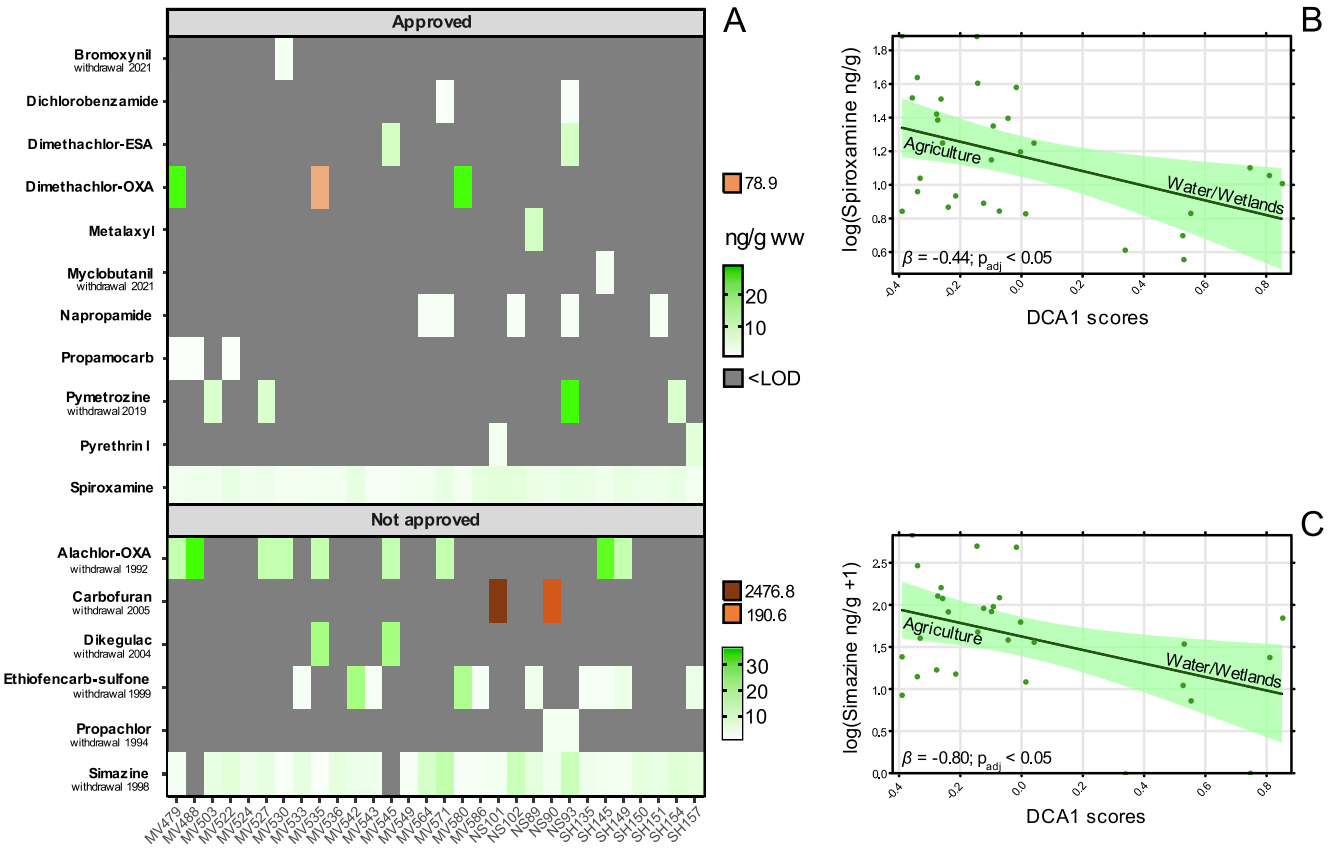

Fig. 5. Detection of approved and expired plant protection products at the time of sampling (until 31/12/2018) in white-tailed sea eagles (HAAL, n = 30) given as heat map (A). Grey tiles refer to samples below the limit of detection (LOD). Summary statistics are given in Table SI-11. Date of withdrawal (in Germany) refers to the parent compound in case of metabolites/transformation products. Significant effects (adj $p < 0.05$) of DCA land cover scores on spiroxamine (B) and simazine (C) are given as predictor effects plots with regression line, residuals (dots), and 95% confidence intervals. Model estimates of all univariate models are given in Table 1.

Rubio et al. (2020a)) including studies on HAALs (Badry et al., 2021; González-Rubio et al., 2020b; Oró-Nolla et al., 2021). Through the application of comprehensive analytical tools using both GC and LC coupled to HR-MS, the current study adds information on novel CECs in combination with underlying food web characterisation as well as on risk assessment with regards to their chemical regulations in Europe.

Our study demonstrated the presence of a large variety of contaminants in the livers of an apex predator from Germany, some of which have not been reported in the literature before. However, 2300+ chemicals remained undetected and their absence (SDL: <1.83 ng g^{-1}) remains difficult to assess as not all investigated target analytes were liver-specific and might be present in other environmental matrices such as wastewater, surface water or soils. Nevertheless, the liver represents the metabolic most competent organ and was therefore chosen as matrix for analysing contaminants with different physicochemical properties. The fact that a compound was not detected in a field biomonitoring study does not relieve a compound from the suspicion of being PBT since the environmental occurrence also always depends on e.g. its use and (local) emission sources. Furthermore, the generic sample preparation protocols and the full scan acquisition mode applied in HRMS instrumentation may have accounted for increased detection limits and lower %recoveries compared to conventional LC- or GC- MS/MS targeted methodologies for a pre-selected and restricted number of compounds (usually from the same chemical class) using Selected Reaction Monitoring (SRM) mode. However, one major advantage of our HRMS analysis is that apart from wide-scope target screening, the acquired chromatograms are accessible for retrospective data treatment, without the need for additional analysis, using suspect and non-target screening strategies that will expand the number of detected compounds in future (Menger et al., 2020).

4.1. Stable isotope values and food web characterization

An important means to control for dietary variations of apex predators feeding on mixed food webs represents the analysis of stable isotopes. During the summer season between 1996 and 2008, linear mixing models using stable isotope values in muscles (n = 75) of HAALs from the same study area revealed that the aquatic environment represents the main food source (91%) with fish accounting for 60% of the diet followed by waterfowl (27%) and game mammals (13%) (Nadjafzadeh et al., 2016). During winter, the contribution of wild ungulates can increase up to 29.5% (Nadjafzadeh et al., 2016). In general, stable isotope values of the present study were lower compared to those in livers of 30 HAALs sampled in the same study region between 1996 and 2003 ($\delta^{13}C$: –23.5 ± 1.1 ‰; $\delta^{15}N$: +13.6 ± 2.4 ‰; Nadjafzadeh et al. (2016)). The lower $\delta^{15}N$ values may be caused by a higher proportion of game mammals throughout the seasons, whereas the lower $\delta^{13}C$ values might reflect an increased uptake of freshwater (vs marine) prey. However, both $\delta^{13}C$ and $\delta^{15}N$ values have shown to decline in species of the coastal food web from northern Germany between 1988 and 2016, which was suggested to be related to an increase in terrestrial carbon sources and changes in nutrient inputs (Corman et al., 2018). In general, German HAALs use, compared to other HAAL subpopulations from Norway and Greenland, a higher proportion of freshwater food sources, which results in considerably lower $\delta^{13}C$ values (Løseth et al., 2019; Nadjafzadeh et al., 2016). Similar to HAALs from southern Sweden, marine HAALs from Germany (e.g. from Usedom) mainly forage on the brackish water of the Baltic Sea, which is characterised by lower salinity and slow water exchange with the North Sea, which might have contributed to the generally lower $\delta^{13}C$ values observed by the current study.

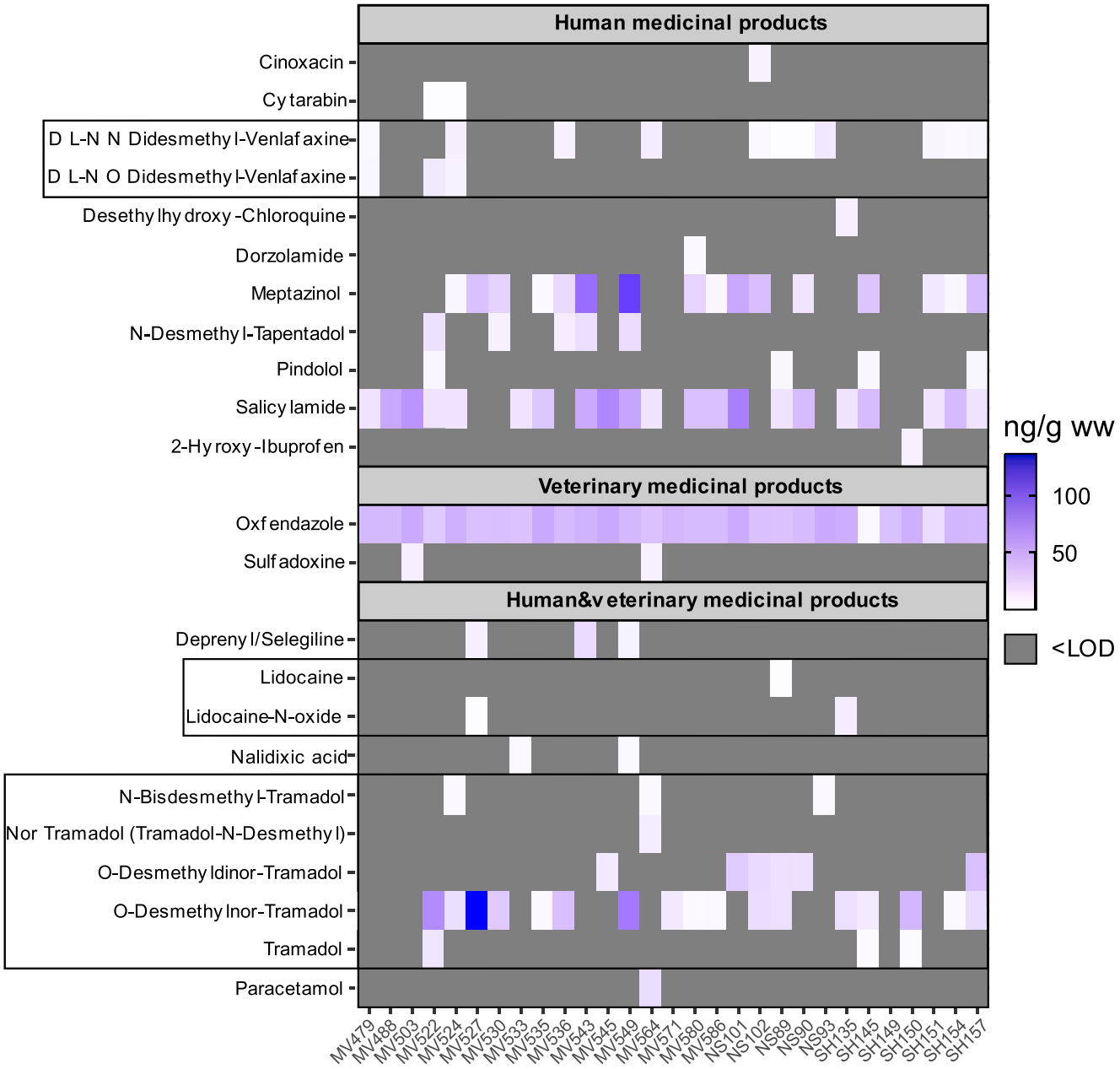

Fig. 6. Detection of medicinal products classed by their registration (human, veterinary, both) in white-tailed sea eagles found dead (HAAL, n = 29) given as heat map. Grey tiles refer to samples below the limit of detection (LOD). Summary statistics are given in Table SI-12. MV542 has been excluded due to potential deliberate treatments. Model estimates of all univariate models are given in Table 1. None of the univariate models significantly (adj $p < 0.05$) explained the variation of oxfendazole.

4.2. Assessment of POP and CEC concentrations among HAAL subpopulations and other predators

POPs listed in the Stockholm Convention were banned on a global scale due to their PBT properties but many POPs are still threatening apex predators in the Baltic Sea region due to biomagnification (de Wit et al., 2020). Among POPs, *p,p*'-DDE was together with ∑PCBs the main driver for population declines of HAALs during the 20th century (Helander et al., 2002; Roos et al., 2012). DDE as well as PCBs represent the dominant legacy POPs in the present study, which is in agreement with other marine apex predators in the Baltic Sea region (de Wit et al., 2020). In western Germany (Federal Republic of Germany), DDT was banned in the early 1970ties (id: SH&NS, Fig. 1), whereas it was still in use until 1988 by the German Democratic Republic (GDR, id: MV, Fig. 1). Concentrations of $\sum_3$DDT (95% *p,p*'-DDE) showed declining trends in eggs of HAALs from northern Germany between 1969 and 2001 (Scharenberg and Struwe-Juhl, 2006), which is in agreement with Swedish HAALs (Roos et al., 2012; Sun et al., 2020a). Concentrations of *4,4*′-DDE in the present study were considerably lower compared to liver concentrations of HAALs from Eastern Germany sampled between 1979 and 1998 (n = 24, median: 6400 (738) ng g^{-1}; Kannan et al. (2003)), which is considered to be related to the local use patterns of DDT in the GDR. In contrast to DDT, PCBs are still suspected to threaten marine apex predators (e.g. Desforges et al., 2018) but associations with reproduction failure in HAALs was considered to be lower compared to *p,p*'-DDE (Helander et al., 2002). Western Germany had one of the highest PCB productions between 1930 and 1983, accounting for ~12% of the global production, whereas production in the GDR was considered to be lower (Breivik et al., 2002). Among northern HAAL sub-populations, ∑PCB levels were, similar to *p,p*'-DDE, highest in Sweden,

where concentrations show a declining trend between 1968 and 2011 (Sun et al., 2020a). Concentrations of $\sum_6$PCBs in the current study were lower compared to those in livers of previously sampled (1979–1998) HAALs from Eastern Germany (dioxin-like $\sum$PCBs median: 6500 (1443) ng g^{-1}; Kannan et al. (2003)) and HAALs from Greenland sampled between 1997 and 2009 ($\sum_{28}$PCBs, median: 540 ng g^{-1}; Jaspers et al. (2013a)). The detected DDE and PCB levels in the current study were below thresholds for reproductive impairment in HAALs (DDE: 120 μg g^{-1} lipid weight (lw); $\sum$PCBs: 500 μg g^{-1} lw; Helander et al. (2002)) based on the conversion from wet weight to lipid weight for DDTs and PCBs in HAAL livers (~1:20) (calculated based on Jaspers et al. (2013a)). However, both POPs showed considerable variations among individuals and may still cause subclinical effects on immunity and oxidative stress as observed for HAAL nestlings from Norway (Hansen et al., 2020; Sletten et al., 2016). Another frequently detected POP was dicofol, which was used in Germany as miticide until 1992. Dicofol was not detected in muscle tissue of bream (*Abramis brama*) from German freshwater sites (LOQ: 10 ng g^{-1}) and therefore not considered to be a relevant aquatic contaminant (Fliedner et al., 2016). Concentrations of the current study were mainly below the LOQ reported by Fliedner et al. (2016), indicating that the frequent detection may be related to biomagnification of comparably low residues in the food web. Other legacy POPs such as β-HCH, hexachlorobenzene and chlordanes were previously detected in HAAL subpopulations (Hansen et al., 2020; Løseth et al., 2019; Sun et al., 2020a). The detection of those POPs in the current study is expected to reflect exposures through remobilisation from soils and sediments as some POPs were ceased out comparably late in the GDR.

PFAS are used in a large variety of products including fire-fighting foams, paints and varnishes or outdoor clothing, which resulted in a ubiquitous distribution in the environment (Land et al., 2018). PFOS represented the main PFSA (98.2%) and PFAS (96.8%) in the current study, which is in line with results observed for eggs of Swedish HAALs and livers of Swedish otters (*Lutra lutra*) (Faxneld et al., 2016; Roos et al., 2013). In Norway, the contribution of PFOS is also dominant but appears to have a lower relative contribution to $\sum$PFAS (Jouanneau et al., 2020; Roos et al., 2013). PFOS levels in livers of 36 HAALs from Eastern Germany (1979–1998) ranged between < 3.9–127 ng g^{-1} with a median of ~29 ng g^{-1} (Kannan et al., 2002). These results indicate that PFOS levels in HAALs considerably increased over the past decades in the study area (47.2–2440 ng g^{-1}; this study). This is in line with increasing PFOS trends in feathers of HAALs from Sweden (1968–2011) (Sun et al., 2019), whereas other northern HAAL subpopulations showed declining PFOS trends after the phase-out in the early 2000s (Jouanneau et al., 2020; Sun et al., 2019). Furthermore, liver concentrations in the current study were higher compared to PFOS concentrations in livers from terrestrial raptors sampled in the vicinity of a PFAS point source in Antwerp, Belgium (barn owl (*Tyto alba*), median: 304.5 ng g^{-1}; Jaspers et al. (2013b): and Eurasian sparrowhawk (*Accipiter nisus*), mean: 236 ng g^{-1}; Meyer et al. (2009)). The high PFOS levels of HAALs from northern Germany (this study) in combination with the high levels from southern Sweden (Faxneld et al., 2016) indicate that emission sources from Germany might contribute to a delayed onset of declining PFOS trends in biota from the Baltic Sea region.

The dominant PFCAs in the present study were PFNA (C_9) > PFDeA (C_{10}) > PFUnA (C_{11}), which is in line with patterns found in livers of Swedish otters (Roos et al., 2013), whereas PFNA (C_9), PFUnDA (C_{11}), PFTrDA (C_{13}) were most dominant in eggs of Swedish HAALs (Faxneld et al., 2016). A dominant contribution of odd chain PFCAs appears to be more pronounced in marine (vs freshwater) environments (Roos et al., 2013) and might, besides matrix specific differences, explain the observed differences in PFDeA detection. In Kannan et al. (2002), the only targeted PFCA, PFOA, was not detected in HAALs from Eastern Germany, which might have been related to the comparably high LOQ of 40 ng g^{-1} ww. In the study by Jaspers et al. (2013b), PFCAs were except for PFOA only sporadically detected in livers of barn owls but at higher concentrations compared to PFCAs in the present study. Similar to PFOS, PFCAs showed an increasing trend in feathers and eggs of HAALs populations from Sweden (Faxneld et al., 2016; Sun et al., 2019). For long-chain PFCAs, atmospheric transport and transformation of precursors were suggested to result in a uniform distribution among northern HAAL subpopulations, whereas for PFOS, spatial water-bound contamination was suggested to be most influential (Faxneld et al., 2016; Roos et al., 2013; Sun et al., 2019). In central Europe, where most industrial activity is located, direct PFCA emissions might have a considerable impact as well. However, since PFCA concentrations in the present study were comparably low, direct emission sources of the targeted PFCAs in the study area seem unlikely.

Among approved PPPs (until 31/12/2018), the fungicide spiroxamine was detected in all individuals. Quantities of sold spiroxamine in Germany ranged between 100 and 1000 tonnes (t) per year during the sampling period (BVL, 2020), making it a frequently sold PPP. Spiroxamine was not detected in a recent multi-target analysis of blood (LOQ: 0.1 ng ml^{-1}) and muscle tissues (LOQ: 10 ng g^{-1}) of terrestrial raptors from Spain (Rial-Berriel et al., 2020; Sabater et al., 2020), whereas 3% of herbivorous game mammals from Poland had residues in their muscles (n = 136, mean: 1.1 ng g^{-1}) (Kaczyński et al., 2021). For spiroxamine, the highest levels are expected to occur in livers (mammals), where it is relatively fast metabolized and excreted (EFSA, 2010). Despite the matrix differences compared to our study, these results indicate that terrestrial spiroxamine exposure via scavenging might only be responsible for a minor part of the observed exposures. Other approved PPPs were only occasionally present in HAALs with dimethachlor metabolites being present in 17% of the individuals, which might be related to aquatic exposure due to their frequent detection in wastewater treatment plant (WWTP) effluents (Gago-Ferrero et al., 2020). Among the expired PPPs, the herbicide simazine was detected in almost all individuals and was also detected in WWTP effluents as well as in soil and sediments from Europe (Chiaia-Hernández et al., 2020; Gago-Ferrero et al., 2020). Furthermore, simazine was only occasionally detected in blood (5%; n = 148) of terrestrial raptors from Spain (Rial-Berriel et al., 2020), which indicates, similar to spiroxamine, that terrestrial exposure might only be responsible for a minor part of the observed exposures. In contrast, carbofuran is despite its ban frequently used to deliberately poison HAALs and other raptors in Europe (Kitowski et al., 2020). Carbofuran poisoning was confirmed as cause of death for the HAAL NS101 via gut and gizzard content and was suspected during necropsy for NS90.

Among the MPs, the anthelmintic agent oxfendazole (VMP; livestock) was detected in all individuals. In a previous study, oxfendazole was together with another anthelmintic agent detected in a liver of a pine marten (*Martes martes*) from the UK and suspected to be related to scavenging on treated livestock (Taylor et al., 2019). In contrast, no oxfendazole residues (LOQ: 0.1 ng mL^{-1}) were found in blood of non-scavenging raptors from Spain (Rial-Berriel et al., 2020), which indicates that scavenging on livestock might have influenced the observed exposures. The second most common MP, salicylamide (HMP, analgesic) is not used in Germany (Table SI-5), which raises the question if salicylamide is a potential metabolization/transformation product from more common and structurally similar MPs such as acetylsalicylic acid. However, salicylamide is also pre-registered under REACH as it used as an intermediate during the manufacture of other substances (Table SI-5). Previous studies detected salicylamide in freshwater along with paracetamol, (hydroxy-)cotinine, DADMAC (C10:C10) and 2-OH-benzothiazole (Diamanti et al., 2020) as well as together with venlafaxine, lidocaine and meptazinol in WWTP effluents (Gago-Ferrero et al., 2020). In the current study especially, coastal HAALs from the island Usedom (Baltic Sea) but also the HAALs close to the North Sea (e.g. NS101&SH145) had considerable residues, which indicates the presence of potential marine exposure sources. Other detected MPs comprise opioid analgesics such as tramadol and its metabolites, which were together with (nor-)lidocaine and (O-desmethyl-) venlafaxine

previously detected in aquatic biota from Germany (bream) and the UK (amphipods) and suspected to be related to WWTP effluents (Boulard et al., 2020; Miller et al., 2021). Both tramadol and lidocaine metabolites were found at similar or higher concentrations in bream compared to their parent compounds (Boulard et al., 2020), which indicates at least some of the metabolites are transferred in the food web of HAALs. Among the stimulants, nicotine metabolites were most frequently detected even though nicotine derivates are in general efficiently eliminated in WWTPs (Buerge et al., 2008). Therefore, the assessment of potential routes of exposure for nicotine in the present study remains difficult to assess and requires further investigation.

4.3. Ecological and spatial variation of POPs and CECs

Many legacy POPs have shown to be biomagnified in food webs of HAALs (de Wit et al., 2020; Helander et al., 2002). However, no significant association between POPs of the Stockholm Convention ($\sum_6$PCB, $\sum_2$DDT) and δ^{15}N was observed, which is in line with observations for $\sum$OCPs/$\sum$PCBs (Løseth et al., 2019), but contrasts observations for *p,p'*-DDE and PCB 153 in Norwegian HAAL nestlings (Eulaers et al., 2013). For freshwater sites, which represent together with brackish water the main food source for German HAALs, lower admixture and higher spatial variation are suggested to result in increased heterogeneity of contaminants levels, which might obscure trophic signals (Elliott et al., 2009). Another confounding factor for the assessment of trophic influences on contaminant levels might have been the use of δ^{15}N bulk values, as baseline δ^{15}N values have shown to vary not only with trophic position but also with agricultural inputs, which might obscure or create spurious relationships with δ^{15}N (Elliott et al., 2021). Due to the unaccounted variation of baseline δ^{15}N, δ^{13}C (as well as δ^{34}S) has especially in marine ecosystems proven to be a better predictor for contaminants in top-predators (Elliott et al., 2021; Løseth et al., 2019). In contrast, the lack of a significant relationship between agricultural land cover scores and legacy POPs in the present study is assumed to be related to the lack of temporal overlap between the time of the latest POP application/emission (1970s/1990s), sample collection (2015–2018) and extraction of the data from the 2018 Corine data set.

For PFOS, the major PFSA in the current study, significant associations with δ^{15}N were reported for trend models in feathers of Norwegian and Swedish HAALs, whereas δ^{15}N was no significant predictor for $\sum$PFCA (Sun et al., 2019). In the blood of peregrine falcon nestlings (*Falco peregrinus*) from Canada, both $\sum$PFSA and $\sum$PFCA significantly increased with δ^{15}N (Sun et al., 2020b). In the current study, only $\sum_6$PFCA levels significantly increased with δ^{15}N, which indicates higher $\sum_6$PFCA levels with preying on piscivorous prey species. However, the non-significant relationship of $\sum_4$PFSA with δ^{15}N (adj $p = 0.33$) was unexpected as PFSAs generally have higher biota to soil accumulation factors compared to PFCAs of equal chain length (Zhao et al., 2013). A possible reason might be related to specific point sources that have potentially obscured trophic signals within the home range of the eagles. For example, both NS93 and NS102 were found in the same catchment area of the river Elbe and showed the highest PFOS concentrations (>2000 ng g^{-1}) among individuals of the present studies as well as compared to raptors from a PFAS contaminated area in Belgium (see above). Potential PFAS sources in our study area (including MV530: 1291 ng g^{-1} PFOS) include a military training ground in Lübtheen (used until 2013) as well as private airports, e.g. from the use of firefighting foams. The lack of association of both $\sum_6$PFCA and $\sum_4$PFSA/PFOS with δ^{13}C is however consistent with results for feathers of adult HAALs from Sweden, whereas δ^{13}C significantly explained $\sum$PFCAs variations in Norwegian HAALs (Sun et al., 2019) and peregrine falcon nestlings from Canada (Sun et al., 2020b).

Among the PPPs, the concentrations of the approved fungicide spiroxamine and expired herbicide simazine increased with the proportion of inland agricultural land cover, which indicates that exposures might be related to local sources. For example, surface runoff and spray drift of spiroxamine might have caused aquatic emissions in the direct vicinity of agricultural fields as spiroxamine rapidly binds to sediments in water systems (EFSA, 2010). We therefore recommend further studies on spiroxamine in bioturbating organisms such as bream from agricultural influenced areas to further investigate potential exposure risks. For simazine, regular monitoring for the EU Water Framework Directive is only recommended for water but not sediments or biota due to its low log K_{ow} (2.2) and low bioconcentration factor (1) (EC, 2010). However, residues of simazine were previously detected in sediments as well as in apex predators (see 4.2), which calls for further studies on potential exposures from simazine impurities (up to 3%) in terbuthylazine formulations (herbicide, sold up to 1000 tons per year BVL (2020)) as well as for studies on potential legacy applications of simazine as algicide in fishing ponds, where HAALs are known to forage.

4.4. Risk assessment and implications for chemicals management

The JANUS software is a helpful tool to unravel a mismatch between predicted laboratory data on PBT properties and observed exposures (Pizzo et al., 2016). As expected, many of those compounds that were predicted to have PBTs or PBs properties (JANUS scores > 0.6; Table SI-5), e.g. most legacy POPs and PFAS, also had high detection rates (>70%). However, some estimated and already regulated PBTs, e.g. PFHxS and PFTrDA had low detection rates, which may reflect the complexity of exposure events for apex predators that are not solely related to intrinsic chemical properties. Furthermore, some of the identified PBTs that were not or hardly detected were used in low quantities in Germany (e.g. fluorene), regulated for a long time (e.g. hexachlorobenzene), or may have been removed by WWTPs.

Among the non-restricted industrial chemicals regulated under REACH, PFASs (particularly PFDeA; PFHpS; PFNA, PFuNA) and galaxolide were the chemicals of highest concern based on their detection rate (>30%) and/or their predicted PBT properties (JANUS: P and/or B score > 0.6). In 2017, the REACH restriction of PFOA, its salts and precursors came into force and was implemented in 2020 (EC, 2017). Our data further support the urge for regulatory action on polyfluorinated compounds, which are currently evaluated as part of the ongoing restriction of PFAS (ECHA, 2020). We have submitted our results to the authorities responsible for the EU-wide restriction of PFAS to support their weight of evidence assessment. Another industrial compound regulated under REACH, galaxolide, is used as synthetic musk in washing and personal care products up to 10,000 tons per year (EU) and is assumed to be bioaccumulative and toxic but not persistent according to JANUS (Table SI-5). On request of the French authority, our data have also been used for the ongoing REACH substance evaluation concerning potential PBT properties. These examples demonstrate that strengthening the collaboration between biomonitoring networks and authorities might help to further promote the regulatory use of centralized, open assess databases like NORMAN (https://www.norman-network.com/nds/) and IPCHEM (https://ipchem.jrc.ec.europa.eu).

In contrast to the other chemical classes, data on use and tonnage are available for most PPPs. Based on a P score of > 0.6 and sold amounts of > 100 tons per year in Germany, exposures to bromoxynil, spiroxamine, and propamocarb were expected. However, only spiroxamine appeared to have a wide-spread exposure in HAALs. The fact that all other approved PPPs were found in few individuals indicates that the majority of PPPs are either not bioaccumulative, rapidly metabolized and excreted by HAALs or are just not applied in the study area as indicated by their low tonnages (Table SI-5). Among the non-approved PPPs, the widely detected PPPs simazine and alachlor-OXA are predicted to be vP/P by JANUS and have high absorption affinity, which might indicate that both substances bind to soils and sediments and are potentially remobilised as described in section 4.3. In contrast, the frequent detection of ethiofencarb-sulfone indicates potential illegal applications in the study area based on the low P and B scores.

Among the MPs, most of the detected substances had a P, B or T score

< 0.6, indicating that the substances are degradable in the environment (low P) and can be metabolised/excreted by organisms (low B). Observed exposures to detected MPs might therefore be related to emissions that have exceeded metabolization/transformation rates. In contrast, oxfendazole (VMP) may persist in the environment as predicted by JANUS (Table SI-5). However, exposure routes via scavenging are not accounted for during registration and should be considered for VMPs used in livestock as exemplified for diclofenac poisoning of scavengers in Spain (Herrero-Villar et al., 2021). Therefore, a regulatory follow-up check of the environmental fate and behaviour of oxfendazole including future monitoring studies is necessary to investigate if oxfendazole contamination is of concern for scavengers. Taken together, the JANUS software has proven to be a reliable tool for the rapid identification of P, B or T properties for the majority of the detected compounds. However, for some known PBT compounds such as brodifacoum, the JANUS tool fails to predict PBT properties, which indicates that hazard assessments cannot yet be based on *in silico* tools alone.

5. Conclusion

Our study shows that HAALs from Germany are exposed to a large cocktail of chemicals across different regulations including more than fifteen POPs and their metabolites, which demonstrates that contamination in German HAALs is still widespread. Even though wildlife species are exposed to multiple chemicals, chemical mixtures are so far not adequately assessed in the European risk assessment (Drakvik et al., 2020). There is an urgent need to promote strategies on how exposure to multiple hazardous chemicals can be more effectively assessed to cover field conditions. Since data on bird toxicity, sales and use of MPs, industrial chemicals regulated under REACH as well as on biocides are non-obligatory within the EU approval or registration, no link can be drawn between predicted environmental emission rates, measured concentrations in HAALs and their effects. However, especially the combination of legacy POPs and PFAS (e.g. for NS93&102, SH150), is suspected to result in cumulative or synergistic effects that may exceed toxic thresholds (Sonne et al., 2021; Sun et al., 2020a) and requires further investigation. Our study supports the general trend, that whilst in recent years great efforts have been undertaken in terms of analytical development to quantify the presence of CECs in biota, our understanding of the risks and possible chronic impacts posed to wildlife species, particularly to apex predators, still lags behind. We therefore recommend that data on the occurrence of CECs in apex predators should be more commonly considered in risk assessments under the different regulatory frameworks, e.g., in a weight of evidence approach, to trigger timely risk management measures before adverse effects in organisms or populations start to manifest.

CRediT authorship contribution statement

Alexander Badry: Conceptualization, Writing – original draft, Formal analysis (statistics), Data curation, Visualization. **Gabriele Treu:** Conceptualization, Writing – original draft, Formal analysis (risk assessment), Data curation, Funding acquisition. **Georgios Gkotsis:** Validation (wide-scope target target methods), Investigation (extraction of CECs and HRMS analysis), Writing - review & editing. **Maria-Christina Nika:** Formal analysis (wide-scope target screening), Writing – review & editing. **Nikiforos Alygizakis:** Formal analysis (analytical data), Writing – review & editing. **Nikolaos S. Thomaidis:** Writing – review & editing, Supervision, Resources. **Christian C. Voigt:** Investigation, Resources, Writing – review & editing. **Oliver Krone:** Conceptualization, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank Susanne Auls for her support during necropsy, Anja Luckner for her support during stable isotope analysis as well as Alexandre Courtiol for giving critical advice on the statistics. We furthermore thank the UBA colleagues Jürgen Arning, Kevin Bauer, Sina Egerer, Anton Friesen, Arne Hein, and Stefanie Jacob for compiling regulatory information on the chemicals. We also thank Christof Herrmann, Torsten Lauth, Wolfgang Mewes, Bernd Struwe-Juhl, Thomas Neumann, Peter Görke and Joachim Neumann for submitting eagle carcasses.

Funding

We gratefully acknowledge the World Wide Fund for Nature, Germany [grant number: 20441661/218/18287CV] for financing the doctoral studies of Alexander Badry. Furthermore, we thank the Klara-Samariter Foundation [grant number: 181019 2] for financing the analysis of the samples. Georgios Gkotsis acknowledges the A. G. Leventis Foundation for the financial support during his PhD studies.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106934.

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Chapter 5: Spatial variation of rodenticides and emerging contaminants in blood of raptor nestlings from Germany

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Published in Environmental Science and Pollution Research (2022)

- https://doi.org/10.1007/s11356-022-20089-1

Including an update of the funding section as an additional funding source for publication was awarded to the Leibniz Institute for Zoo and Wildlife Research:

- https://doi.org/10.1007/s11356-022-23702-5

Detailed author contributions:

OKro and AB conceptualised the work and conducted the blood sampling together with OKrü, NC and TG. OKro was responsible for the project administration and funding acquisition. The chemical analysis of the samples was conducted in collaboration with the Julius Kühn-Institut in Berlin, where AB conducted his work in the laboratory of DS. AB was responsible for recovery testing, sample preparation, extraction, and data evaluation. DS established the analytical methodologies and supervised the analysis and data evaluation. OKro, HB, NC, TG, HI, OKrü, TM, GM, WN, and RZ identified the breeding sites of the raptor species and organised the ringing campaigns. The manuscript was drafted by AB with input from OKro, DS, NC, HI, and GT. AB conducted the statistical analysis and visualisations.

Environmental Science and Pollution Research (2022) 29:60908–60921
https://doi.org/10.1007/s11356-022-20089-1

RESEARCH ARTICLE

Spatial variation of rodenticides and emerging contaminants in blood of raptor nestlings from Germany

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Received: 5 January 2022 / Accepted: 1 April 2022 / Published online: 18 April 2022

Abstract

Wildlife exposures to pest controlling substances have resulted in population declines of many predatory species during the past decades. Many pesticides were subsequently classified as persistent, bioaccumulative, and toxic (PBT) and banned on national or global scales. However, despite their risks for non-target vertebrate wildlife, PBT substances such as anticoagulant rodenticides (ARs) are still permitted for use in Europe and have shown to threaten raptors. Whereas risks of ARs are known, much less information is available on emerging agrochemicals such as currently used PPPs and medicinal products (MPs) in higher trophic level species. We expect that currently used PPPs are relatively mobile (vs. lipophilic) as a consequence of the PBT criteria and thus more likely to be present in aqueous matrices. We therefore analyzed blood of 204 raptor nestlings of three terrestrial (red kite, common buzzard, Montagu's harrier) and two aquatic species (white-tailed sea eagle, osprey) from Germany. In total, we detected ARs in 22.6% of the red kites and 8.6% of the buzzards, whereas no Montagu's harriers or aquatic species were exposed prior to sampling. ΣAR concentration tended to be higher in North Rhine-Westphalia (vs. North-Eastern Germany) where population density is higher and intense livestock farming more frequent. Among the 90 targeted and currently used PPPs, we detected six substances from which bromoxynil (14.2%) was most frequent. Especially Montagu's harrier (31%) and red kites (22.6%) were exposed and concentrations were higher in North Rhine-Westphalia as well. Among seven MPs, we detected ciprofloxacin (3.4%), which indicates that risk mitigation measures may be needed as resistance genes were already detected in wildlife from Germany. Taken together, our study demonstrates that raptors are exposed to various chemicals during an early life stage depending on their sampling location and underpins that red kites are at particular risk for multiple pesticide exposures in Germany.

Keywords Biomonitoring · Birds of prey · Plant protection products · Rodenticides · Medicinal products

Responsible Editor: Ester Heath

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Introduction

Agricultural intensification and associated chemical pollution resulted in environmental contamination and wildlife exposures over the past decades (Köhler and Triebskorn, 2013; Tang et al. 2021). Especially pest controlling substances have shown to persist in the environment, bioaccumulate in food webs, and reach toxic concentrations in predatory species (de Wit et al. 2020; Gómez-Ramírez et al. 2019; Kean et al. 2021). Raptors are particularly sensitive to anthropogenic pollution as many species have suffered from substantial population declines during the second half of the twentieth century (Helander et al. 2002; Shore and Taggart 2019). While numerous pesticides were consequently classified as persistent organic pollutants (POPs) and banned on a national or global scale during the 1970s and 1980s, residues of many POPs are still detectable in various species across Europe (de Wit et al. 2020; Kean et al. 2021). Under current European chemical legislations such as the Regulation on Biocidal Product Regulation (Regulation (EU) 528/2012) or Plant Protection Products (Regulation (EC) No. 1107/2009), substances are tested for persistent, bioaccumulative, and toxic (PBT) properties prior to their approval, which led to the elimination and restriction of already marketed substances. However, the identification of PBT properties is usually based on physicochemical properties and laboratory studies using aquatic, lower trophic level species such as fish (e.g., OECD No. 305). Studies on wildlife species, especially apex predators, are therefore important for adding information on chemical exposures of higher trophic level species under field conditions. Such information can then be used, e.g., in a weight of evidence approach for strengthening the connection between science and policy to ultimately improve chemical legislations (Wang et al. 2021).

Even though pesticides, i.e., biocides and plant protection products (PPPs), are assessed for PBT properties prior to their approval, certain known PBT compounds such as anticoagulant rodenticides (ARs) are still in use today due to a lack of suitable alternatives. The first generation of ARs was first introduced in the 1950s and subsequently supplemented by more persistent second-generation ARs (SGARs) due to the increasing resistance of rodents towards the first generation (Rattner et al. 2014). Today, ARs are registered in Germany as biocides to control populations of rodents in, e.g., urban areas and livestock farms, whereas their approval as PPPs (to protect agricultural crops) has expired and is only granted in exceptional cases. Due to their universal toxicity to vertebrate wildlife and potential to bioaccumulate in food webs, ARs are threatening raptors and other predators in Europe (Badry et al. 2021; Geduhn et al. 2015; Roos et al. 2021). In Germany, exposure to ARs has been shown to affect not only terrestrial compartments but also aquatic species, which was suggested to be related to their widespread use in sewer systems (Kotthoff et al. 2018; Regnery et al. 2019b, 2020).

Whereas exposure risks of many wildlife species to ARs and legacy PPPs are known, much less information is available on emerging agrochemicals such as currently registered PPPs and medicinal products (MPs) in higher trophic level species. Emission sources of currently used PPPs contrast those of legacy pesticides and comprise spray drift, agricultural surface runoff (Zhang et al. 2018), and direct exposures in the case of ground breeding birds (Bro et al. 2015). Recent studies analyzing liver residues indicated that raptors from Germany are exposed to currently used PPPs (Badry et al. 2021, 2022), whereas only limited information is available for PPPs other than neonicotinoids in raptor blood in Europe (Byholm et al. 2018; Rial-Berriel et al. 2020; Taliansky-Chamudis et al. 2017). For MPs, emission sources depend on their use as veterinary (VMP) or human medicinal product (HMP). Agriculturally related exposures to VMPs are for example linked to animal manure fertilization and scavenging on livestock, whereas HMPs enter the environment via wastewater or leaches from landfills (Shore et al. 2014; Wöhler et al. 2020). Both HMPs and VMPs were previously detected in liver and plasma of European raptors which included among others non-steroidal antiinflammatory drugs (NSAIDs) and antibiotics (Badry et al. 2021, 2022; Gómez-Ramírez et al. 2020).

All three contaminant groups (ARs, PPPs, and MPs) have been prioritized based on their respective risks for pan-European raptor monitoring (Badry et al. 2020). For investigating the extent of exposure of these three contaminant groups we focused on three terrestrial species, namely, the common buzzard *(Buteo buteo*, hereafter BUBT), the red kite (*Milvus milvus*, hereafter MIML), and the Montagu's harrier (*Circus pygargus*, hereafter CIPY). BUBTs and MIMLs are both facultative scavengers that inhabit agriculturally influenced habitats such as forest patches and open grasslands (Heuck et al. 2013; Schindler et al. 2012), whereas CIPYs are ground nestling obligate hunters in, e.g., barley or wheat fields (Arroyo et al. 2002). The diet of all three species consists of small mammals depending on their abundance with a varying contribution of avian prey and invertebrates (reviewed in Badry et al. 2020). Besides terrestrial species, we also included both (semi-) aquatic raptors occurring in Europe, namely, the white-tailed sea eagle (*Haliaeetus albicilla*, hereafter HAAL) and the osprey (*Pandion haliaetus*, hereafter PAHA) as ARs, PPPs, and MPs were previously detected in aquatic species from Germany (Badry et al. 2022; Boulard et al. 2020; Kotthoff et al. 2018). Whereas PAHAs are exclusively foraging on fish, HAALs are mixed

food web feeders that forage mainly on fish and waterfowl with a varying contribution of terrestrial carrion depending on season and availability (Nadjafzadeh et al. 2016).

The current work builds upon previous research investigating the exposure levels to ARs and agriculturally related substances in livers of avian apex predators from Germany (Badry et al. 2021, 2022). The analysis of apparently healthy nestlings was expected to overcome a potential sampling bias when analyzing internal organs of deceased individuals. Information on chemical exposures under field conditions is crucial to develop risk management measures for already identified PBT substances (i.e., ARs) and for supporting hazard assessments in European chemicals legislations. Specifically, we aim to (i) investigate the occurrence of currently used PPPs in blood as these substances are expected to be relatively mobile (vs. lipophilic) as a consequence of the PBT criteria and might therefore be present in rather aqueous matrices (i.e., blood). Furthermore, we aim to (ii) investigate the spatial contamination among the study populations as the exposure and associated risk factors for pesticide exposure (e.g., livestock farming and urbanization Badry et al. 2021; Geduhn et al. 2015)) differ among the sampling regions.

Methods

Sampling

The sampling campaigns took place between May and August of 2019 and 2020 in Germany depending on the hatching dates and associated ringing dates of the five species (Fig. 1). The sampling of most nests was conducted when the nestlings were older than 3 weeks in order to reflect mainly dietary exposure routes (vs. potential maternal transfer). Biometric data (body weight, wing length) and

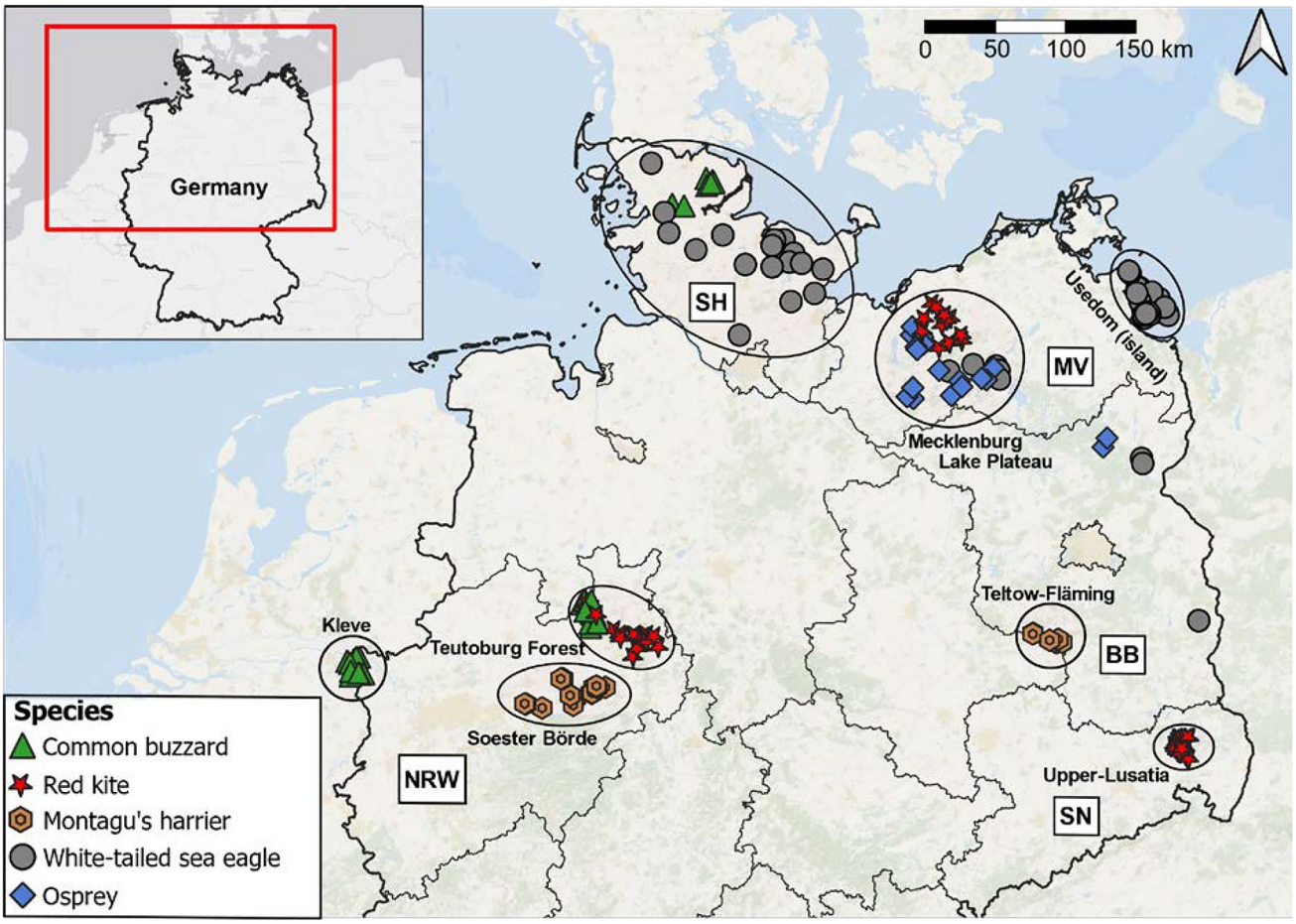

Fig. 1 Sampling locations of the investigated raptor species within the federal states of Germany. Grey boxes refer to the abbreviations of the federal states: *NRW* North Rhine-Westphalia, *SH* Schleswig–Holstein, *MV* Mecklenburg-Western Pomerania, *BB* Brandenburg, *SN* Saxony. Green triangles refer to common buzzards (*Buteo buteo* (BUBT)), red stars to red kites (*Milvus milvus* (MIML)), brown doubled hexagons to Montagu's harriers (*Circus pygargus* (CIPY)), grey circles to white-tailed sea eagles (*Haliaeetus albicilla* (HAAL)), and blue squares to ospreys (*Pandion haliaetus* (PAHA))

reproductive status (number of nestlings per nest) are given in Table SI-1. One 0.7–1-mL blood sample per nest was taken from the *v. cutanea ulnaris* of one of the oldest/fittest nestlings during the local ringing campaigns to keep disturbances at the nest minimal. Blood sampling was conducted using sterile syringes with cannulas of 0.4–0.6-mm diameter. After sampling, we removed the cannula from the syringe and transferred the blood to K3EDTA Vacuette® containers. Most of the blood samples were frozen directly in the field whereas some samples were cooled using ice packs and frozen within 18 h after sampling (− 20 °C). When possible, we opportunistically searched for prey remains in the nests. In total, we took one blood sample from 204 nests from five raptor species in 2019 ($n = 96$) and 2020 ($n = 108$). The five species comprised the MIML ($n = 53$), BUBT ($n = 35$), CIPY ($n = 29$), HAAL ($n = 64$), and PAHA ($n = 23$). All CIPYs were sampled directly within cereal fields in approximately 50 × 50 m protection zones.

Sampling locations

General information on land cover data classes of the sampling areas can be found in Figure SI-1. Briefly, the *BUBTs* were sampled mainly in three locations: the Teutoburg Forest area, the District of Kleve in North Rhine-Westphalia, and the northern parts of Schleswig–Holstein (Fig. 1). The Teutoburg Forest area is part of the central uplands in North Rhine-Westphalia (including the boarder region of lower saxony) and is influenced by mixed coniferous-deciduous forests, cereal fields in open areas, and livestock farming. The district of Kleve is located in North Rhine-Westphalia next to the border with the Netherlands and is influenced by livestock farming and agroforestry. Indications on the presence of intensive livestock farming are taken from the reported spatial sales of veterinary antibiotics in 2019 (Wallmann et al. 2020). The third sampling location, Schleswig–Holstein, is a federal state that is characterized by (field) agriculture, especially cereals and crops for fodder production as well as livestock farming. Furthermore, Schleswig–Holstein comprises various types of surface waters including rivers, lakes, and coastal waters of the North and Baltic Sea.

The *MIMLs* of the study were sampled in the Teutoburg Forest area in Western Germany, northern parts of Mecklenburg-Western Pomerania, and the Saxonian part of Upper Lusatia in Eastern Germany. Northern parts of Mecklenburg-Western Pomerania are characterized by similar agricultural types as Schleswig–Holstein with cereals being the dominant crop type followed by crops used for fodder production. The third sampling location in the Saxonian part of Upper Lusatia represents a rural area that is characterized by numerous small lakes of which some are used for aquaculture.

The *CIPYs* were sampled in the Soester Börde, a lowland region in the vicinity of the Teutoburger Forest area that is extensively used for growing cereals, mainly wheat, barley, maize, and rapeseed. A few samples were also taken from cereal fields in the Teltow-Fläming district in the south of Berlin (Eastern Germany), where field agriculture is also frequent.

The investigated *HAALs* originated from three sampling regions: the German part of the Baltic Sea island Usedom, the Mecklenburg Lake Plateau, and the federal state of Schleswig–Holstein. The island Usedom is characterized by mixed coniferous-deciduous and waterlogged forest as well as by Bodden and open coastal waters of the Baltic Sea. The Mecklenburg Lake Plateau, where also the *PAHAs* were sampled, has comparably low human population density and is characterized by a well-preserved landscape including a national park, numerous lakes, and mixed coniferous-deciduous forests.

Selection of analytes

The selection of analytes followed the same rationale as in Badry et al. (2021) for liquid chromatography (LC)-mass spectrometry (MS)/MS compounds but included considerably more PPPs. In total, 90 PPPs (45 herbicides, 31 fungicides, 12 insecticides, 2 metabolites), of which 78 were approved during the start of the sampling campaign (05/2019), were included in the analysis (Table SI-2). Furthermore, the analysis included all currently registered ARs in Germany (brodifacoum, bromadiolone, chlorophacinone, coumatetralyl, difenacoum, difethialone, flocoumafen, and warfarin) as well as four widely used human medicinal products (ciprofloxacin, diclofenac, ibuprofen, sulfadiazine) and three veterinary antibiotics (enrofloxacin, marbofloxacin, sulfamethazine).

Sample extraction and analysis

The frozen blood samples were stored at − 80 °C after arrival at the analytical laboratory and were thawed before analysis. The sample treatment is presented step by step in Table SI-3. The blood samples (0.2 mL) were aliquoted in polypropylene tubes, spiked with a surrogate mixture for ongoing validation of analytical performance, and filled up to a final volume of 2 mL using acetonitrile. After adding a steel ball (Ø = 2 mm), we vortexed the samples and put them in an ultrasound bath for 5 min. After centrifugation (10 min, 5000 rpm), we transferred the aliquot to a new polypropylene tube. The procedure was repeated once by adding again 2 mL of acetonitrile and the supernatants were combined. Aliquots of 0.2 mL were then reduced to dryness and resuspended in internal standards and methanol/water

for LC–MS/MS methods A, B, C, and E and in acetonitrile/water for method D (Table SI-4). After a brief ultrasound bath, the samples were filtrated through a syringe filter and stored at − 20 °C until analysis by LC–MS/MS.

The measurement of analytes was performed with a QTRAP-Triple Quad Linear Ion Trap 6500 + (SCIEX) in electrospray ionization mode. The identification and quantification of analytes were done with retention time and a precursor — product ion — transition (Table SI-5). For a multilevel calibration, we used 11 concentration levels from 0.01 to 20 pg μL^{-1}. All analytes in all samples were quantified against a matrix-matched standard and the criterion for the acceptance of the calibration curve was the correlation coefficient ($r^2 > 0.99$). The analyte concentrations were determined by the bracketing calibration method and calculated from the peak areas with the internal standards (Table SI-5). The calibration level with a relative standard deviation (RSD) below 20%, between the bracketing injections in a batch, was accepted as the lowest calibration level. The validation of the analytical procedure was checked by recovery tests using spiked pig blood (10, 100, and 1000 ng mL^{-1}) stored in polypropylene tubes as well as in K3EDTA Vacuettes® (for rodenticides) to exclude potential effects of K3EDTA (used as anticoagulant in the blood sampling tubes) on rodenticide analysis. The mean recovery ($n = 5$) and the repeatability for each spike level are given in Table SI-6a. Additionally, we added surrogates to all samples (recovery and investigated samples) for ongoing validation of the analytical procedure. Mean recoveries and RSD of surrogate reproducibility are given in Table SI-6b. The pig blood samples, as well as the sample processing procedure, caused no detectable levels of the target analytes. The confirmation of the identity of an analyte was done with the linear ion trap mode with dynamic fill time. A substance was accepted when its enhanced product ion spectra in the sample (with intensity > 500 cps) matched more than 80% of those in the matrix standards in the same analysis sequence. All signals of confirmed analytes had a signal to noise ratio of > 6:1. The lowest calibration level of all batches was lower or equal to the calibration level to which the reporting limit (RL) refers. The measured concentrations of the analytes were neither surrogate nor recovery corrected.

Spatial visualization and statistical analysis of contaminant data

All map-based visualizations were created using QuantumGIS software version 3.10.2 (QGIS Development Team 2020). We extracted all land cover classes in the sample area from the Corine Land Cover 2018 (EEA 2018) to visualize general land cover gradients (Figure SI-1). All other visualizations were created using the R package "ggplot2" (Wickham et al. 2016). We applied the non-parametric Mann–Whitney test (two-sided) using R version 4.1.2 (R Core Team. R 2021) for analyzing spatial differences in ΣAR and bromoxynil concentrations between terrestrial raptors (BUBT, MIML, CIPY) sampled in North Rhine-Westphalia, where intense cereal and livestock farming prevails, and terrestrial raptors sampled in North-Eastern parts of Germany (Geduhn et al. 2015; Wallmann et al. 2020) where population density is lower and intense agriculture less frequent (Figure SI-1). Concentration below the reporting limit was replaced with zero for statistical analysis and the level of significance was set to $p < 0.05$. No comparison among regions was possible for the (semi-) aquatic raptors (HAAL, PAHA) as both species are only resident in North-Eastern Germany. Concentrations are given as median (interquartile range: IQR) in ng mL^{-1} and refer to samples with detectable residues (Table SI-7), while "n" refers to the total sample number and "n^+" to the number of nestlings that contained detectable contaminant residues in their blood.

Results

In total we detected five out of eight ARs (brodifacoum, difenacoum, difethialone, coumatetralyl, warfarin), six out of 90 PPPs (bromoxynil, fenpropidin, fenpropimorph, 2-methyl-4-chlorophenoxyacetic acid (MCPA), spiroxamine, terbuthylazine), and one out of seven MPs (ciprofloxacin) in our study (Fig. 2; Table SI-7).

Anticoagulant rodenticides (ARs)

In total, we detected at least one AR in 7.4% ($n^+ = 15$) of the 204 individuals (Fig. 2A, B). These ARs comprised brodifacoum (2.5%, $n^+ = 5$, RL: 5 ng mL^{-1}), difenacoum (2.0%, $n^+ = 4$; RL: 2.5 ng mL^{-1}), coumatetralyl (1.5%, $n^+ = 3$; RL: 0.5 ng mL^{-1}), warfarin (1.5%, $n^+ = 3$, RL: 0.5 ng mL^{-1}), and difethialone (0.5%, $n^+ = 1$; RL: 2.5 ng mL^{-1}), whereas bromadiolone (RL: 5 ng mL^{-1}), chlorophacinone (RL: 10 ng mL^{-1}), and flocoumafen (RL: 0.5 ng mL^{-1}) were not detected in any of the blood samples.

The species with the highest detection rate of ΣARs was the MIML (22.6%, 7 (9.8) ng mL^{-1}; Fig. 2A, B) with brodifacoum (9.4%, 13 (5) ng mL^{-1}) being most frequently detected followed by difenacoum (7.6%, 6.5 (7.8) ng mL^{-1}), coumatetralyl (5.7%, 1 (0.5) ng mL^{-1}), and warfarin in one individual (1 ng mL^{-1}). The only other species exposed to ARs was the BUBT (8.6%, 1 (13); Fig. 2B) which had residues of warfarin in two individuals (1 ng mL^{-1} each) as well as of difethialone (27 ng mL^{-1}) in one individual. No AR residues were detected in CIPYs, HAALs, and PAHAs (Fig. 2B). The spatial visualization of ΣARs among the five species in 2019 and 2020 shows that in both years AR exposure occurred predominantly in MIMLs and BUBTs

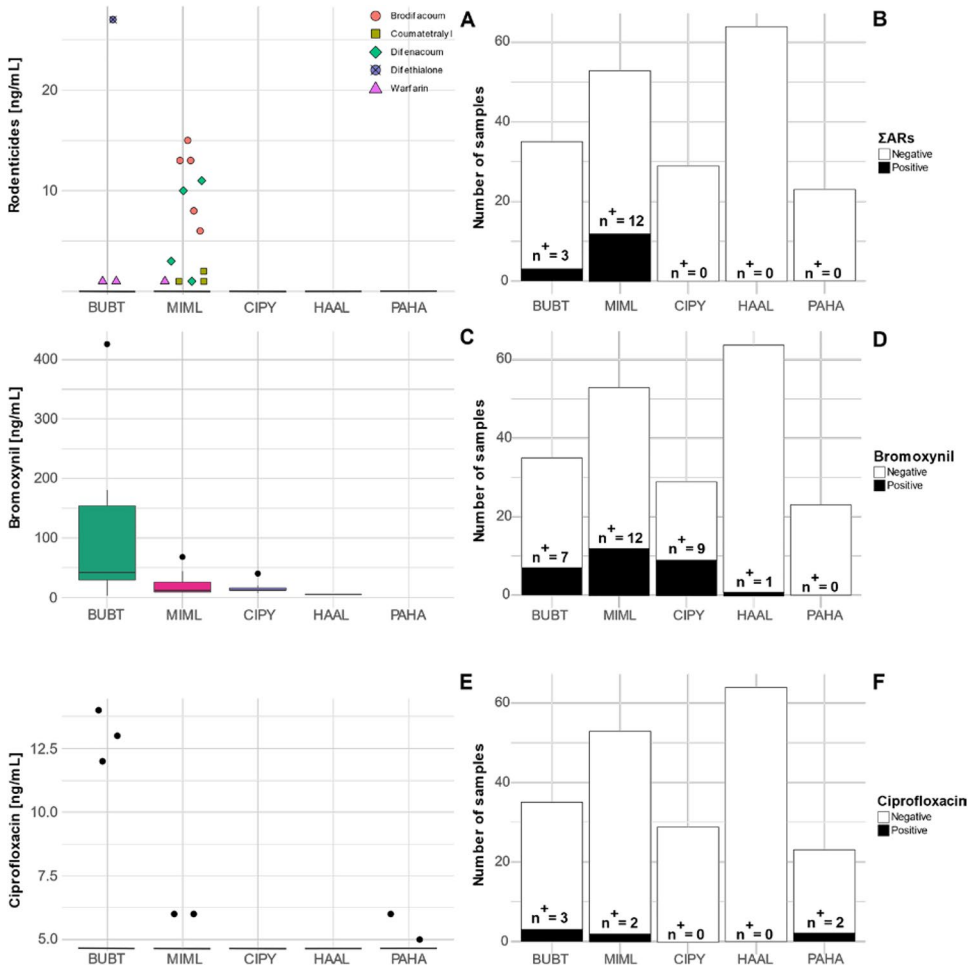

Fig. 2 Concentrations of detected ARs (brodifacoum, difenacoum, difethialone, coumatetralyl, warfarin) (**A**) and ciprofloxacin (**E**) is given by dot plots and bromoxynil (**C**) given as boxplot (for samples > RL, reporting limit). The lower and upper hinges of the box correspond to the 25th and 75th percentile with the median given as horizontal line. The upper whisker extends from the hinge to the largest value no further than 1.5*IQR from the hinge. The lower whisker extends from the hinge to the smallest value at most 1.5*IQR of the hinge. The respective sample numbers (*n*) and samples with concentration > RL (n^+) are given per species in **B**, **D**, and **F**. BUBT: *Buteo buteo* (common buzzard), MIML: *Milvus milvus* (red kite), CIPY: *Circus pygargus* (Montagu's harrier), HAAL: *Haliaeetus albicilla* (white-tailed sea eagle), PAHA: *Pandion haliaetus* (osprey)

from North Rhine-Westphalia (Figure SI-2). This is furthermore supported by the Mann–Whitney test, where terrestrial raptors from North Rhine-Westphalia showed higher ΣAR contamination compared to terrestrial raptors sampled in North-Eastern Germany ($W = 1879.5$, p-value = 0.05).

Plant protection products (PPPs)

Among 90 analyzed PPPs, 82 were expected to be used in Germany at least in 2019 based on their sales figures (active substances; Table SI-2) and periods of grace of the four expired PPPs (epoxiconazole, fenpropimorph, pymetrozine, quinoxyfen). In total six PPPs were detected in the blood of the five investigated raptor species during 2019 and 2020 with bromoxynil showing the highest detection rate (14.2%, $n^+ = 29$; Fig. 2D) followed by fenpropidin (2%, $n^+ = 4$), fenpropimorph (1.5%, $n^+ = 3$), spiroxamine (1.5%, $n^+ = 3$), MCPA (1%, $n^+ = 2$), and terbuthylazine (0.5%, $n^+ = 1$) (Fig. 3). Among the five species bromoxynil exposure predominantly occurred in terrestrial raptors (MIML, BUBT, CIPY) from North Rhine-Westphalia (Figure SI-3). This is again supported by the Mann–Whitney test, where terrestrial raptors from North Rhine-Westphalia had significantly higher bromoxynil contamination compared to terrestrial raptors sampled in North-Eastern Germany ($W = 1968$, p-value < 0.05).

For bromoxynil, the highest detection rate occurred in CIPYs (31%, 12 (4) ng mL^{-1}) followed by MIMLs (22.6%, 11.5 (16.8) ng mL^{-1}), BUBTs (20%, 42 (124.5) ng mL^{-1}), and one HAAL (5 ng mL^{-1}) (Fig. 2C). No PPPs other than bromoxynil were detected in MIML and no PPPs at all were detected in blood of PAHAs. All residues of the fungicide fenpropidin were detected in HAALs (6.3%, 6 (4.3) ng mL^{-1}), whereas fenpropimorph was detected in two BUBTs (2 ng mL^{-1} each) and in one HAAL (3 ng mL^{-1}) (Fig. 3). Similar to fenpropidin, all spiroxamine residues were detected in HAALs (4.7%, 3 (3.5) ng mL^{-1}), whereas MCPA was detected only in two CIPYs (1.5 (0.5) ng mL^{-1}). Terbuthylazine was found only in one HAAL (4 ng mL^{-1}) (Fig. 3).

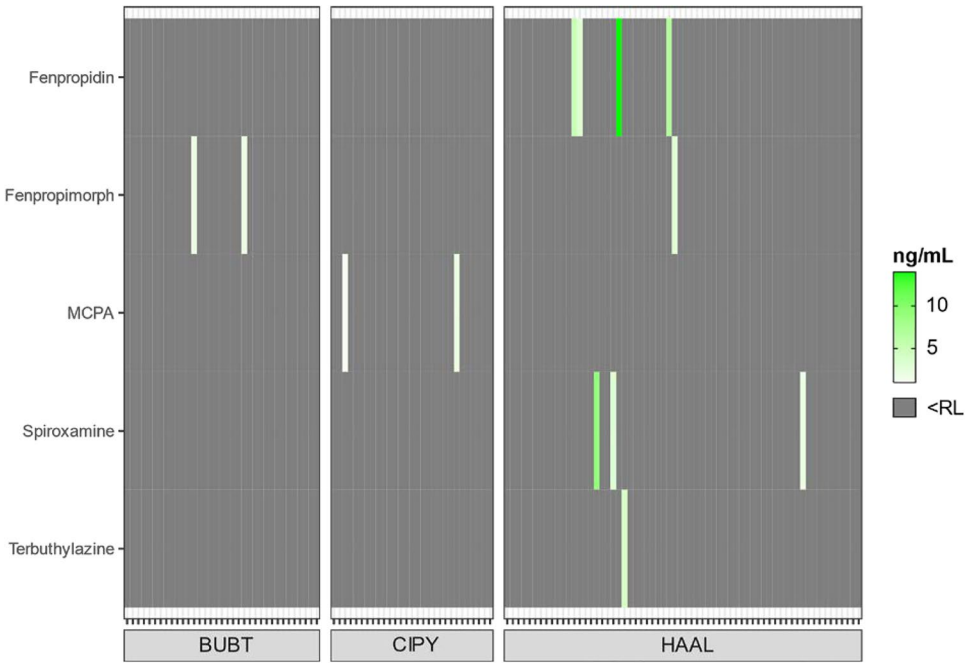

Fig. 3 Heat map of detected PPPs other than bromoxynil (see Fig. 2) in blood of BUBT: *Buteo buteo* (common buzzard, $n = 35$), CIPY: *Circus pygargus* (Montagu's harrier, $n = 29$), and HAAL: *Haliaeetus albicilla* (white-tailed sea eagle, $n = 64$) nestlings. Grey tiles in the heat map refer to samples below the reporting limit (RL) (Table SI-6a)

Medicinal products (MPs)

The only detected HMP was the fluoroquinolone antibiotic ciprofloxacin (RL: 5 ng mL^{-1}) in 3.4% ($n^{+} = 7$) of the individuals, whereas diclofenac (RL = 1 ng mL^{-1}), ibuprofen (RL = 5 ng mL^{-1}), and sulfadiazine (RL = 0.5 ng mL^{-1}) were not detected. Furthermore, none of the VMPs (enrofloxacin: RL = 2.5 ng mL^{-1}, marbofloxacin: RL = 5 ng mL^{-1}, sulfamethazine: RL = 0.5 ng mL^{-1}) were detected.

Ciprofloxacin was detected in three BUBTs (8.6%; 13 (1) ng mL^{-1}), two MIMLs (3.8%, 6 ng mL^{-1} each), and two PAHAs (8.7%, 6 and 5 ng mL^{-1}) (Fig. 2 E and F). In contrast, no ciprofloxacin residues were detected in CIPYs and HAALs. All ciprofloxacin exposures occurred in 2019 in three BUBTs from Kleve in North Rhine-Westphalia as well as in two MIML and two PAHA from North-Eastern Germany (Figure SI-4).

Discussion

Anticoagulant rodenticides (ARs)

An increased risk for raptors and other predators to be exposed to ARs when preying on small mammals is well characterized and ARs have shown to be frequently detected in liver tissues of deceased raptors across Europe (López-Perea and Mateo, 2018) including Germany (Badry et al. 2021). ARs accumulate in livers where they exert their main mode of action by inactivating the vitamin K epoxide reductase (Rattner et al. 2014), whereas their half-lives in blood (< 2 days for chicken) are considerably lower (Horak et al. 2018). In Germany, most AR formulations consist of a single active ingredient and only a few formulations use combinations of two ingredients (e.g., difenacoum and brodifacoum) to overcome resistances in areas with high rodent infestation status (Regnery et al. 2019a). In the present study, we detected AR residues in blood of nestlings from only two terrestrial species, MIML and BUBT. A previous study reported AR residues in almost 15% of adult and nestling barn owls (*Tyto alba*) and common kestrels (*Falco tinnunculus*) from Spain, which was suggested to be related to a constant AR exposure through their prey (Rial-Berriel et al. 2020). The exposure rate of the terrestrial species from the current study was comparable (12.8%) but reporting limits for brodifacoum (5 ng mL^{-1}), bromadiolone (5 ng mL^{-1}), and chlorophacinone (10 ng mL^{-1}) were higher compared to Rial-Berriel et al. (2020), which might have led to an underestimation of exposures for some ARs. Nevertheless, the investigated MIMLs in the present study had higher exposure rates (22.6%) and higher concentrations of the two most common ARs (brodifacoum and difenacoum) compared to the rodent predators from Spain in Rial-Berriel et al. (2020). This might be related to multiple exposure pathways of MIMLs as the species is a facultative scavenger and might have been exposed via foraging on sublethally exposed rodents as well as acutely poisoned rodents. Thus, our study emphasizes the particular risk of MIML for AR poisoning in Germany, which is in agreement with a study on liver samples from deceased MIMLs (Badry et al. 2021). Interestingly, the detection of ARs in blood of MIML nestlings predominantly occurred in the Teutoburger Wald

(North Rhine-Westphalia, Western Germany), whereas the investigated MIMLs from Eastern (Saxony) and Northern Germany (Mecklenburg-Western Pomeranian) were exposed only once (Figure SI-2). The detection rate of BUBTs (8.6%) was lower compared to the MIML in our study. Interestingly the detection rate of BUBTs was similar to those in blood of juvenile red-tailed hawks (*Buteo jamaicensis*, $n = 97$), which represents the North American sister species of the European BUBT (Abernathy et al. 2018). Similar to the MIML, all exposures of BUBTs occurred in North Rhine-Westphalia as well, which may be attributed to higher anthropogenic influence (Figure SI-1) and intense livestock farming in the region (Wallmann et al. 2020). In general, ΣAR contamination in terrestrial raptors from North Rhine-Westphalia was higher compared to terrestrial raptors from North-Eastern Germany ($p = 0.05$). This is in agreement with a previous study on red foxes (*Vulpes vulpes*), where individuals were highly exposed to ARs in North Rhine-Westphalia as well (Geduhn et al. 2015). The diet of a rodent specialist, the barn owl, consisted around livestock farms in North Rhine-Westphalia mainly of non-target rodents from the taxon *Microtus* followed by *Sorex* spp. and *Apodemus* spp. (Geduhn et al. 2016). During the period (April–June) that coincides with our sampling campaign (May–July), rodents of the taxon *Apodemus* were the dominant prey items and regularly showed brodifacoum residues in their livers during baiting (Geduhn et al. 2016, 2014). Whether exposure pathways via foraging on non-target rodents such as *Apodemus* spp. represent a relevant exposure pathway for the investigated opportunistic raptors (MIML and BUBT) in our study area requires further investigation. However, foraging on rodents around livestock farms is considered to represent an important exposure pathway for both species based on their ecological traits (reviewed in Badry et al. 2020). In contrast to the MIML and BUBT, the current study did not detect AR residues in CIPYs, which was unexpected and might be related to foraging on non-rodent prey prior to sampling as CIPYs are opportunistic rodent predators depending on season and availability (Arroyo et al. 2002; Mirski et al. 2016). Furthermore, CIPY sampled in the current study nested directly in cereal fields, where the approval of ARs as PPPs (to protect agricultural crops) has expired and is only granted in exceptional cases. Interestingly, there was a population low of the common vole (*Microtus arvalis*) in the sampling area Soester Börde during 2019 and 2020 (HI, unpublished data), which might have resulted in an enhanced use of alternative prey such as birds and insects. However, as we are lacking systematic information on the diet prior to sampling we cannot disentangle whether their local foraging pattern or the ban of ARs as PPPs prevented CIPYs from exposures. However, this holds usually true for field studies in general, since dietary information, chemical exposure conditions, and information on the toxicokinetic behavior of a chemical (e.g., derived from laboratory study) are usually not assessable or unknown in field studies. An absence of ARs in blood of a raptor that is known to forage on small mammals was furthermore reported for eagle owls (*Bubo bubo*) from Spain, which was suggested to be related to the fast depletion of ARs in blood within days (Gómez-Ramírez et al. 2012). Therefore, new study designs using, e.g., consecutive blood samples from the same individual to cover a broader range of recent exposures in combination with the analysis of livers from deceased adult birds would help to evaluate the actual risk of ARs for CIPY and other raptors. In general, none of the investigated blood samples showed bromadiolone residues, which might contrast with results from other European countries (Italy, France, Netherlands, Romania) where bromadiolone was also registered as PPP until 31/05/2021 (Regnery et al. 2019a). Similar to CIPYs, no ARs were detected in nestlings of the investigated (semi-) aquatic species (HAAL and PAHA). Both species were sampled in North-Eastern Germany, where human population density is lower, and the intensification of agricultural land use is less pronounced compared to North Rhine-Westphalia (Figure SI-1). However, in Badry et al. (2021), 38% ($n = 60$) of the HAALs from North-Eastern Germany had AR residues in their liver but at lower concentrations compared to, e.g., the MIML. The absence of AR residues in the blood of HAAL nestlings and contradicting findings in livers of adults might be related to a combination of a generally lower AR contamination in North-Eastern Germany, shorter half-lives of ARs in blood, and the comparably high reporting limits for some of the targeted ARs in the present study. Furthermore, ARs accumulate over time with adults being at greater risk compared to juveniles (Badry et al. 2021; Roos et al. 2021), which might have further complicated their detection in nestlings. For the PAHA, the results of the current study are in line with Badry et al. (2021), where also no AR residues were detected in liver tissues of 13 PAHAs from a similar study region. These results indicate that piscivorous raptors in North-Eastern Germany might not be threatened by ARs, although the relatively small sample size (PAHA) limits an extrapolation on the population level. Further studies on aquatic predators (e.g., great cormorant (*Phalacrocorax carbo*), grey heron (*Ardea cinerea*), or Eurasian otter (*Lutra lutra*)) including prey species in highly populated areas as well as in areas of intensive livestock farming, such as North-Western Germany, might reveal further insights into potential biomagnification of ARs in aquatic food webs.

Plant protection products (PPPs)

Recent studies targeting emerging contaminants (including PPPs) in raptor tissues such as liver and muscle detected a few PPPs as well as a few human and veterinary MPs,

whereas the majority of target compounds were not detected (e.g., Badry et al. 2021; Sabater et al. 2020; Taylor et al. 2019). Similar results were obtained in the study on raptor blood by Rial-Berriel et al. (2020), where few currently approved and expired PPPs were detected. None of the detected PPPs in this study was detected by Rial-Berriel et al. (2020) where fenpropidin, fenpropimorph, spiroxamine, and terbuthylazine were also targeted. Whereas Rial-Berriel et al. (2020) detected the fungicide metrafenone (approved) in 2.7% of the blood samples, we did not detect metrafenone in our study. The most frequently detected PPP in our study was the herbicide bromoxynil, which was mainly found in the terrestrial raptors (BUBU, MIML, CIPY). Bromoxynil was approved during the study period in 2019 and 2020 but its approval expired (31/07/2021) due to a high risk for wild mammals from dietary exposures as well as for child residents (EC, 2020). In 2019, between 25 and 100 t of bromoxynil were sold in Germany (BVL 2020) for spraying it against broadleaved weeds (post-emergence) for miscanthus, alfalfa, red clover, grass (propagation), maize, and sorghum (EFSA 2018). Interestingly, bromoxynil contamination was significantly higher in terrestrial raptors (BUBT, MIML, CIPY) from North Rhine-Westphalia compared to those from North-Eastern Germany (Figure SI-3), which might be related to the intensive maize farming in, e.g., the Soester Börde and surrounding regions. Direct bromoxynil exposure to CIPY via spray application seems unlikely as concentrations were broadly similar to the tree nesting BUBT and MIML. A high risk for secondary poisoning was identified for bromoxynil octanoate, especially for earthworm-eating birds and mammals (EFSA 2017), which might explain exposures for BUBT and MIML as both species are known to forage on earthworms around the breeding time. Especially, the observed comparably high residues found in three BUBTs (127–426 ng mL^{-1}) require further investigation with regard to bioaccumulation and potential adverse effects. For instance, although regulatory guidelines exist to ensure that commercial PPPs will not adversely affect bird populations, there are currently no test guidelines within the regulatory assessment specifically designed to evaluate bioaccumulation and biotransformation in birds (Kuo et al. 2022).

Other PPPs besides bromoxynil were detected at lower concentrations and detection rates. The currently approved fungicides fenpropidin (sold amount in 2019: 100–250 t) and spiroxamine (sold amount in 2019: 250–1000 t), as well as the approved herbicide terbuthylazine (sold amount in 2019: 250–1000 t; see BVL (2020)), were detected in only a few HAALs, whereas the other species were not exposed. Fenpropidin and spiroxamine are used via foliar spraying against fungal diseases of cereals (EFSA 2007, 2021), whereas terbuthylazine is applied via foliar spraying in maize and sorghum fields against annual and perennial grasses (EFSA 2019). These analytes were also included in the target screening of 30 HAAL livers using UHPLC-QTOF-MS/MS (Badry et al. 2022), where spiroxamine was detected in all individuals (LOD: 0.08 ng g^{-1}). However, during the sampling period of the current study (spring-early summer), herbicides have shown to be more frequent, whereas fungicides are used later during the year to protect developed crops from fungal diseases (Brühl et al. 2021). Spiroxamine residues were furthermore detected in wild boar (*Sus scrofa*) and roe deer (*Capreolus capreolus*) muscles from Poland (Kaczyński et al. 2021), which are both common prey species of HAALs in Germany but not for the species analyzed in Rial-Berriel et al. (2020), where spiroxamine was not detected (LOQ: 0.1 ng mL^{-1}). Terbuthylazine was one of the most frequently detected PPPs in insect traps from nature conservation areas in Germany (Brühl et al. 2021) and was previously detected in dermal swap samples from amphibians (Schenke et al. 2020) as well as in fecal samples (terbuthylazine-2-hydroxy) of Eurasian skylarks (*Alauda arvensis*) from Germany (Esther et al. 2022). Furthermore, terbuthylazine is formulated together with bromoxynil in one of the previously approved PPP products in Germany (Zeagran® ultimate), which indicates similarities in exposure pathways for both substances. Fenpropidin was detected in four and terbuthylazine in one HAAL, whereas no residues were detected in HAAL livers by Badry et al. (2022) (screening detection limit < 1.83 ng g^{-1}) and blood of terrestrial raptors in Rial-Berriel et al. (2020) (LOQ: 0.1/0.4 ng mL^{-1}), which might reflect matrix-specific differences in case of liver (vs. blood) as well as differences in feeding ecology compared to non-scavenging terrestrial raptors.

The only detected fungicide in a terrestrial raptor was fenpropimorph in two BUBTs. Similar to the other fungicides, fenpropimorph (sold amount in 2019: 100–250 t/a) was used via foliar spraying in, e.g., in cereal fields (EFSA, 2008), but its approval expired on 30/04/2019 (period of grace: 30/10/2020). Fenpropimorph residues have been previously reported in liver of a potential prey species (hedgehog: *Erinaceus europaeus*; Schanzer et al. 2021) of medium-sized terrestrial raptors from Germany. However, because no systematic or opportunistic dietary information was available for the nests of the exposed BUBTs, no conclusion can be drawn on potential sources and exposure pathways. Furthermore, we detected the herbicide MCPA (sold amount in 2019: 250–1000 t) in two CIPY nestlings sampled in cereal (barley) fields, where MCPA is applied from spring to early summer to control the growth of broadleaved weeds (EC, 2008). The absence of all targeted PPPs in PAHAs indicates that aquatic exposures via foraging on fish in inland habitats are probably not responsible for the observed exposures in HAALs. However, further systematic dietary investigations including exposure levels in prey species are needed

to verify this assumption. Surprisingly, no PPPs other than bromoxynil were detected in MIMLs, which was unexpected as MIMLs are likely to be at risk for multiple exposures due to their opportunistic foraging behavior as facultative scavenger in agricultural landscapes. A limitation of the current study was that mainly parent compounds (i.e., dimethachlor) were analyzed although transformation products of PPPs (i.e., dimethachlor-oxa or ethiofencarb-sulfone) have shown to be present livers of HAALs (Badry et al. 2022). However, information on the metabolism of PPPs in avian wildlife including their distribution in internal organs and blood is scarce, which complicates the identification and selection of relevant metabolites.

Human medicinal products (HMPs)

A previous target screening for 2441 contaminants in livers of deceased HAALs from Germany revealed that MPs (and transformation products) represented the majority of the detected compounds followed by legacy pollutants and PPPs (including transformation products) (Badry et al. 2022). Recently, wildlife species have been proposed as potential sentinels for detecting antimicrobial resistance in Germany due to their potential to act as reservoirs and dispersers of antimicrobial resistance genes (Plaza-Rodríguez et al. 2021). Among others, fluoroquinolones were prioritized within the critically important category for which risk management strategies are needed (WHO 2018). In the current study, we only detected the HMP ciprofloxacin in three BUBTs, two MIMLs, and two PAHAs in 2019 but not in 2020 (Figure SI-4). Sales of ciprofloxacin accounted for 32,980 t in 2009 (Bergmann et al. 2011) and ciprofloxacin is a known metabolite of enrofloxacin in mammals, where both show fast elimination in plasma of < 12 h after administration (Rao et al. 2002). Treated livestock or companion animals that were treated shortly before sampling might have therefore been a potential source of ciprofloxacin for the facultative scavengers (BUBT and MIML). Furthermore, ciprofloxacin was found in high levels in sewage sludge from Germany (Bergmann et al. 2011), which might have affected exposures of the terrestrial species as well. The comparably high concentrations in the BUBTs may be a cause of concern as experimental fluoroquinolone admission in bird eggs has shown to result in adverse effects on embryonic development (Hruba et al. 2019). Ciprofloxacin was furthermore reported in a HAAL liver from North-Eastern Germany (Badry et al. 2021), which was suggested to be related to aquatic exposures as ciprofloxacin is frequently detected in wastewater treatment plant effluents across Europe (Loos et al. 2013). However, no ciprofloxacin residues were found in blood of HAAL nestlings from this study but in blood from PAHA nestlings in North-Eastern Germany, which further indicates that aquatic exposure via fish might be the main update pathway. Taken together, our results demonstrate that terrestrial and aquatic exposure pathways for raptors to fluoroquinolones exist, which requires further investigation especially since the presence of ciprofloxacin resistance has already been reported for bacteria in wildlife from Germany (Plaza-Rodríguez et al. 2021). In contrast to fluoroquinolones, no residues of NSAIDs were detected in the current study, which contrasts observations in Badry et al. (2021), where ibuprofen residues were detected in 23.8% of HAAL livers as well two northern goshawks (*Accipiter gentilis*) and one MIML. However, half-lives of ibuprofen in blood are comparably short and peak after 1–2 h after administration in plasma of humans (Garrard 2014), which might explain why ibuprofen was not detected in the current study.

Veterinary medicinal products (VMPs)

For veterinary antibiotics, sales are registered in Germany since 2011 and sales of the targeted veterinary fluoroquinolones (enrofloxacin and marbofloxacin) in 2019 were 4770 and 1155 t each (Wallmann et al. 2020). In contrast to our study, enrofloxacin was previously detected in a liver from a northern goshawk from Berlin as well as in a MIML that was either treated prior to death or foraged on treated prey items (Badry et al. 2021). Furthermore, enrofloxacin (but not ciprofloxacin (LOQ: 25 ng mL^{-1})) was detected in plasma of 29 griffon vulture nestlings (*Gyps fulvus*) from Spain, which was suggested to be related to foraging on livestock carcasses (Gómez-Ramírez et al. 2020). As previously discussed, the absence of enrofloxacin in blood of raptors in the current study may also be related to the short half-lives of fluoroquinolones in bird blood (Cox et al. 2004). In agreement with results for raptor livers in Badry et al. (2021), we did not detect the NSAID diclofenac. In contrast to Spain (see, e.g., Herrero-Villar et al. 2021), diclofenac is not used as VMP in Germany, which seems to protect facultative scavengers from exposure.

Conclusion

Our study demonstrated that raptor nestlings are exposed to various ARs, PPPs, and one fluoroquinolone antibiotic across Germany, which is in agreement with previous studies on tissues of deceased raptors. However, a limitation of our study remains the final assessment of the analytical results, especially those below our reporting limits as toxicokinetic data, such as the half-life in blood of raptors, metabolization rates, and distribution behavior in raptors, are largely unknown.

Our results for ARs confirm previous observations in livers of deceased raptors demonstrating that MIMLs are at particular risk for AR exposure in Germany (Badry

et al. 2021). Furthermore, BUBTs from the countryside have shown to be exposed to ARs as well, which indicates that urban BUBT populations might be at particular risk as shown for northern goshawks from Berlin (Badry et al. 2021). In general, AR exposure of both species seems to be more dominant in North Rhine-Westphalia, which might be related to the high population density and intense livestock farming in North-Western Germany. On the other hand, the absence of ARs in CIPY indicates that the ban of ARs as PPPs reduces exposures in cereal fields but further studies using consecutive blood samples and/or livers of adult birds are needed to confirm this observation. The absence of ARs in blood of HAAL and PAHA nestlings indicates that nestlings of piscivorous species living in lower populated areas such as North-Eastern Germany might not be at high risk for AR exposures.

Among the PPPs, bromoxynil was the most frequently detected substance and showed, similar to ARs, the highest concentration in terrestrial species from North Rhine-Westphalia. Further studies on acute and long-term effects on wildlife species should be investigated despite its withdrawal in 2021 since potential long-term risks from dietary exposure were identified for wild mammals in its final renewal report (EC, 2020). Other PPPs such as spiroxamine, fenpropidin, or fenpropimorph were only occasionally detected in a few individuals, whereas the majority of the targeted PPPs was not detected. However, some fungicides might have been applied during later stages of our sampling campaigns (Brühl et al. 2021), which calls for further investigations on fungicide exposures during summer since, e.g., spiroxamine has shown to be frequently detected in livers of deceased HAALs (Badry et al. 2022). For MPs, the detection of the fluoroquinolone ciprofloxacin in BUBTs, MIMLs, and PAHAs calls for general risk mitigation measures to reduce the environmental impact of antibiotics in the environment as resistance genes were already detected in wildlife from Germany (Plaza-Rodríguez et al. 2021).

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11356-022-20089-1.

Acknowledgements We acknowledge the following people for their crucial help during the sampling campaign: Manuela Merling de Chapa, Falko Gleichner, Margret Bunzel-Drüke, Antje Drangusch, Meinolf Ottensmann, Tony Rinaud, Youri van der Horst, Paul Sömmer, Torsten Lauth, Andreas Bass, Lisa Giese, and Ragna Einicke. We furthermore thank Martina Hoffmann and Ina Stachewicz-Voigt for their support during the residue analysis, Sabine Schiller for the technical support, and Anton Friesen for the critical advice.

Author contribution Alexander Badry: conceptualization, investigation, writing — original draft; review and editing; formal analysis, data curation, visualization; Detlef Schenke: methodology, resources, data curation, validation, writing — review and editing, project administration; Helmut Brücher: investigation; Nayden Chakarov: investigation, writing — review and editing; Thomas Grünkorn: investigation; Hubertus Illner: investigation, writing — review and editing; Oliver Krüger: investigation; Torsten Marczak: investigation; Gerard Müskens: investigation; Winfried Nachtigall: investigation; Ronald Zollinger: investigation; Gabriele Treu: writing — review and editing; Oliver Krone: conceptualization, investigation, writing — review and editing, supervision, project administration, funding acquisition.

Funding Open Access funding enabled and organized by Projekt DEAL. Financial support was provided by the World Wide Fund for Nature, Germany (grant number: 20441661/218/18287CV) for the doctoral studies of Alexander Badry. Furthermore, the Klara-Samariter Foundation (grant number: 181019 2) financed the field work and the analysis of the samples.

Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval All blood samplings fulfilled the ethical requirements and animal experiments by the respective federal states of Germany were approved: Brandenburg: 2347-A-10–1-2019, Mecklenburg-Western Pomerania: 7221.3–3.2–004/19, North Rhine-Westphalia: 81–02.05.40.19.007, Schleswig–Holstein: V244-26613/2019, and Saxony: DD24.1–5131/475/6.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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Chapter 6 - General discussion

The overall objective of this thesis was to identify and characterise current chemical threats for birds of prey from different feeding guilds in Germany. Apart from national monitoring, this thesis also aimed to contribute to harmonising pan-European raptor biomonitoring schemes. Chapter 2 identified the most suitable sentinel species for pan-European biomonitoring for a set of priority compounds (i.e. Pb, Hg, ARs, PPPs and MPs) based on distribution and key ecological criteria such as diet, habitat and migration. The common buzzard and tawny owl (*Strix aluco*) have proven to be the most suitable species for the majority of the considered contaminant groups. The selection of one over the over depends on how critical scavenging is as an exposure pathway and whether partial migration (common buzzard) is likely to compromise the aims of any biomonitoring programme. Whereas these priority contaminants have been shown to threaten vertebrates in Europe, only limited information is available for birds of prey in Germany. Chapter 3, therefore, investigated the exposures to a subset of these priority contaminants (i.e. ARs, PPPs and MPs) for birds of prey from different feeding guilds in Germany. The analysis of liver tissues demonstrated that ARs cause the most severe threat among the investigated contaminants. Red kites and urban northern goshawks showed exposure rates to ARs of >80%, and concentrations frequently exceeded toxicity thresholds. The observed landscape effect of urban areas on AR exposure is particularly remarkable as northern goshawks are not primarily foraging on rodents. Of the two in Germany occurring raptor species that utilise aquatic food webs, only the (semi-) aquatic white-tailed sea eagle was exposed to ARs in livers. In contrast, the piscivorous osprey showed no ARs residues in a comparably small sample size. Chapter 4 focused on the identification of novel threats by analysing 2,441 legacy and emerging contaminants in the livers of white-tailed sea eagles as indicator species. In total, 85 chemicals were detected, demonstrating that mixed food web feeders are exposed to a large diversity of aquatic and terrestrial contaminants. The most frequently detected class of compounds were, despite their low predicted PBT scores, MPs, followed by POPs and PPPs. Compounds that threatened white-tailed sea eagles in the past, like 4,4′-DDE and PCBs, were present in all samples below toxicity thresholds. However, there is currently only limited information available on the toxicity of chemical mixtures in wildlife. Especially the combination of POPs with other hazardous compounds like PFAS requires further investigation. The blood analysis in nestlings from chapter 5 confirmed that red kites are at particular risk for AR exposure, whereas exposure rates in common buzzards were lower. No AR residues were detected in the Montagu's harrier and the aquatic species (i.e. white-tailed sea

eagle, osprey). The ground-breeding Montagu's harrier showed a similar extent of exposure to PPPs (i.e. bromoxynil) compared to the tree-nestling terrestrial raptors. In general, concentrations of ARs and bromoxynil were higher in terrestrial species from North-Rhine Westphalia compared to North-Eastern Germany.

6.1 Chapter 2 - Choosing sentinel species for pan-European biomonitoring – prospects and pitfalls

Choosing a harmonised sentinel species for pan-European biomonitoring represents a challenging task due to the diversity of landscapes and different climate zones within Europe. Nevertheless, harmonised monitoring approaches are crucial to evaluate the effectiveness of regulatory outcomes of European environmental and chemical legislations. There are various raptor monitoring programs in Europe (Derlink et al. 2018; Gómez-Ramírez et al. 2014), often including species of high conservation value and limited distribution ranges, resulting in a fragmented approach. There have been considerable efforts to harmonise biomonitoring programs, e.g. in terms of the sample matrix and monitoring protocols (Espín et al. 2020; Espín et al. 2016), but the selection of sentinel species represented a critical knowledge gap.

6.1.1 Selecting pan-European sentinel species based on the distribution and ecological criteria

In a first step, priority contaminant groups were selected based on expert knowledge from a workshop in Thessaloniki in 2019 and a literature review on their threats to European vertebrate wildlife. Among the abiotic contaminants, two non-essential metals, namely Pb and Hg, were selected. Exposures to Pb in raptors are primarily related to its use in hunting ammunition and foraging on game species (Krone 2018). In contrast, Hg has more diffuse exposure that are generally related to, e.g. agricultural and industrial emissions (Sun et al. 2019b). Among the organic contaminants, the selection focused on ARs, pesticides (e.g. PPPs) and MPs, due to described adverse effects on wildlife in 1.3 (chapter 1).

The common buzzard and tawny owl have proven to be the most suitable species for most of the considered contaminants. The selection of one over the other depends on the importance of contaminant exposures from carcasses (i.e. scavenging) and residency within a territory. Other species might be more suitable for certain contaminants with specific emission sources, such as golden eagles for Pb or vultures for NSAIDs. Northern goshawks have proven to be particularly suitable for studies, including far northern regions in Europe, due to their widespread distribution and residency (Table 2). Species such as the barn owl (*Tyto alba*) or common

kestrel (*Falco tinnunculus*) might be suitable additions for studying rodent-related chemical exposures in regions where they occur (e.g. SGARs in Geduhn et al. 2016)).

6.1.2 Methodological considerations for selecting a pan-European sentinel species

A general limitation of using raptors for large-scale monitoring represents the aquatic environment as only two species with limited distribution range are present in Europe (i.e. white-tailed sea eagle and osprey). These species are arguably still valuable sentinels for regional contamination monitoring, like white-tailed sea eagle for the Baltic Sea region (Helander et al. 1982; Zampoukas et al. 2014) or the osprey for piscivorous food web studies (e.g. Bean et al. 2018; Lazarus et al. 2015). However, more widespread species, such as Eurasian otters (*Lutra lutra*), might be more suitable sentinels for European freshwater environments. For the marine environment, there is no common species that is distributed across all European Seas. However, marine mammals are generally considered to represent suitable sentinels for regional contaminant monitoring programs (Desforges et al. 2022). Chapter 2 assumed that passive monitoring schemes using carcasses of raptors might be most feasible for pan-European terrestrial biomonitoring, as active monitoring schemes using, e.g. blood, requires ethical permits, trained personnel, and higher costs. By focusing on carcasses, the sample matrix is limited to internal tissues (and feathers) as remaining blood, e.g. in the heart vessels, might already be coagulated when the carcass is found. In general, the choice of sample matrix also depends on the contaminants of interest (i.e. target analytes), and the liver was, together with blood, considered to be most effective for pan-European biomonitoring (Espín et al. 2016).

Table 2: Raptors with the highest number of advantageous key ecological traits for pan-European monitoring averaged among the considered contaminant groups. Advantageous criteria are depicted in green and limiting criteria are depicted in yellow. References for the traits are given in Table SI-3 of Chapter 2. The definition of the main region is based on United Nations Statistics Division (1999) Geoscheme.

Species	Distribution	Foraging trait	Diet	Habitat	Migration
Tawny owl (*Strix aluco*)	4/4 main regions	Active hunter	Small mammals Small birds Insects	Wide-habitat niche Farmland with forest patches Urban habitats	Resident
Common buzzard (*Buteo buteo*)	4/4 main regions	Active hunter& facultative scavenger	Mainly small mammals (if abundant) Insects Birds	Agricultural habitats Forest patches Urban habitats	Partial migrant
Northern goshawk (*Accipiter gentilis*)	4/4 main regions	Active hunter	Mainly avian prey Minor proportion of mammals	Forest habitats Forest patches Urban habitats	Resident
Common kestrel (*Falco tinnunculus*)	4/4 main regions	Active hunter	Mainly rodents Birds (enhanced in cities) Invertebrates	Agricultural habitats Urban habitats	Partial migrant
Barn owl (*Tyto alba*)	3/4 main regions (missing in Fennoscandia)	Active hunter	Mainly rodents (specialist)	Agricultural habitats Urban habitats	Resident

In the first step of the applied selection process, raptor species were shortlisted based on their distribution within the four main regions of Europe defined by the United Nations Geoscheme (United Nations Statistics Division 1999). Dividing Europe based on broad categories in combination with the subsequently applied advantageous criteria (number of resident countries within a main region) brings the benefit of quickly shortlisting the most widely distributed species in Europe. However, it comes at the cost of overestimating local distribution hotspots of comparably rare species at border regions. An example represents the golden eagle in the western European main region, where they only occur in the alpine parts of Germany, Austria, Switzerland and France (BirdLife International 2019). However, alpine areas are not representative of Germany and France as they only constitute a minor part of the respective countries. This issue was specifically addressed in chapter 2. It has proven to not be influential for the sentinel selection for Pb, mainly due to the lack of widely distributed scavengers of game mammal carcasses in Europe (BirdLife International 2017).

Among the prioritised contaminant groups, especially ARs and pesticides had similarities in the selection process. The only difference was that facultative scavenging was only considered an advantageous trait for ARs. This was mainly attributed to exposures to both compound classes in agriculturally influenced landscapes. Since 2021, ARs are no longer approved as PPPs in any European country (European Commission 2022), which restricts their use to biocidal applications around livestock farms, buildings and sewage systems. An exception represents the use of specific ARs as PPPs during rodent outbreaks (e.g. Jacob et al. 2020). Based on this regulatory change, the preferred habitat for selecting a sentinel species for pan-European AR monitoring is now restricted to farmland, urban areas, and vicinity to human settlements (vs agricultural habitats). This change is not considered to be influential as the shortlisted species (e.g. tawny owl, common buzzard) also occur in the vicinity of human settlements (i.e. farmlands, urban areas) and are therefore expected to cover biocidal exposure pathways (Table 2).

For some contaminant groups like Pb and VMPs, foraging trait and specific diet (carcasses) was considered to represent the major source of exposure for vertebrate wildlife (Krone et al. 2009; Shore et al. 2014). However, the distribution of obligate scavengers (i.e. vultures) is very limited in Europe (BirdLife International 2017), which excludes them from pan-European biomonitoring. Switching to facultative instead of obligate scavengers might circumvent the limited distribution but comes at the cost of including exposure pathways from other sources as well. This is especially true for opportunistic facultative scavengers that have a comparably

large dietary niche, such as the common buzzard or the red kite. Therefore, species with smaller dietary niches (e.g. vultures or golden eagles) are recommended to supplement pan-European biomonitoring schemes for contaminants that are primarily associated with foraging on game mammal carcasses (e.g. Pb) or livestock carcasses (e.g. VMPs). A major difference in the selection of sentinel species for (V)MPs was the consideration of migratory behaviour due to the expected fast metabolisation of MPs in tissues (e.g. Cox et al. 2004). This is particularly known for parent compounds in mammalian tissues, whereas information on bird tissues is scarce (Kuo et al. 2022). In general, the consideration of migratory behaviour had only a minor influence on the choice of candidate species for MP monitoring, as the selection process focused, similar to pesticides, on terrestrial exposure to MPs in agricultural landscapes.

In summary, the applied trait-based approach has proven to be a robust methodology for selecting sentinel species for large-scale monitoring schemes. It has been shown to reduce the number of potential sentinels to only a few species, namely the common buzzard and the tawny owl. Both species are among the most frequently collected species in freezers of European natural history museum, which underlines the feasibility of pan-European biomonitoring using carcasses (Ramello et al. 2022). For some contaminants such as Pb, these monitoring approaches should be supplemented with regional monitoring campaigns including species at particular risk to avoid potential underestimations of chemical exposures. The selection of candidate species is expected to contribute to the development of a harmonised pan-European biomonitoring scheme that will serve as a proof of concept for the presented trait-based approach. For example, the Leibniz Institute for Zoo and Wildlife Research provided livers of common buzzards to the LIFE APEX project, which applied a European-wide analysis for a wide range of contaminants (Gkotsis et al. 2022). Based on the results of this chapter, the COST Action ERBFacility provided additional evidence on the suitability of tawny owls for large-scale monitoring by performing an in-depth analysis of population contextual data (Ratajc et al. 2022).

6.2 Chapter 3 - From pan-European biomonitoring to chemical threats for birds of prey in Germany

After identifying the most suitable sentinel species for pan-European biomonitoring, the main topic of this dissertation dealt with the identification of chemical threats for birds of prey from different feeding guilds in Germany. In the first step, the analysis focused on the livers of deceased birds of prey. A particular focus was on ARs as they are known to threaten raptors in Europe (López-Perea and Mateo 2018). In contrast, information on the other organic priority

contaminants, such as currently used PPPs and (V)MPs in bird tissues, is scarce. The selection of species for chapter 3 was based on representing different feeding guilds of birds of prey from Germany rather than their suitability for pan-European biomonitoring (Gómez-Ramírez et al. 2014). Therefore, the selection of candidate species differs from the selected sentinel species in chapter 2.

6.2.1 Exposure to anticoagulant rodenticides among feeding guilds in relation to toxicity thresholds

Although threats of ARs to vertebrate wildlife are well documented in, e.g. Spain, UK and France (chapter 2, table SI-13), little is known about ARs exposure in Germany except for a study on barn owls and red foxes (*Vulpes vulpes*) (Geduhn et al. 2016; Geduhn et al. 2015). Urban northern goshawks and red kites showed ARs residues in >80% of the livers. The results for the red kite were similar to reports from the United Kingdom (UK) and Spain (see chapter 3). In contrast, this study was the first to demonstrate widespread AR exposure in northern goshawks, a species that is known to primarily forage on other birds. The majority of the investigated northern goshawks originated from Berlin, where northern goshawks established a stable population. A recent study analysed the diet of urban and rural northern goshawks and found a higher proportion of scavenging birds, such as crows and magpies, in the diet of urban northern goshawks (Merling de Chapa et al. 2020). Scavenging birds might be secondarily exposed to ARs in urban areas via carcasses of poisoned rodents. A previous study on songbirds from Germany reported that passerines frequently enter bait boxes (Walther et al. 2021b). Songbirds might therefore represent and additional exposure route for northern goshawks and sparrowhawks, which showed exposure to bromadiolone in three individuals. However, further studies on ARs in potential prey species are needed to identify the main exposure route for urban northern goshawks.

The investigated northern goshawks frequently exceeded the toxicity threshold of 100 ng g^{-1} and 200 ng g^{-1} ∑SGARs in their livers (Figure 1). These threshold values are based on coagulopathy in exposed captive eastern screech owls (*Megascops asio*) (Rattner et al. 2014a) as well as on a probabilistic analysis of hepatic SGAR residues and associated toxicosis in great horned owls (*Bubo virginianus*) and red-tailed hawks (*Buteo jamaicensis*) (Thomas et al. 2011). However, there are significant species differences in sensitivity, and some raptor species are considerably more sensitive to ARs than, e.g. common regulatory test species (northern bobwhite) (Rattner et al. 2011; Rattner et al. 2010; Thomas et al. 2011). Sublethal effects of ARs in wildlife are poorly characterised yet, which, together with intra- and interspecific

differences, complicates the assessment of hepatic ARs residues. (Rattner and Harvey 2021; Rattner et al. 2014b). The reason for these differences might be related to polymorphisms in the sequence of the target enzyme, the vitamin-k-epoxide reductase, which has not been sequenced for raptors yet (Rattner and Harvey 2021). In general, SGARs, particularly brodifacoum, are considered the most toxic for raptors by causing prolonged effects that increase with each exposure event (Rattner and Harvey 2021; Rattner et al. 2020). Brodifacoum was, together with difenacoum (SGAR), most frequently detected in this study, which corresponds to the estimated market shares in Germany (Regnery et al. 2019). In France, bromadiolone was most frequently detected in raptors and vultures (Moriceau et al. 2022). The frequent detection of bromadiolone might be related to the prolonged use of bromadiolone as PPP in France (until 2021) vs only biocidal applications in Germany. Due to the frequent detection and high concentrations of SGARs in this study, adverse effects such as coagulopathy, anaemia and toxicosis seem likely for some of the individuals, especially those exceeding 200 ng g^{-1} ∑SGARs. Recently, the impacts of ARs have been linked to the population level of raptors, such as a declining abundance of common kestrels in the UK (Roos et al. 2021). Furthermore, local extinctions of red kites from Spain were reported in response to general poisonings (Mateo-Tomás et al. 2020).

Impacts on the population level in Germany would be particularly critical for red kites, as more than 50% of the global breeding pairs live in Germany (Heuck et al. 2013). In total, 31% of the red kites exceeded the threshold of 100 ng g^{-1} and 11.9% the threshold of 200 ng g^{-1} ∑SGARs when excluding a single deliberate AR poisoning (Figure 1). In Moriceau et al. (2022), 100% of the red kites from France showed AR residues, with 43.8% (n=16) of the individuals exceeding the threshold of 100 ng g^{-1} ∑SGARs. The exceedance was not linked to individuals with acute toxicosis or signs of clotting failure (Moriceau et al. 2022). These observations are similar for most individuals in chapter 3 and might be related to 1) difficulties detecting pathological signs of AR toxicosis in carcasses and 2) intra- and inter-species variations in sensitivity to ARs. In this study, red kites were subject to multiple poisonings, including environmental AR poisoning (i.e. >100 ng g^{-1} ∑SGARs), a deliberate AR poisoning, and two deliberate insecticide poisonings with dimethoate. Red kites are known to suffer from poisonings throughout Europe, and poisonings have resulted in local extinctions of red kites, especially in regions with low population densities (Mateo-Tomás et al. 2020).

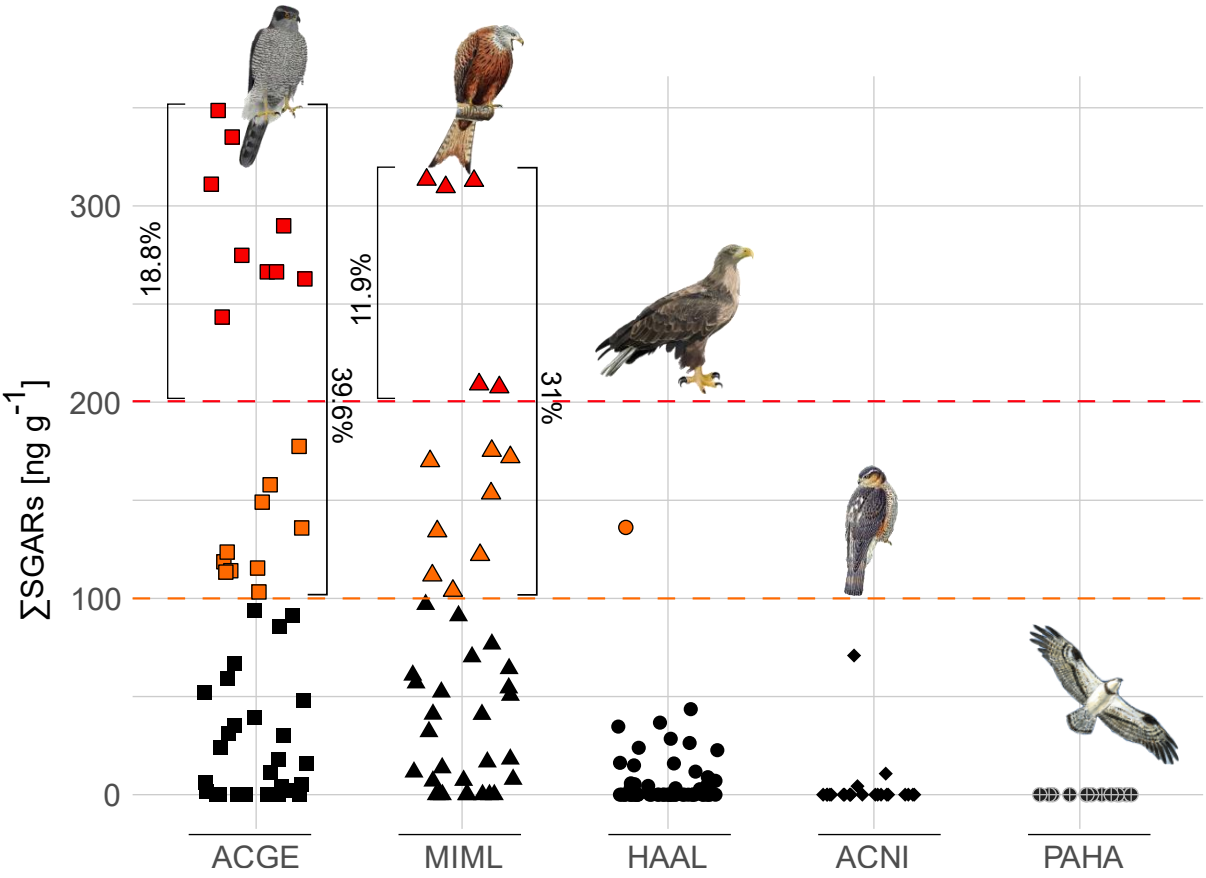

Figure 1: Scatter plot of ∑SGAR concentrations in livers grouped per species. Individuals exceeding the threshold of 100 ng g^{-1} ∑SGARs are depicted in orange, and individuals exceeding the threshold of 200 ng g^{-1} ∑SGARs are depicted in red. ACGE: *Accipiter gentilis* (northern goshawk, squares), MIML: *Milvus milvus* (red kite, triangles); HAAL: *Haliaeetus albicilla* (white-tailed sea eagle, circles); ACNI: *Accipiter nisus* (sparrowhawk, diamond); PAHA: *Pandion haliaetus* (osprey, crossed circle). One red kite (Bra305; brodifacoum: 4853.5 ng g^{-1}; difenacoum: 69.4 ng g^{-1}) was not displayed due to deliberate poisoning. Concentrations below the reporting limit were replaced by zero. The figure was created using the package ggplot2 in R version 4.1.2 (R Core Team 2021; Wickham 2016).

For white-tailed sea eagles, exposures were lower compared to northern goshawks and red kites, which was expected as white-tailed sea eagles do not frequently forage on rodents (Nadjafzadeh et al. 2016). However, one white-tailed sea eagle exceeded the threshold of 100 ng g^{-1} ∑SGARs (Figure 1), which demonstrates that adverse effects might also occur in a mixed food-web feeder. In general, concentrations were lower compared to a recent study from Poland, which investigated the liver of white-tailed sea eagles that died from suspected poisoning (Sell et al. 2022). In this study, 100% of the individuals showed AR residues and 50% (n=40) of the individuals exceeded the threshold of 100 ng g^{-1} and 25% the threshold of 200 ng g^{-1} SGARs (Sell et al. 2022). The authors suggest that red foxes as potential prey and a lack of regulation and control for the sale of AR products might have caused the high exposure of white-tailed sea eagles from Poland. Interestingly, American bald eagles, which are closely related to the white-tailed sea eagle, also showed a comparable high detection rate of 83% (n=116) in their livers

(Niedringhaus et al. 2021). The results were similar to golden eagles (83%, n=17) (*Aquila chrysaetos*) that are known to predate rodents and other mammals (Niedringhaus et al. 2021). These results demonstrate that mixed food web feeders can be frequently exposure to ARs as well. The absence of ARs in ospreys from our study indicated that aquatic exposures, e.g. from the AR use in sewage systems, might not be the main exposure source for the investigated white-tailed sea eagle from Germany. However, further studies using larger sample sizes and including piscivorous species from regions of higher population density and intense livestock farming are needed to investigate potential aquatic trophic transfers.

6.2.2 Factors influencing the exposure to anticoagulant rodenticides

Modelling factors that influence exposure to the targeted contaminants was only possible for ARs as the detection rate for PPPs and MPs was too low. For ARs, it is known that the distance to livestock farms and urban areas influences exposures (Geduhn et al. 2015; López-Perea et al. 2019). A limitation of our study was that the locations of livestock farms (including the type of farming) were missing. Agricultural influences in the study were quantified using satellite images from geographic information systems. They referred to field agriculture rather than livestock farming, where ARs were used as PPPs in the past. In general, modelling the landscape composition and biological factors for individuals from opportunistic sampling collections is challenging due to a lack of reference sites and spatiotemporal clustering of variables (e.g. northern goshawk and urban area). Nevertheless, similar to other studies, the applied modelling approach identified influential factors that can be linked to causation. For example, the contribution of urban areas was identified as the most influential factor rather than field agriculture per se, which is in agreement with a previous study on raptors (López-Perea et al. 2019). Furthermore, exposure pathways of terrestrial raptors in Canada and the US were mainly related to suburban and urban areas and foraging on target and non-target rodents (Elliott et al. 2022; Hofstadter et al. 2021). This is in agreement with results from Geduhn et al. (2014), where target and non-target rodents were frequently exposed around livestock farms in Germany. However, a recent study on Norway rats (*Rattus norvegicus*) in livestock farms reported that individuals died after baiting in places that are hardly accessible to predators (Walther et al. 2021a). The authors suggested that predators are therefore primarily exposed to ARs via living rodents or other non-target mammals (Walther et al. 2021a). These observations contrast with results from a previous study in which half of the exposed Norway rats did not die under cover and were more active during the daytime by moving further to open areas (Cox and Smith 1992). Elliott et al. (2022) suggested that target rats represent a critical exposure pathway for owls in more urbanised habitats. In Berlin, an acutely poisoned Norway rat was

found dead on a path in a park area (Fennpfuhlpark, 28/05/2022) during daytime with an ∑SGAR concentration in the liver of 2,015 ng g^{-1} and 9,640 ng g^{-1} in the stomach content (analysis: Julius-Khn Institut, Berlin). This observation calls for further studies on target and non-target prey species and suggests that rats are accessible for predatory wildlife in urban areas.

Apart from urbanisation, age class has been shown to influence exposures, which is in agreement with previous studies (e.g. Roos et al. 2021). The high exposure in adults (vs juveniles) is expected to reflect the bioaccumulation of ARs throughout the lifespan. No difference was observed for sex, which indicates that the widespread food web contamination of ARs seems to overrule potential exposure differences based on varying foraging strategies between males and females. Nutrition condition (as a proxy for the accumulation of lipophilic contaminants) did not show to influence AR concentrations, which indicates that lipophilicity alone is not responsible for the accumulation of ARs in raptors. A study on the dietary accumulation of flocoumafen in Japanese quails found that the hepatic concentration did not increase with exposure (Huckle et al. 1989). The authors concluded that the specific binding site for ARs limits the accumulation. The affinity to the vitamin k epoxide reductase might therefore be the dominant factor for the accumulation rather than lipophilicity alone.

6.2.3 Exposure medicinal products in relation to their known environmental occurrence

Besides ARs, we detected four out of seven MPs in the livers of birds of prey. The analysis focused on individuals that were found dead to exclude birds that received deliberate treatments before death. Among the detected MPs, ibuprofen (HMP) showed the highest detection rate (14.9%). In 2020, ibuprofen (18.6 million prescriptions) was one of the most prescribed HMPs in Germany (Ludwig and Mhlbauer 2021). Conventional wastewater treatment plants have been shown to insufficiently eliminate ibuprofen (Gago-Ferrero et al. 2020; Langenhoff et al. 2013). Therefore, the high consumption rates are expected to exceed the elimination capacity, which may be responsible for the frequent detection in surface waters (e.g. Bergmann et al. 2011; Loos et al. 2013). This might also explain the detection of ibuprofen in white-tailed sea eagles, a species that is predominantly feeding on fish and other species of the aquatic food web, such as waterfowl (Nadjafzadeh et al. 2016). Similar to white-tailed sea eagles, residues were also found in Eurasian otters from the UK that are also known to feed on fish and waterfowl (Richards et al. 2011). Interestingly, waterbirds from Italy were exposed to ibuprofen and other HMPs as well, which was suggested to be related to incomplete wastewater removal (Distefano et al. 2022). In contrast to white-tailed sea eagles, ospreys did not show any

exposures in this study. The absence might be related to the local exposure conditions in the habitats, the comparably small sample size, and the exclusive piscivorous foraging behaviour of ospreys. Based on the results from chapter 3, ibuprofen is expected to enter aquatic food webs, which calls for further risk mitigation measures at wastewater treatment plants. For example, advanced treatment steps such as ozonation are applied to degrade contaminants. However, such measures often come at the cost of creating transformation products for which even less ecotoxicological information exists (Merkus et al. 2022).

Among the fluoroquinolones, enrofloxacin (VMP) and its metabolite ciprofloxacin (HMP) were detected in a single red kite. It was suspected that this red kite might have received an unreported veterinary treatment or foraged on medicated livestock based on the exceptionally high concentrations of enrofloxacin (1655 ng g^{-1}). A recent study investigated the presence of fluoroquinolones in livestock carcasses from a wildlife feeding station in Spain. The study reported enrofloxacin of up to 3359 ng g^{-1} and ciprofloxacin concentrations 1550 ng g^{-1} in the plasma of griffon vultures that visited the feeding stations (Herrero-Villar et al. 2022). Despite the fact that feeding stations are not provided to scavengers in Germany, the observed exposure in the red kite might therefore be caused by foraging on medicated livestock. The relatively high concentration of ciprofloxacin in one white-tailed sea eagle is considered to be a result of aquatic exposures from the use of ciprofloxacin as HMP rather than metabolisation from enrofloxacin. This assumption is based on 1) the absence of enrofloxacin in the same white-tailed sea eagle and 2) a presumable low metabolisation rate for the conversion of enrofloxacin to ciprofloxacin in birds (American Black Vultures (*Coragyps atratus*)) after administration (Waxman et al. 2021).

6.2.4 Exposure to plant protection products and deliberate poisoning

Among the 30 targeted PPPs, we only detected two insecticides and one metabolite. The neonicotinoid thiacloprid was detected in two red kites during autumn and spring of 2009 and 2015. In general, neonicotinoids seem to be rapidly metabolisable in avian tissues (Bean et al. 2019), which indicates that the spatiotemporal context is critical for the detection. This is supported by a study on neonicotinoid exposure in farmland birds after sowing (Lennon et al. 2020a) as well as a study that detected residues in gamebirds during autumn sowing (Lennon et al. 2020b). The majority of the 30 PPPs was not detected, which might be related to 1) the spatiotemporal context of exposures and potential rapid metabolisation and excretion 2) the fact that not all targeted PPPs are liver-specific and may rather occur in other matrices (e.g. blood or kidney). Nevertheless, the exposure to currently used PPPs requires further investigation as

a rapid metabolism and distribution to other organs does not exclude adverse effects. Information on the metabolism of PPPs is also crucial for developing target methods for metabolites and transformation products that are specific to avian organisms (Kuo et al. 2022). Apart from environmental exposures, three deliberate poisonings of red kites were detected, one with brodifacoum (SGAR) and two with dimethoate (banned insecticide). Deliberate poisoning of raptors is a well-known threat for red kites and other raptors in Europe (e.g. Berny et al. 2015; Kitowski et al. 2020; Molenaar et al. 2017) and might contribute to the declined survival rates of red kites in Germany (Katzenberger et al. 2019).

6.3 Chapter 4 – Bridging the gap from legacy pollution to emerging contaminants and chemical mixtures

In addition to investigating chemical threats by three classes of priority contaminants, chapter 4 focused on the identification of 2,441 legacy and emerging contaminants. The applied methodology was first established in aquatic matrices such as surface water, wastewater, sediment and fish (Diamanti et al. 2020; Gago-Ferrero et al. 2020; Nikolopoulou et al. 2022). Therefore, many of the target analytes were expected to be contaminants of the aquatic environment. Analysing them for the first time in a (semi-)aquatic apex predator was expected to generate further insights into their accumulation in food webs. Choosing one of the two in Germany occurring raptor species that feed on the aquatic food web (white-tailed sea eagle and osprey) depends on the consideration of the dietary niche and the importance of migratory behaviour. The analysis focused on the white-tailed sea eagle as the species is resident throughout the year. Furthermore, the broad dietary niche of white-tailed sea eagles has resulted in multiple chemical exposures in the past and made the species particularly susceptible for chemical contamination. White-tailed sea eagles are therefore expected to provide insights into the accumulation of contaminants from different exposure routes, which may be indicative for other raptor species as well.

6.3.1 Feeding ecology of the investigated white-tailed sea eagles

In general, the foraging behaviour of the investigated white-tailed sea eagles was similar to those in Nadjafzadeh et al. (2016) by demonstrating that freshwater/brackish water fish and piscivorous birds represent the most important prey items. The stable isotope values for $\delta^{15}N$ are furthermore similar to those of white-tailed sea eagles from the southwestern parts of Finland (mean ± 2*SE: 12.4 ± 0.7‰ (this study) vs mean ± SD: 12.09 ± 1.83‰) (Vainio et al. 2022). In contrast to Baltic white-tailed sea eagles, other subpopulations inhabit coastal habitats in Nordic regions, e.g. Norway, Islands or Greenland. These regions are characterised by a more

pristine coastal environment with higher diversity of breeding sites of avian prey species. In general, northern subpopulations have a higher intake of marine prey, which generally results in lower $\delta^{13}C$ values (e.g. in Løseth et al. 2019).

6.3.2 Detection of co-occurring chemicals and their relation to stable isotope values

In total, 85 chemicals were detected in the livers of white-tailed sea eagles, from which most belonged to the class of MPs followed by legacy POPs and PPPs (Figure 2). The frequent detection of MPs is expected to be influenced by the fact that 45% of the target analytes were MPs (and transformation products) but also demonstrates that MPs frequently enter food webs of apex predators. The high detection rate of legacy POPs (e.g. DDTs and PCBs) and PFAS was expected as these compounds are known to bioaccumulate in apex predators from the Baltic Sea region (e.g. de Wit et al. 2020). The large number of PPPs (and transformation products) demonstrates the importance of extending current target lists, as there was only limited information available on the accumulation of these compounds in other apex predators (see 4.2, chapter 4). Especially the frequent detection of the currently approved PPP spiroxamine requires further investigation. Among the expired PPPs, two deliberate poisonings were detected with the expired PPP carbofuran. Carbofuran is, despite its ban in 2005, used to deliberately poison raptors in Europe (Kitowski et al. 2020). Both spiroxamine and the expired PPP simazine were found with increasing concentration in agricultural landscapes. These results indicate that spiroxamine applications result in wildlife exposures and a potential persistence of simazine in agricultural landscapes.

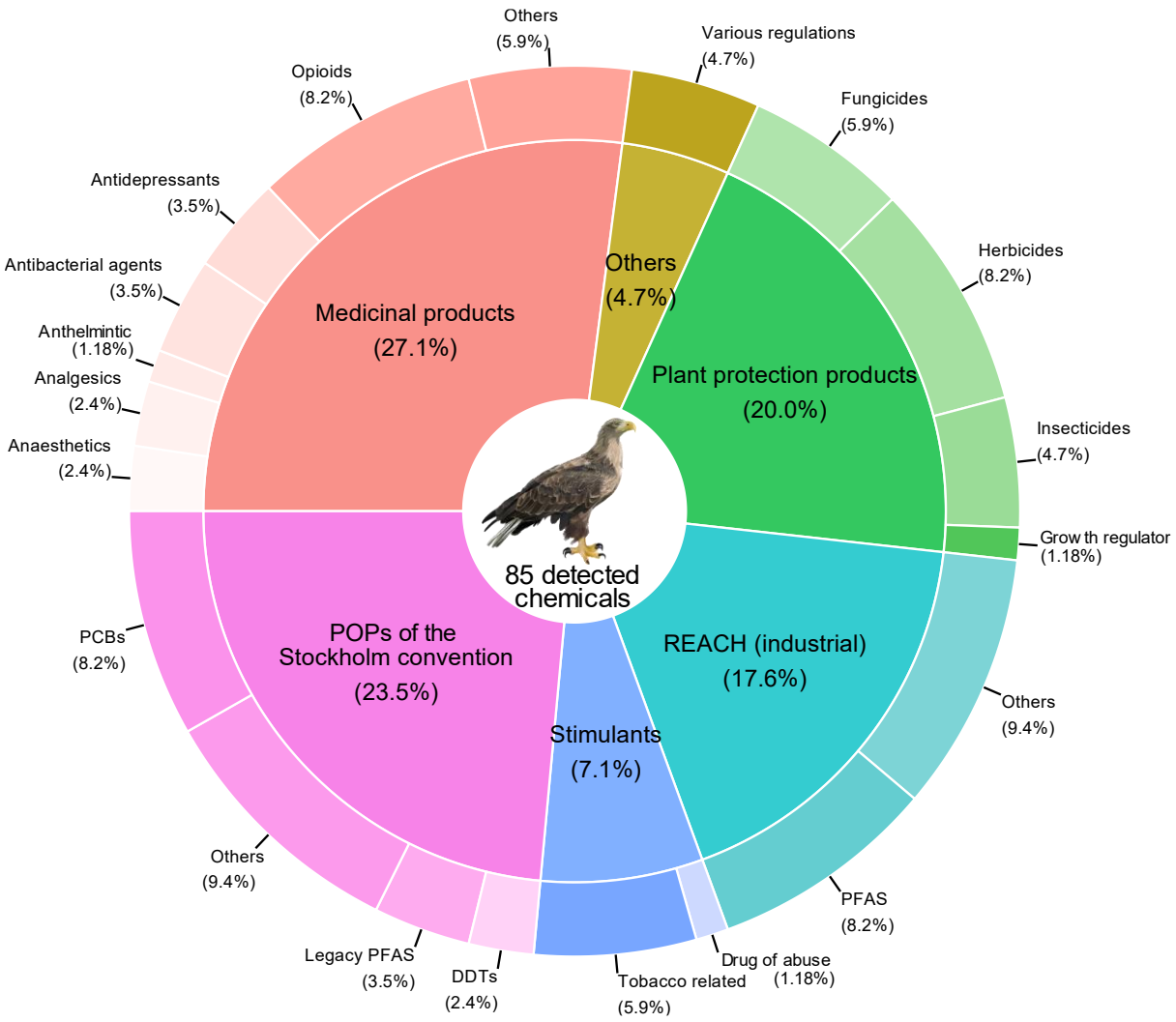

Figure 2: Classes and subclasses of detected chemicals in livers of 30 white-tailed sea eagles from northern Germany. Percentages refer to the number of detected chemicals within the given (sub-)class. Veterinary and human medicinal products are given in the same category (medicinal products) for visualisation purposes. Metabolites and transformation products were included in the regulatory classes of their respective parent compounds. The figure was created using the webr package in R version 4.1.2 (Moon 2020; R Core Team 2021).

Chapter 4 demonstrated that legacy POPs such as 4,4′-DDE and PCBs are still among the most dominant contaminants in white-tailed sea eagles in terms of concentration. However, in contrast to certain marine mammals (Desforges et al. 2018; Williams et al. 2020), these concentrations were below a reported toxicity threshold for reproductive impairment in white-tailed sea eagles (Helander et al. 2002). As POPs heavily impacted the Baltic Sea region in the past, further studies on marine mammals are highly recommended, especially for species suffering from anthropogenic pressures, such as harbour porpoises (*Phocoena phocoena*) (Gkotsis et al. 2022; Siebert et al. 2020). None of the bioaccumulating POPs (Σ_2DDT, Σ_6PCB) and Σ_4PFSAs were significantly associated with δ^{15}N, which was unexpected as the heavier stable nitrogen isotope (^{15}N) accumulates along trophic levels. (Løseth et al. 2019; Sun et al.

2019a). The particularly high PFOS concentration of some individuals (NS93, NS102 and MV530) in the catchment area of the river Elbe might have been a result of a point pollution source. Such non-linear behaviour in the data might explain the lack of significant relation between Σ_4PFSAs and δ^{15}N. In general, the applied modelling approach only considered univariate models due to the small sample size (n = 30). This limits the statistical power of the analysis and might, together with the discussed problems of using bulk δ^{15}N (Elliott et al. 2021), explain the lack of association with the other contaminants.

6.3.3 Comparison of the applied wide-scope target screening to other high-resolution measurements in European apex predators

It is increasingly recognised that conventional multi-target methods only capture a minor fraction of currently registered or authorised contaminants on the chemical market. As a consequence, there is only limited information available on CECs in European raptors (reviewed by González-Rubio et al. 2020). To address this gap, wide-scope target screening methods (chapter 4), as well as suspect and NTS workflows, are increasingly developed for biota matrices (Dürig et al. 2022a; Rebryk et al. 2022). Wide-scope target screening methodologies use generic extraction protocols and high-resolution mass spectrometers (HRMS) and rely, similar to conventional target methods, on a representative mix of isotopically labelled reference standards. Using reference standards not only allows for the identification of a compound but also its quantification. Gkotsis et al. (2022) applied a wide-scope target screening for 2,273 liquid chromatography (LC) amendable contaminants (non-volatile, polar to semi-polar substances) on marine, freshwater and terrestrial apex predators (liver) and prey species (fish, muscle) from the UK, the Netherlands, Sweden and Germany. The study detected 145 contaminants, of which the majority also belonged to MPs, followed by PPPs and PFAS (Gkotsis et al. 2022). In contrast to chapter 4, the study by Gkotsis et al. (2022) did not analyse gas chromatography (GC)-amendable contaminants (volatile, hydrophobic substances) such as POPs (Table SI-4, chapter 4). A recent study analysed 2,448 contaminants using GC- and LC-HRMS for 26 eggs of peregrine falcons, Eurasian curlews (*Numenius arquata*), little owls (*Athene noctua*) and eagle owls (*Bubo bubo*) from southwestern Germany. In contrast to Gkotsis et al. (2022), the study by Gkotsis et al. (2023) reported a dominant contribution of PPPs (including POPs) followed by PFAS, MPs and industrial chemicals (including POPs). In general, only 58 compounds were detected in the eggs analysed by Gkotsis et al. (2023), of which the majority were lipophilic. Differences between Gkotsis et al. (2023) and chapter 4 are expected to be related to food web differences of the studied species (terrestrial vs semi-aquatic) and matrix differences (eggs vs livers).

Target screening methods such as the one described above rely on costly analytical standards that are only available for a fraction of the produced chemicals on the European market. Therefore, suspect screening (using prior information such as e.g. mass ratio or predicted retention time) and NTS (prioritising chromatographic peaks based on, e.g. statistically increasing peak areas in a time series) become increasingly important. Both suspect screening and NTS are important complementary methodologies to derive qualitative and semi-quantitative data on CECs (Aalizadeh et al. 2021; Hollender et al. 2019; Schymanski et al. 2015). For example, Dürig et al. (2022a) applied NTS methodologies using LC-HRMS for a times series (1965-2017) of muscle samples from Swedish white-tailed sea eagles. In this study, 207 features with increasing temporal trends were tentatively identified, of which four were of anthropogenic origin. Features refer to chromatographic peaks consisting of retention time, peak area and mass-to-charge ratio and can be assigned to a chemical formula with a certain level of confidence (Schymanski et al. 2014). The detected features in Dürig et al. (2022a) were assigned to two pharmaceuticals (tolterodine, aphidicolin), one cosmetic (octoxynol-2) and one endogenous compound that is also produced as an industrial chemical (octadecatentraenoic acid). Another study applied NTS workflows using GC-HRMS in biota from the Baltic Sea in Sweden tentatively identified more than 135 anthropogenic features based on their significant time trends (Rebryk et al. 2022). The study included muscle tissues of white-tailed sea eagles (1965-2017), eggs of common guillemots (*Uria aalge*, 1986-2019) and blubber of harbour porpoises (1988-2019). Similar to the conclusions of this study, many legacy POPs, such as PCBs or DDTs, showed declining trends, whereas certain CECs (e.g. plasticiser, contaminants from polymer industry) increased (Rebryk et al. 2022). In Rebryk et al. (2022) white-tailed sea eagles contained the lowest number of CECs (4/14 detected CECs), from which only two compounds (1-hexylcyclohexene and 2,6-bis(1,1-dimethylethyl)phenol) showed increasing trends. A recent food web study analysed the species mentioned above together with lower organisms from the Baltic Sea using GC-HRMS (Rebryk and Haglund 2022). In this study, Rebryk and Haglund (2022) tentatively identified 253 features that showed significant trophic magnification factors (TMFs). TMFs are a measure for the increase of a contaminant concentration per trophic level (vs biomagnification factor for a specific predator/prey pair) (Vainio et al. 2022). Among legacy POPs (median TMF_{PCBs}:18 , TMF_{DDTs}: 6.9), also CECs (median TMF: 4.4) were detected, such as e.g. polymer additives (TMFs: 2.8-7.8), halogenated flame retardants (TMFs: 3-13) and a UV blocker (TMF: 3.6) (Rebryk and Haglund 2022). Legacy POPs (e.g. PCBs and related compounds) showed the highest TMFs and were most closely associated with white-tailed sea eagles, which also had the highest trophic level (4.25)

among the investigated species (Rebryk and Haglund 2022). Similar to chapter 4, Rebryk et al. (2022) also identified the synthetic musk galaxolide, but in harbour porpoises, not in white-tailed sea eagles. Galaxolide was also detected in other European apex predators (Gkotsis et al. 2022), which indicates widespread contamination of this compound. Legacy POPs, such as DDT derivates and PCBs, as well as emerging contaminants, such as galaxolide were also in human post-mortem tissues (including the liver) (Baumer et al. 2021). Apart from galaxolide, none of the tentatively identified CECs in white-tailed sea eagles from Dürig et al. (2022a) or Rebryk et al. (2022) was detected in chapter 4. The HRMS chromatograms of chapter 4 were stored in the NORMAN digital sample freezing platform (Alygizakis et al. 2019), a database system that allows for future retrospective suspect screening, e.g. for the above-mentioned compounds. Establishing NTS methods in biota matrices is therefore crucial to continuously extending specific target and suspect screening lists.

Dürig et al. (2022a), Rebryk et al. (2022) and Rebryk and Haglund (2022) used the muscle of white-tailed sea eagles as the sample matrix, whereas chapter 4 focused on the liver to cover a broad range of LC- and GC-amendable compounds. Except for matrix differences, there were also temporal differences between the studies, as chapter 4 only included samples from recent years (2015-2018). A general issue when analysing biota matrices is related to comparably high matrix effects that require additional clean-up steps (Badry et al. 2022a). Together with generic sample extraction protocols, this can result in lower sensitivity and higher detection limits for some chemical classes compared to specific target methods. The issue was demonstrated for brodifacoum in chapter 4 when comparing the results with the overlapping individuals analysed in chapter 3. Nevertheless, applying comprehensive analytical methodologies using both GC- and LC-HRMS in the livers of an apex predator has shown to be able to detect a wide range of contaminants.

6.3.4 Regulatory implications based on *in-silico* predictions of persistent, bioaccumulative and toxic properties

The applied prioritisation scheme used the quantitative structure–activity relationship (QSAR) tool JANUS. The QSAR model estimates PBT properties based on experimental and predicted data by including associated uncertainties (Pizzo et al. 2016). In general, the JANUS tool has proven to be supportive by identifying mismatches between the regulatory classification and observed exposures. However, the JANUS scores are based on the behaviour of previously known PBT substances, which might limit its applicability for future unknown modes of persistence, bioaccumulation and/or toxicity. A prominent example from the past are PFAS,

whose accumulation depends on their protein binding affinity rather than their lipophilicity, which was the main driver for the bioaccumulation of many POPs. The JANUS tool classified both POPs and perfluorosulfonic acids (PFSAs) as bioaccumulative, whereas PFCAs were not classified as bioaccumulative. This estimation is in line with results from a study Zhao et al. (2013), who reported generally higher biota to soil accumulation factors for PFSAs than PFCAs. Interestingly, approved PPPs with predicted persistence, such as bromoxynil, myclobutanil and pymetrozine, expired shortly after the sampling period. In contrast, napropamide and spiroxamine are still approved, and especially the frequent detection of spiroxamine requires further investigation. In contrast to the expectations, most detected compounds were MPs rather than known/predicted bioaccumulating substances like POPs or PFAS. These results are expected to be influenced by the selection of target analytes but also demonstrate that many MPs can enter higher trophic levels in aquatic food webs (Gkotsis et al. 2022). MPs are frequently detected contaminants in the aquatic environment when emissions from wastewater treatment plant effluents exceed removal rates, which is why some MPs are considered 'pseudo-persistent' contaminants (Barceló and Petrovic 2007). In general, MPs are considered to be metabolisable and excretable in mammals, which might explain their low B scores (JANUS). However, for certain MPs such as diclofenac, metabolism pathways are different in birds which have led to fatal consequences for vultures (Herrero-Villar et al. 2021; Oaks et al. 2004). The frequent detection of compounds that are not expected to be persistent or bioaccumulative demonstrates that chemical exposures in apex predators are complex and do not solely rely on intrinsic physicochemical properties. For example, the landscape and feeding ecology of a species but also the sales and usage of a chemical are expected to influence wildlife exposure. However, accessing data for sales is challenging as such information is confidential for biocides or only given in ranges for PPPs and industrial chemicals. Publishing indices that are based on the relative sales (e.g. 0-1) might help to develop exposure indices, which could then be integrated in *in silico* hazard toolboxes to conduct a preliminary risk assessment.

Taken together, chapter 4 demonstrated that white-tailed sea eagles are exposed to a large variety of anthropogenic chemicals, some of which have never been described in literature before. Legacy pollutants such as DDTs and PCBs have been shown to still represent a considerable contamination burden with detection rates of up to 100%. Most detected compounds were MPs, which is expected to be related to incomplete wastewater removal and their large representation among the target analytes. The analysed white-tailed sea eagles have been shown to predominantly forage on aquatic food webs which is in line with a previous

study on the food choice of white-tailed sea eagles from the study region (Nadjafzadeh et al. 2016). Compared to northern subpopulations, German white-tailed sea eagles forage to a lesser degree on marine food webs that are considered to be less polluted compared to inland freshwater habitats due to higher dilution and admixture (Elliott et al. 2009). Chemical burdens of white-tailed sea eagle subpopulations outside of the Baltic Sea environment might therefore be lower. Further studies considering the ecological and geographical differences are needed to assess general exposure risks for white-tailed sea eagles, e.g. as part of the monitoring activities in the MSFD (Zampoukas et al. 2014). Additionally, studies using NTS workflows in the terrestrial environment, such as in Dürig et al. (2022b) or Hornek-Gausterer et al. (2021), are needed for extending target/suspect lists with analytes that are specific for those compartments. This would be particularly valuable for future studies using terrestrial sentinel species, such as common buzzards or tawny owls (see chapter 2).

6.4 Chapter 5 – Distribution of prioritised contaminants in the blood of raptor nestlings from different feeding guilds

The final chapter of the dissertation applied an active monitoring scheme using blood from raptor nestlings to increase the spatiotemporal resolution of contaminants signals. Sampling the blood of nestlings has the advantage of knowing the precise nest location and life history of the individuals. It might further overcome a potential sampling bias when focusing on tissues from deceased birds. In contrast, a limitation of analysing blood is that many compounds that are known to threaten apex predators accumulate in lipophilic tissues. Besides these bioaccumulative compounds, persistent and mobile chemicals came into focus of chemical regulation recently. Such compounds are not retained by environmental barriers and rapidly distribute in the aquatic environment (Hale et al. 2020). Analysing blood as an aqueous matrix was expected to provide further insights into the exposure of non-bioaccumulative compounds in birds of prey. In contrast to chapter 3, chapter 5 restricted the analysis to LC-amendable compounds because hydrophobic (GC-amendable) compounds were excepted to rather accumulate in lipophilic tissues.

6.4.1 Distribution and spatial variation of anticoagulant rodenticides among feeding guilds

Similar to chapter 3, mainly SGARs (e.g. brodifacoum and difenacoum) were detected in the blood of the investigated species. In general, the half-life of ARs is lower in the blood than in the liver, which results in lower detection rates than in chapter 3. Nevertheless, the results from this chapter are in line with the observations from chapter 3 by demonstrating that red kites are

particularly at risk for AR exposure (22.6%, n = 53, median: 7 ng mL^{-1}). A previous analysis in the blood of red kites nestling in Franche-Comté showed AR residues in 30% (median: 6.1 ng mL^{-1}) of the individuals (Powolny et al. 2020), which is remarkedly consistent with results from this study. In contrast, a study on red kites from the Pyrenees and adjacent regions found higher exposure rates (55%, n=20) (Oliva-Vidal et al. 2022a). Anthropogenic landscape features (e.g. livestock farm density) and ecological factors (e.g. local foraging pattern) might be responsible for differences in the exposure. For example in the Pyrenees, red kites have been shown to more frequently forage on carcasses of carnivores (Oliva-Vidal et al. 2022b), which might have caused a higher AR exposure in this region. The results for ARs in the blood of red kites demonstrate that a considerable number of individuals might be exposed to ARs throughout their lifespan. Further studies investigating the potential effects of ARs on the population level are therefore recommended, especially since farmland birds are globally declining (Moreau et al. 2022). A recent experimental study investigated the sublethal effects of chlorophacinone (FGAR) in six free-ranging red-tailed hawks (*Buteo jamaicensis*) and detected signs of thermoregulatory dysfunction (piloerection) and coagulopathy (Vyas et al. 2022). In chapter 5, only one FGAR (warfarin) was detected in a few common buzzards (8.6%, n=35), which is the European sister species of the North American red-tailed hawk. In general, common buzzards can have similar AR exposure rates to those of red kites (López-Perea and Mateo 2018), whereas others (including the current study) report lower exposure rates for common buzzards (Moriceau et al. 2022). As both species are generalists, differences in AR exposures might be related to their dietary plasticity in the respective sampling regions. However, further studies including dietary information before sampling would be needed to confirm this assumption. Surprisingly, Montagu's harriers did not show dateable AR residues in their blood, which was unexpected since small mammals can represent an important prey item for the species (Terraube and Arroyo 2011). Montagu's harriers are ground-breeding raptors in cereal fields that were sampled in approximately 50x50 meter protection zones. For harriers, little is known about their exposure to ARs in Europe except for bromadiolone exposure in a single Montagu's harrier in France (Berny et al. 1997) and three Marsh harriers (*Circus aeruginosus*) from Denmark (Christensen et al. 2012). Two hen harriers (*Circus cyaneus*) from France also showed, similar to the results of this study, no AR exposures (Moriceau et al. 2022). However, a species from the same family, the Réunion harrier (*Circus maillardi*), was frequently exposed to ARs on French oversea territory (Coeurdassier et al. 2019). The comparably short half-live of ARs in the blood and the lack of dietary information prior to sampling calls for further studies on liver tissues of deceased Montagu's harrier to exclude potential risks for the species.

Even though Montagu's harriers were not exposed in this study, terrestrial birds of prey (red kite, common buzzard and Montagu's harrier) from North-Rhine Westphalia showed higher ΣAR concentrations compared with terrestrial species from North-Eastern Germany ($p = 0.05$; Figure 3). These results suggest that a higher population density and more intensive livestock farming (e.g. in North-Rhine Westphalia) are important drivers for AR accumulation in predators (Geduhn et al. 2015; López-Perea et al. 2019). In contrast to the other terrestrial species, the common buzzard also inhabits urban areas, which has been linked to increased AR exposure (chapter 3). It is therefore strongly recommended to investigate the risks of urban common buzzards as these populations are likely to be particularly impacted by AR exposure.

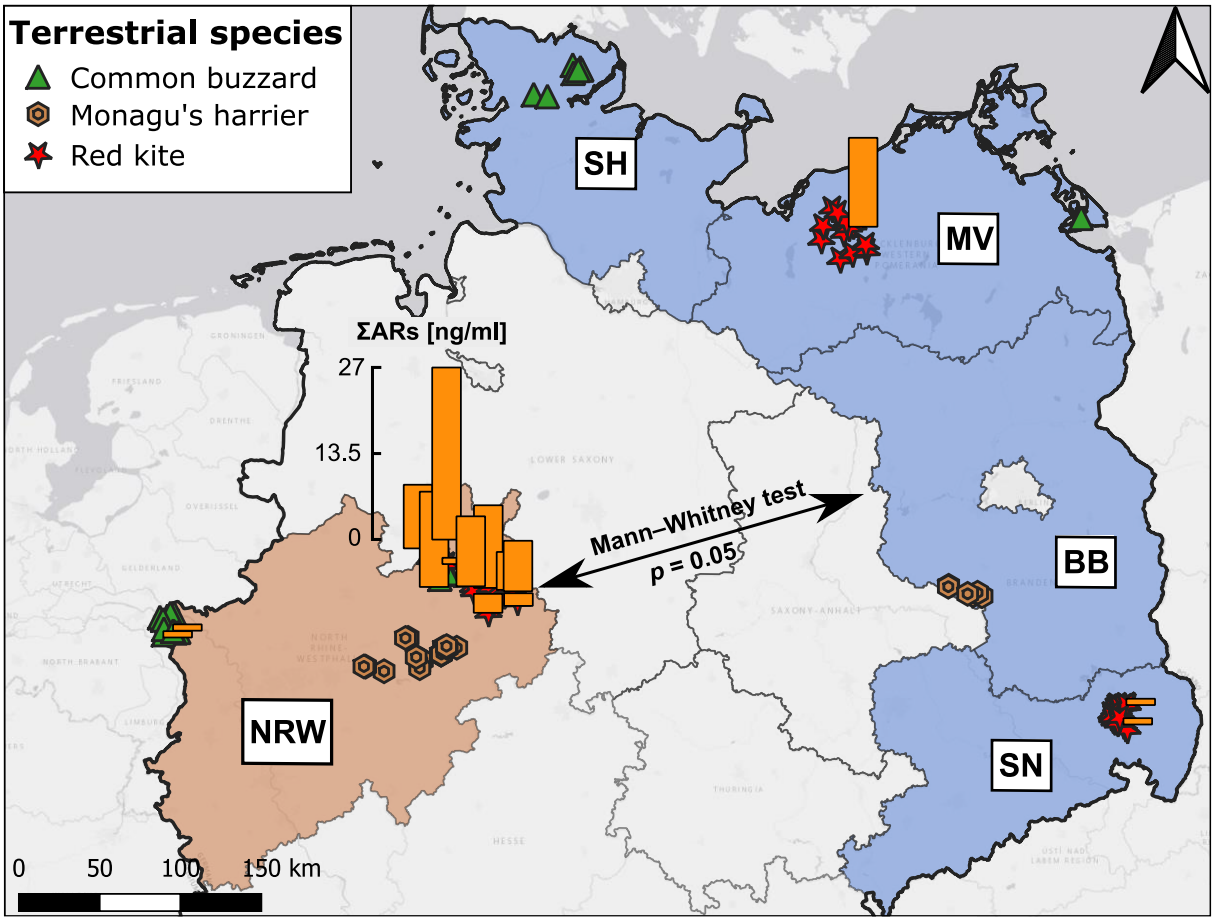

Figure 3: Spatial variation of ΣARs [ng ml^{-1}] in the blood of terrestrial birds of prey from North-Rhine Westphalia, including the border region of Lower Saxony (NRW, red) versus North-Eastern Germany (blue) given as histograms (orange). SH: Schleswig–Holstein, MV: Mecklenburg-Western Pomerania, BB: Brandenburg, SN: Saxony. Green triangles refer to common buzzards (*Buteo buteo*), red stars to red kites (*Milvus milvus*), and brown doubled hexagons to Montagu's harriers (*Circus pygargus*). The figure was created using the QuantumGIS software version 3.10.2 (QGIS Development Team 2020).

A divergence between exposure in liver tissues of adults (chapter 3) and the blood of nestlings was observed for white-tailed sea eagles. The short half-lives of ARs in blood and presumably low concentrations (based on chapter 3) of species inhabiting North-Eastern Germany are

expected to be responsible for the absence of ARs in the blood of white-tailed sea eagles. The absence of ARs in the blood of osprey is consistent with results in livers from chapter 3 and reports from other countries (Lemarchand et al. 2012; Thornton et al. 2022; Weir et al. 2018). These results indicate that ospreys are generally not at risk for ARs exposures.

6.4.2 Exposure to plant protection products and medicinal products in relation to their sales and spatial variation

PPPs were detected in all species except for ospreys. The most frequently detected PPP was the herbicide bromoxynil in 14% of the individuals. The median concentrations in Montagu's harrier were similar (red kite) or lower (common buzzard) compared to the other terrestrial tree-nesting raptors. Therefore, overlaps in their dietary niche (see Table SI-3, Chapter 2) are expected to be most influential for the observed exposures rather than spray applications in cereal fields. Interestingly, the authorisation of bromoxynil ended after the sampling period in 2021. However, during the past two years, the sales increased from 25-100 t in 2019 to 250-999 t in 2021 (period of grace 14/09/2021) (BVL 2022). This indicates 1) that bromoxynil was increasingly used in 2021 and 2) that the investigated species might have been more frequently exposed. In general, bromoxynil concentrations were significantly higher in terrestrial birds of prey from North-Rhine Westphalia (vs North-Eastern Germany; $p < 0.05$, Figure 4). This indicates that local land use patterns such as intense field agriculture, e.g., the Soester Börde and surrounding regions, caused increased wildlife exposures.

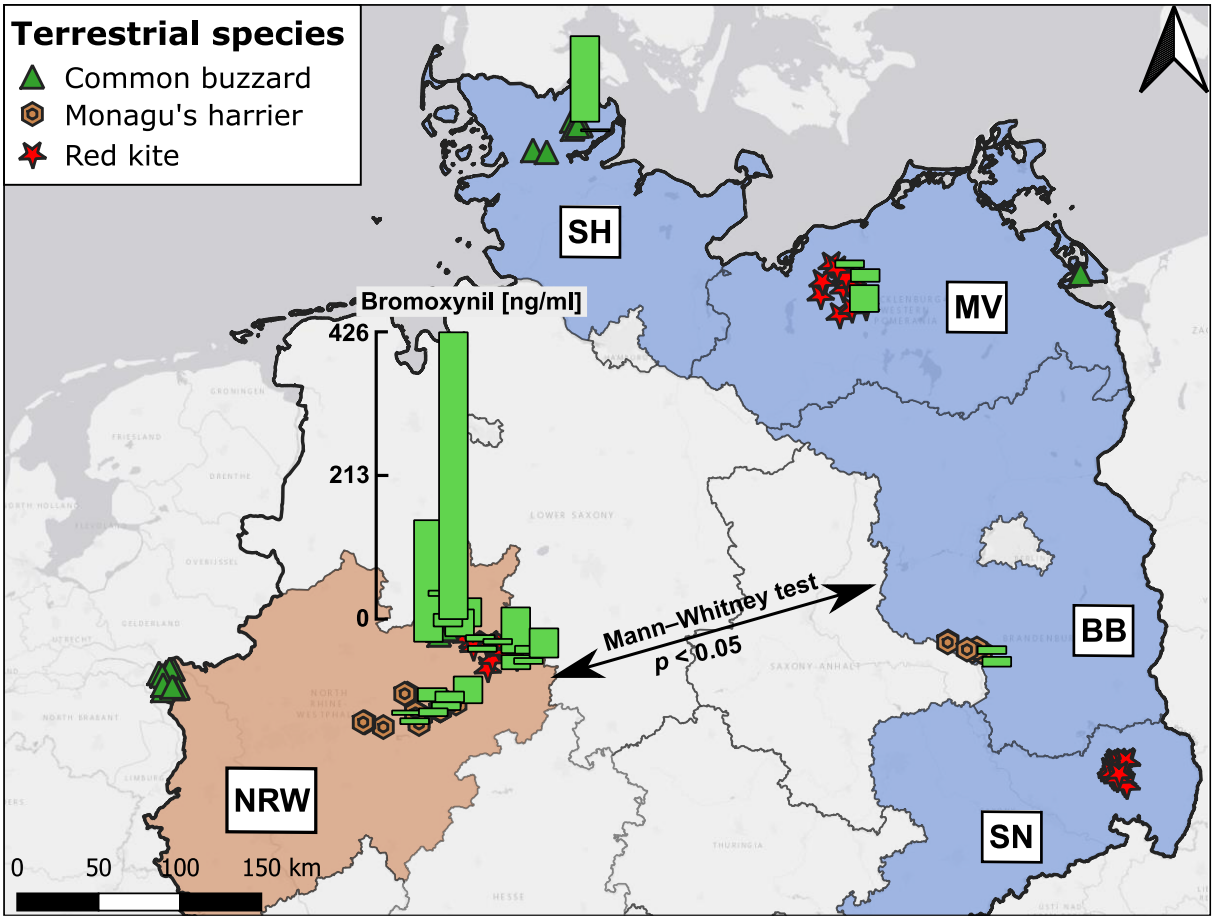

Figure 4: Spatial variation of bromoxynil [ng ml^{-1}] in the blood of terrestrial birds of prey from North-Rhine Westphalia, including the border region of Lower Saxony (NRW, red) versus North-Eastern Germany (blue) given as histograms (light green). SH: Schleswig–Holstein, MV: Mecklenburg-Western Pomerania, BB: Brandenburg, SN: Saxony. Green triangles refer to common buzzards (*Buteo buteo*), red stars to red kites (*Milvus milvus*), and brown doubled hexagons to Montagu's harriers (*Circus pygargus*). The figure was created using the QuantumGIS software version 3.10.2 (QGIS Development Team 2020).

Other PPPs besides bromoxynil were only sporadically detected. This indicates, similar to the results of chapter 3, that most targeted in-use-PPPs are not accumulating in the investigated species. However, sales of spiroxamine also increased from 250-1000 t in 2019 to 1000-2499 t in 2021, which makes spiroxamine one of the most frequently sold PPP in Germany (BVL 2022). Similar to results from chapter 4, spiroxamine was also detected in the blood of white-tailed sea eagles but at lower detection rates. Spiroxamine is currently authorised in the EU until 31/12/2023 (European Commission 2022). Based on the results of chapters 4 and 5, it is recommended to include spiroxamine in target lists for studies on mixed food web feeders such as the white-tailed sea eagle (chapter 4). For both bromoxynil and spiroxamine, studies on potential adverse effects on higher trophic level species are missing, which complicates the final assessment of the observed exposures. For the bromoxynil formulation, bromoxynil-octanoate, a high risk for secondary poisoning was identified (European Food Safety Authority

2017), which highlights the need of considering formulations in target lists. In addition to formulations, such compounds should also comprise metabolites and transformation products. However, limited information is currently available to predict the formation/occurrence of such compounds in avian organisms (Kuo et al. 2022). Information on avian metabolism is expected to be particularly valuable for MPs that are designed to be metabolisable in humans and/or livestock. Chapter 5 demonstrated the presence of the HMP ciprofloxacin in the blood of common buzzards, red kites and osprey. The different feeding ecologies of the species indicate that multiple environmental emission sources for fluoroquinolone antibiotics exist. In contrast to the results of chapter 3, ibuprofen was not detected in the blood of white-tailed sea eagles (or any other species), which might be related to the comparably high detection limit (5 ng ml^{-1}) and potential rapid metabolisation of ibuprofen (Garrard 2014). A general limitation of chapter 5 was that mainly parent compounds were included in the target list, as chapter 4 demonstrated that metabolites and transformation products of MP were frequently detected in the livers. The further development of NTS workflows in biota matrices is therefore recommended for identifying additional metabolites in avian organisms. Moreover, studies using plasma (vs blood) and specific extraction protocols for NSAIDs (vs generic extraction in this multi-target analysis) might yield lower detection limits and thus provide further insights into the risks of HMPs for raptors feeding on aquatic food webs.

6.5 Recommendations for reducing the chemical impacts on wildlife

6.5.1 Limiting the use of anticoagulant rodenticides and improving sanitary measures

In Germany, SGARs are only allowed to be used by professional users based on established risk mitigation measures. However, consumer sales of SGARs are still possible due to a lack of national legal provisions on biocidal sales (Regnery et al. 2019). Apart from a sales restriction, additional measures such as restricting the outdoor use of particularly toxic SGARs (i.e. brodifacoum) might reduce the wildlife impact of ARs. Such measures have been shown to influence the exposure of raptors in Canada, but it remained unclear whether they also reduced the impact of AR poisoning (Elliott et al. 2022).

Norway rats are known to have high resistance against FGARs around livestock farms in the north-western parts of North-Rhine Westphalia, which resulted in the increased use of more potent SGARs (i.e. brodifacoum/difethialone) (Esther et al. 2022). This is expected to have contributed to the observed higher exposures of ARs in terrestrial birds of prey from North-Rhine Westphalia in chapter 5. The application of additional sanitary measures at livestock

farms (e.g. removing open feeding sites) as well as reducing the accessibility of buildings has been shown to delay the reoccurrence of rodents and to increase the control success in the post-treatment period (Esther et al. 2022). Together with limiting the outdoor use of ARs, these measures are recommended to reduce the wildlife impact of ARs. This is especially important since alternatives such as mechanical traps or other chemical solutions, such as alphachloralose, cholecalciferol or phosphine/cyanide gas releasers, are less favoured in the EU due to animal welfare considerations or limited usability and efficacy (Hohenberger et al. 2022). The lack of suitable alternatives calls for further risk mitigation, as current measures do not prevent raptors from exposure. These measures should primarily focus on non-chemical solutions to prevent rodent infestations in the first place. Chemical solutions should ideally comply with the safe-by-design ambition of the Chemical Strategy for Sustainability (European Commission 2020b). One way might be the encapsulation of the active ingredient with compounds such as cellulose that cannot be digested by carnivorous species such as raptors (Hohenberger et al. 2022). Furthermore, this would overcome the bait shyness of previously approved rodenticides by causing a delay in the occurrence of acute toxic effects (Hohenberger et al. 2022). However, whereas capsulation might prevent primary exposures of carnivorous species, it does not prevent secondary exposures, which is considered to be the dominant form of exposure for raptors. Digital traps and monitoring systems might provide an additional measure to more precisely prevent non-target primary exposures (Hohenberger et al. 2022). Furthermore, banning rolled oat baits such as those used in Walther et al. (2021b) is expected to prevent primary exposures of songbirds. Such measures were already implemented in North America (Elliott et al. 2022). Further systematic approaches, including non-chemical solutions and the design of safer chemical alternatives, are needed to prevent non-target exposures and secondary wildlife poisoning.

6.5.2 Understanding the problems of persistent and bioaccumulative chemicals

In general, the highest concentrations in livers of white-tailed sea eagles from Germany were reached by persistent and bioaccumulative compounds such as DDTs, PCBs and PFOS. However, concentrations of DDTs and PCBs were below toxicity thresholds for reproductive impairment. Even though concentrations were lower compared to levels during the 20th century, it is important to understand that declining levels of persistent chemicals are not linked to their environmental disappearance. Declining trends are rather associated with their dilution, distribution to environmental sinks (e.g. sediments) or long-range transport to polar regions (Chiaia-Hernández et al. 2022; Muir et al. 2019). As discussed by Scheringer et al. (2022), chemical and environmental legislations primarily focus on toxicity, whereas the main global

chemical problems are associated with persistent chemicals. When persistent chemicals are continuously released into the environment, they are expected to have an increased chance of exceeding known or unknown toxic thresholds (Cousins et al. 2019; Scheringer et al. 2022). This is considered to be especially problematic for PFAS that are currently still in use. For example, concentrations of certain PFAS in rainwater are now exceeding recently updated drinking water guideline values (Cousins et al. 2022). Due to the complexity of assessing toxicities for thousands of PFAS, five member states of the EU are currently preparing a PFAS restriction dossier for all chemicals that contain at least one fully fluorinated methyl or methylene carbon atom (European Chemicals Agency 2022). The restriction proposal is expected to be submitted in January 2023 and restricts a whole group of substances rather than compounds for which there is enough scientific evidence. For PFAS, already regulated, longer-chained PFAS were increasingly replaced by shorter-chained homologues that have shown similar hazardous properties (Gomis et al. 2015). Restricting a whole group of chemicals, therefore, represents an important step towards avoiding regrettable substitutions.

Today, the production of chemicals outpaces the capacity for conducting hazard and risk assessments (Johnson et al. 2020; Treu et al. 2022). Furthermore, the effects of environmentally relevant chemical mixtures are so far not adequately assessed in European risk assessments (Drakvik et al. 2020; Kortenkamp and Faust 2018). It is argued that the knowledge of adverse effects will always remain incomplete due to a potentially infinite number of possible effects (Cousins et al. 2019). These examples demonstrate that there is a high degree of uncertainty for assessing toxicity, especially for sublethal and population-level effects in higher-trophic-level wildlife species. This becomes particularly apparent for raptors and ARs as some species have shown to be considerably more sensitive than common regulatory test species (e.g. northern bobwhite) (Rattner et al. 2011). Moreover, for many persistent and bioaccumulating compounds, including DDT and PCBs, links to the toxic effects were only retrospectively established after they had already caused substantial damage. Therefore, chemical regulation should focus more on persistence and bioaccumulation to protect apex predators before adverse effects on the individual or population level manifest. Focusing on persistence in the first place complies with the sustainable use of chemicals by enabling the possibility of stopping emissions once additional information, e.g. on adverse effects, becomes apparent (Cousins et al. 2019). In general, monitoring data are considered to represent an important addition for identifying chemical risks under field conditions and should be more frequently considered in regulatory risk assessments (Treu et al. 2022). From an academia perspective, storing monitoring data inaccessible online databases (e.g. NORMAN Database System) is, together with the provision

of user-specific guidance, recommended to increase the regulatory uptake of monitoring data in future (Badry et al. 2022a; Treu et al. 2022).

7. Conclusion

This dissertation demonstrated the suitability and importance of using birds of prey as sentinels for a wide range of environmental contaminants on a national and continental scale. The selection of candidate species for pan-European biomonitoring has shown that the common buzzard and tawny owl are among the most suitable species based on their widespread distribution, large habitat niche and residency. However, other species may be better sentinels for specific monitoring schemes, such as the golden eagle for Pb or the northern goshawk for studies including far northern European parts. In the next step, pilot monitoring studies involving harmonised sampling across Europe of the selected species are recommended to assess spatiotemporal contaminants trends. Such studies should be accompanied by the analysis of dietary proxies (e.g. stable isotope values) as individuals might feed on different trophic levels across Europe. In general, the applied trait-based approach for identifying raptor biomonitors has proven robust and can also be applied to other continents and contaminants.

Concerning chemical threats for birds of prey from Germany, this dissertation demonstrated the presence of various environmental contaminants, some of which are still registered or approved under European chemical legislations. Especially the frequent detection ARs, which are known to cause adverse effects in vertebrates, is alarming. Terrestrial species known to forage on rodents, such as red kites, but also mainly avivorous species from urban areas, such as northern goshawks, showed detection rates in livers of >80%, and concentrations frequently exceeded toxicity thresholds. The results are particularly concerning for red kites since more than 50% of the global breeding pairs live in Germany. The frequent detection of ARs in a mainly avivorous species such as the northern goshawk indicates widespread food web contamination in urban areas. Studies on rodent-predating species from urban areas, such as common buzzards, are therefore recommended to characterise exposure risks for urban wildlife further. The results of ARs in the blood of nestlings confirm that red kites are at particular risk for exposure and indicate that some individuals might be exposed throughout their lifespan. However, little is known about the potential chronic and sublethal effects of ARs in raptors, which represents a critical knowledge gap. Concentrations of ARs were generally higher in the blood of terrestrial species from regions of high population density and intense livestock farming (i.e. North-Rhine Westphalia). These regions might serve as a starting point for assessing the impact of ARs on the local annual abundance of red kites, as done for common kestrels in the UK. In addition, further studies on potential prey species are needed to identify the main exposure routes around

livestock farms and in urban areas. Such information is crucial for developing further risk mitigation measures to prevent secondary wildlife poisoning.

The two in Germany occurring raptor species that feed on aquatic food webs are only resident in North-Eastern Germany, of which only the (semi-) aquatic white-tailed sea eagle was exposed to ARs in the liver. Based on the results, species from North-Eastern Germany seem to have a generally lower risk for AR exposure. However, the potential for aquatic trophic transfers in adult white-tailed sea eagles requires further investigation. Studies on piscivorous species (e.g. great cormorant (*Phalacrocorax carbo*)) in North-Western Germany are recommended to provide further insights into the potential biomagnification of ARs in aquatic food webs. In general, the results on ARs demonstrate that birds of prey are exposed to ARs depending on their feeding ecology and habitat use. Urban species and rodent-predating species from North-Western Germany are expected to be at the highest risk for exposure. These results call for stricter mitigation measures, such as improving sanitary measures at livestock farms and urban areas and limiting the outdoor use of particularly toxic SGARs.

Apart from AR, which represented the most severe threat among the investigated contaminants, POPs such as DDTs, PCBs and PFOS showed the highest concentrations in the livers of white-tailed sea eagles. Even though concentrations of DDTs and PCBs were below proposed toxicity thresholds, they might still contribute to currently unknown additive or cumulative effects with other frequently detected contaminants. However, chemical mixtures are not adequately assessed in European risk assessments, and little is known about the effects of chemical mixtures in general. Especially the combination of DDTs, PCBs and PFOS requires further investigation as those compounds are known to cause adverse effects when tested individually. In total, 85 chemicals were detected in livers of white-tailed sea eagles, which demonstrates the particular risk for multiple chemical exposures of a mixed food web feeder. There is an urgent need to promote strategies on how exposure to multiple hazardous chemicals can be more effectively assessed under field conditions. Despite the ban of PFOS and PFOA by the Stockholm Convention and the ongoing PFAS restrictions in the EU, exposures to PFAS are expected to prevail due to their high environmental persistence. Together with DDTs and PCBs, these examples demonstrate a need to better address environmental persistence and bioaccumulation for protecting apex predators, as information on toxic effects were only discovered after they caused substantial damage.

In addition to persistent and bioaccumulative compounds, many MPs were detected at lower concentrations. HMPs were mainly detected in white-tailed sea eagles, indicating aquatic

exposures due to high prescription volumes and incomplete wastewater removal. Further studies on exclusively piscivorous species, in combination with the analysis of fish sampled in the same spatiotemporal context, are expected to provide further insights into the trophic transfers of MPs. In contrast to HMPs, VMPs were less frequently detected and assumed to be related to scavenging on medicated livestock or companion animals. The frequent detection of compounds that were not expected to be persistent or bioaccumulative demonstrates that chemical exposures of apex predators are complex and do not solely rely on chemical properties but also on feeding ecology, landscape and chemical use pattern. Among PPPs, approved and expired compounds were detected, some of which were used to deliberately poison birds of prey, such as red kites and white-tailed sea eagles. In general, only a few currently approved PPPs were frequently detected (e.g. spiroxamine), whereas others, such as bromoxynil, expired shortly after the sampling period of the presented studies. Based on the result of this dissertation, I recommend that persistence and bioaccumulation, together with monitoring data and ecological factors (e.g. feeding ecology), are better taken into account in regulatory risk assessments to protect birds of prey before adverse effects in individuals or populations manifest.

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9 Appendix

9.1 Supplementary information – Chapter 2

Towards harmonisation of chemical monitoring using avian apex predators: Identification of key species for pan-European biomonitoring

Supplementary information

Table SI-1: Environmental contaminants prioritised as key candidate compounds for pan- European raptor biomonitoring schemes by ~ 30 experts attending the ERBFacility Workshop in February 2019. Scores were received from participants in three groups. Scores (1-10) were assigned to the respective contaminants with 1 being considered as most important. Contaminant with average scores < 4 were selected for consideration within the current paper and are indicated by a green background colour.

COMPOUND	Group 1	Group 2	Group 3	Average	(Average * 3)/ number of groups returning a score
Pharmaceuticals (e.g. NSAIDs)	1	4	1	2	2.0
Agrochemicals (pesticides)	3	1	3	2.34	2.3
Anticoagulant rodenticides	4	3	4	3.67	3.7
Metals (e.g. Pb, Hg)	5	5	1	3.67	3.7
Perflourinated compounds,	1		5	3	4.5
Carbanates		2		2	6.0
Organochlorines	7	7	7	7	7.0
Brominated and newer Flame Retardants		6	8	7	7.0
Molluscicides	6			6	18.0
Antibiotics			6	6	18.0
Micro-plastics	8			8	24.0
Personal care products			9	9	27.0
Polycyclic aromatic hydrocarbons			10	10	30.0

Table SI-2: Total number of raptor species mentioned for biomonitoring schemes within Europe at the ERBFacility Workshop in February 2019. The presence of species within one of the four European main regions [1] is indicated in a binary system with 1 indicating that a species is present in at least three countries of the respective main region and 0 indicating that a species is present in less than three countries within a the respective main region based on [2]. A red colour indicates that the species is absent in at least two main regions.

Species	Eastern Europe	Northern Europe	Southern Europe	Western Europe
Bearded vulture	0	0	1	1
Egyptian vulture	0 (Bulgaria)	0	1	0 (France)
Eurasian griffon vulture	0 (Bulgaria)	0	1	0 (France)
Cinereous vulture	0 (Bulgaria)	0	1	1

Short-toed snake-eagle	1	1 (baltics)	1	0
Lesser spotted eagle	*1*	*1 (baltics)*	*0*	*0*
Greater spotted eagle	*1*	*1*	*0*	*0*
Booted eagle	*1*	*0*	*1*	*0*
Spanish imperial eagle	*0*	*0*	*(0) Spain&Portugal*	*0*
Eastern imperial eagle	*1*	*0*	*0*	*0*
Golden eagle	1	1	1	1 (mostly alpine)
Bonelli's eagle	*0*	*0*	*1*	*0*
White-tailed sea eagle	1	1	0	0
Common buzzard	1	1	1	1
Rough-legged buzzard	0	1	0	0
European honey buzzard	1	1	1	1
Red kite	1	0	1	1
Black kite	1	0	1	1
Western marsh harrier	1	1	1	1
Hen harrier	1	1	1	1
Montagu's harrier	1	1 (baltics)	1	1
Eagle owl	1	1	1	1
Barn owl	1	1	1	1
Tawny owl	1	1	1	1
Long-eared owl	1	1	1	1
Little owl	1	1	1	1
Short-eared owl	*0*	*1*	*0*	*1*
Scops owl	*1*	*0*	*1*	*0*
Tengmalm's owl	1	1	1	1
Common kestrel	1	1	1	1
Lesser kestrel	*0*	*0*	*1*	*0*
Peregrine falcon	1	1	1	1
Osprey	*0*	*1*	*0*	*0*
Eurasian sparrowhawk	1	1	1	1
Northern goshawk	1	1	1	1

Table SI-3: Reduced number of suggested candidate species for pan-European monitoring for prioritised environmental pollutants based on species distribution [2]. EE =Eastern Europe. NE = Northern Europe, SE = Southern Europe, WE = Western Europe. **WE*** = mainly alpine regions, **NE*** = only Baltic states, **NE**** = absent in Scandinavia and Iceland, **SE*** = only montane habitats.

Species	Distribution	Food web	Feeding trait	Diet	Habitat type	Migration
Eagles						
Golden eagle (*Aquila chrysaetos*)	• EE • NE • SE • **WE***	• Mainly terrestrial	• Active hunter [3-6] • Facultative scavenger [3, 6, 7]	• Mainly medium sized mammals [3-6] • Birds [3-6] • Reptiles [3, 4] • Carrion [3, 6] (enhanced during winter) [8] • Dietary variations among populations [6]	• Open areas [9, 10] • Montane areas [11, 12] • Steep slopes [10] • Avoidance of human disturbances [10] • Moorland [12]	• Mainly resident [13, 14] ➔ highly territorial [12] • Dispersal of subadults in northern Europe and alpine regions [9, 11, 15]
Short-toed snake-eagle (*Circaetus gallicus*)	• EE, • **NE*** • SE	• Terrestrial	• Active hunter [16]	• Mainly snakes [16] • Other reptiles [16] • Invertebrates [17]	• Open forest plots [18]	• Long-distance (trans-Saharan) [19]
Buzzards						
Common buzzard (*Buteo buteo*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [20-23] • Facultative scavenger [24]	• Mainly small to medium-sized mammals [20-23] • Insects [21, 22] • Birds [20-22] • Reptiles [20, 21]	• Low to moderate intensified agricultural areas [18, 25, 26] • Forest mosaics [18, 25] • Occasionally urban habitats [27]	• Partial migration in autumn and winter depending on weather conditions [28] • Partial migration to southern European parts [28]
European honey buzzard (*Pernis apivorus*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [29, 30]	• Mainly invertebrates [29, 30]	• Lack of clear habitat preferences [31]	• Long-distance (southern and eastern Africa) [32]

Kites						
Black kite (*Milvus migrants*)	• EE • SE • WE	• Mixed (terrestrial and freshwater)	• Active hunter [26, 33] • Facultative scavenger [34]	• Carrion [34] • Fish [33] • Mammals [26] • Birds [26] ➔Largely opportunistic	• Open habitats [35] • Preferentially near water (rivers and freshwater marshes) [26, 36] • Foraging along linear landscapes (e.g. roads) [37] • Foraging on dump sites [38]	• Mostly long distance (western Africa) [39] • Partly in the Mediterranean area [39]
Red kite (*Milvus milvus*)	• EE • SE • WE	• Mainly terrestrial	• Active hunter [40] • Facultative scavenger [24]	• Mainly small mammals [40, 41] • Carrion [41] • Insects [40, 41]	• Open grassland (low shrubs) [42, 43] • Forest edges [43] • Farmland and pastures [42, 44]	• Migration to the Mediterranean peninsula [45]
Harriers						

Hen harrier (*Circus cyaneus*)	• EE
	• NE
	• SE
	• WE
		• Mixed (terrestrial and freshwater) [46]	• Active hunters [46, 47]	• Avian prey
				  ○ Waterfowl [46]
				  ○ Gamebirds [46, 47]
				  ○ Non-game birds [46, 47]
				• Mammals [46, 47]
				• Wider niche compared to Western marsh harriers [46]
					• Natural grass mosaics [26, 48]
					• Avoidance of agriculture [26, 48]
					• Moorland [47, 48]
						• Partial migration [49]

Montagu's harrier (*Circus pygargus*)	• EE
	• **NE***
	• SE
	• WE
		• Terrestrial	• Active hunters [50-52]	• Small mammals [50-52]
				• Avian prey [50]
				  ○ Game birds [51]
				• Insects [50]
				➔ Individual diet
					• Agricultural habitat [50, 51]
					  ○ Open grassland [53]
					  ○ Abandoned pastures [53]
						• Long-distance migration (sub-Saharan Africa) [54]

				specialisation occurs [50]		
Western marsh harrier (*Circus aeruginosus*)	• EE • **NE*** • SE • WE	• Mixed (freshwater and terrestrial) [46]	• Active hunters [46, 55, 56]	• Small mammals [46, 55] [56] • Birds [46, 55, 56] ○ Waterfowl [46, 56]	• Natural habitats like reedbeds [56, 57] • Agricultural habitat [58] • Freshwater marshes [26, 57]	• Long-distance migration of populations from EE and NE (sub-Saharan Africa) [59]
Falcons						
Common kestrel (*Falco tinnunculus*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [60-63]	• Mainly rodents [60-63] • Avian prey (more dominant in urban areas) [60-62] • Insects [60-62] • Reptiles [60, 61]	• Agricultural land [25, 64] ○ Open grassland habitats [25] • Urban areas [60-62]	• Partial migration (mainly to SE but also to northern Africa) [65]
Peregrine falcon (*Falco peregrinus*)	• EE • NE • SE • WE	• Mainly terrestrial	• Active hunter [66-68]	• Avian prey (specialist) [66-68]	• Urban areas[66, 69] • Cliff habitats [68, 70, 71] • Cultivated habitats [68, 71]	• Resident [68] to migrating (in northern regions) [72, 73]
Hawks						
Eurasian Sparrowhawk (*Accipiter nisus*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [74-76]	• Avian prey (specialist) [74-76]	• Forest habitats [77-79] • Urban areas [79-81]	• Partial migration to southern European parts [28]

Northern Goshawk (*Accipiter gentilis*)	• EE
	• NE
	• SE
	• WE
		• Terrestrial	• Active hunter [82-84]	• Mainly avian prey [82, 83]
				  ○ Other raptors [83, 85]
				  ○ Non-game birds [82-84]
				  ○ Gamebirds [82]
				• Mammals [82-84]
					• Forest habitats [83, 86]
					• Urban habitats [87]
					• Grass-/shrubland [79]
						• Resident but post fledging dispersal up to 1000 km occurs in northern European parts [88, 89]

Owls						

Eurasian Eagle owl (*Bubo bubo*)	• EE
	• NE
	• SE
	• WE
		• Terrestrial	• Active hunter [90-93]	• Mainly mammals [90-92]
				• Avian prey [90-93]
				  ○ raptors [90, 92, 93]
				• Rarely: fish (rarely) [90], reptiles and invertebrates [92, 93]
				• Largest prey items among owls (more than 200 g) [94]
					• Habitat patches [91, 95]
					  ○ Forest edges [90]
					• Agricultural habitat [90, 96]
					• Adaption to human influenced habitats [90, 96]
						• Resident and territorial [96, 97]

Barn owl (*Tyto alba*)	• EE • **NE**** • SE • WE	• Terrestrial	• Active hunter [98-100]	• Small mammals (rodent specialist) [98-100] • Rarely birds [98-100] • Rarely invertebrates [94, 100]	• Mainly agricultural habitats [98-101] ○ Grassland [98, 100, 101] • Urban habitats [102]	• Mainly resident but short-range dispersal occurs (< 450 km) [103-105]
Little owl (*Athene noctua*)	• EE • **NE**** • SE • WE	• Terrestrial	• Active hunter [93, 100, 106]	• Small mammals [93, 100, 106] • Invertebrates [93, 100, 106] • Rarely birds [93, 100, 107] • Rarely reptiles [100]	• Open agricultural landscapes [108-111] • Vicinity to human settlements [108-111]	• Resident with short range dispersal (< 100 km) [112]
Long-eared owl (*Asio otus*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [93, 113-115]	• Mainly small mammals [93, 113-115] • Birds [93, 113-115] • Rarely Insects [113-115]	• Forest edges/Agroforestry [116-118]	• Mainly resident but migrates from Fennoscandinavia when prey becomes scarce [119, 120]
Tawny owl (*Strix aluco*)	• EE • NE • SE • WE	• Terrestrial	• Active hunter [121-123]	• Small mammals [121-123] • Small birds [121-123] • Rarely amphibians [121-123] • Rarely arthropods [121-123]	• Wide-habitat niche [124] • Urban habitats [121, 125] • Forest and forest patches [124, 126, 127] • Open farmland [126, 127]	• Resident [128]

Tengmalm's owl (*Aegolius funereus*)	• EE • NE • **SE*** • WE	• Terrestrial	• Active hunter [129-131]	• Mainly small mammals [129-131] • Rarely birds [129-131] • Very rarely insects [129]	• High elevations montane or subalpine habitats [124, 132] • Forest/forest patches [133, 134] • Farmland area [133]	• Resident with dispersal up to 580 km [135]

Table SI-4: European raptors feeding on aquatic food webs. EE =Eastern Europe. NE = Northern Europe, SE = Southern Europe, WE = Western Europe.

Aquatic species	Distribution	Food web	Feeding trait	Diet	Habitat type	Migration
White-tailed sea eagle (*Haliaeetus albicilla*)	• EE • NE • (WE: GER, AUT)	• Mixed (marine, freshwater and terrestrial)	• Active hunter [6, 136-139] • Facultative scavenger [6, 136, 138-140]	• Mainly Fish [6, 136-138] • Waterfowl [6, 136-138] • Game mammals [6, 136-139] (scavenging enhanced during autumn/winter)[139] • High dietary variations among populations [6, 139]	• Forest patches near freshwater habitats [136, 138, 141] • Marine habitats like brackish water, forested coast, treeless fjords [141-143] • High sensitivity to human disturbances [141]	• Resident and territorial but dispersal occurs up to 450 km [142, 144, 145]
Osprey (*Pandion haliaetus*)	• NE • (EE: Poland, Bulgaria) • SE: (Canary Islands, Balearic	• Aquatic (freshwater and marine)	• Active hunter [146-149]	• Fish (specialist) [146-148]	• In vicinity to freshwater habitats [146, 148, 150] ○ forest dominated [151] ○ agricultural land [152] • In vicinity to the coast [151, 153, 154] ○ Cliff nesting [151,	• Long-distance migration (mainly to West Africa) [155, 156] • Non-migratory in the Canary Islands [154]

	Islands, Portugal) • (WE: Germany, France)				153, 154]	

Table SI-5: European vultures. EE =Eastern Europe. NE = Northern Europe, SE = Southern Europe, WE = Western Europe. **WE*** = mainly alpine regions, **SE*** = only montane habitats.

Vultures						
Bearded vulture (*Gypaetus barbatus*)	• **SE*** • **WE***	• Terrestrial	• Obligate scavenger [157-159]	• Carrion ○ Mainly mammals (including livestock) [157-159] ○ Rarely birds [157, 158] ○ Rarely reptiles [157]	• Rugged montane habitats [160, 161] ○ Steep alpine habitats [161, 162] • Avoidance of human disturbance [160, 163]	• Resident (dispersal < 200 km) [161]
Cinereous vulture (*Aegypius monachus*)	• SE • (EE: Bulgaria) • (WE: France)	• Terrestrial	• Obligate scavenger [164, 165]	• Carrion ○ Small to medium sized mammals (including livestock) [164, 165] ○ Rarely poultry [164, 165] ○ Very rarely reptiles [165]	• Rugged montane habitats [166, 167] • Lower altitude mountain areas [167] ○ Open Mediterranean woodlands [168] • Avoidance of human disturbance [166, 167]	• Resident (dispersal < 600 km)[169]
Egyptian vulture (*Neophron percnopterus*)	• SE • (EE: Bulgaria) • (WE: France)	• Terrestrial	• Obligate scavenger [164, 165, 170, 171]	• Carrion ○ Mainly mammals (including livestock) [164, 165, 170, 171] ○ Occasionally birds [170, 171] including poultry [164, 165]	• Mainly lower altitude mountain areas [173, 174] • In vicinity to landfills and livestock [175] • Higher acceptance of human disturbance	• Resident but potential for long-distance dispersal (< 600 km) [176]

				○ Rarely reptiles and amphibians [164, 165, 171] ○ Garbage [172] ○ Very rarely fish [165, 171]	[173, 175]	
Eurasian griffon vulture (*Gyps fulvus*)	• SE • (EE: Bulgaria) • (WE: France)	• Terrestrial	• Obligate scavenger [164, 172, 177]	• Carrion ○ Specialists for medium to large mammalian carcasses including livestock [164, 172, 177] ○ Poultry [164, 172] ○ Increasing number of smaller mammals in extreme food conditions [172]	• Low to Mid-Mountainous cliffs [177-181] • Depopulated farming areas [180, 181] • Avoidance of human disturbance [180, 182]	• Resident. (dispersal < 150 km) [183]

Table SI-6: Used key word and Boolean operators in Google Scholar and Web of Science for collecting toxicological data of identified candidate species for pan-European monitoring of prioritised pollutants.

Lead	**AND**	Latin **OR** English species name	**AND**	Liver
Mercury	**AND**	Latin **OR** English species name	**AND**	Liver **OR** feather
Dieldrin **OR** organochlorine*	**AND**	Latin **OR** English species name	**AND**	Liver
veterinary* **OR** pharmaceutical*	**AND**	Latin **OR** English species name	**AND**	Liver

Table SI-7: Selection criteria for pan European Pb monitoring.

	Distribution	**Food web**	**Foraging trait**	**Diet**	**Migration**
Advantageous	• Present in at least three countries within a main region	• Terrestrial	• Active hunter & facultative scavenger	• Game mammals and/or • Waterfowl	• Resident
Limited	• Absence in three or more countries within a main region	• Mixed (marine/freshwater)	• Active hunter	• No preference for game-species	• Partial migration
Exclusion	• Absent in a main region	• Aquatic	• Obligate scavenger	• Other	• Long-distance migration

Table SI-8: Mean concentration of Pb in livers of identified candidate species for pan- European monitoring. N is the number of animals tested for liver residues. Weighted arithmetic means were calculated for studies giving Pb concentrations in subcategories (e.g. cause of deaths, age class etc.).

Species	Countries	N	Mean liver Pb (µg/g)	References
Golden Eagle	Switzerland	55	4.89	[184]
	Sweden	103	0.62	[185]
	Switzerland	3	22.18	[186]
	Germany	3	0.31	[186]
	Austria	1	0.41	[186]
	UK	5	Median: 0.34	[187]
	Norway	116	4.55	[188]
White-tailed sea Eagle	Norway	115	0.76	[188]
	Finland	110	5,95	[189]
	Finland	9	4.60	[190]
	Poland	22	33.62	[191]
	Germany Austria	52 5	7.03	[192]
	UK	1	<0.1	[187]
	Sweden	116	10.59	[193]
Common Buzzard	UK	56	Median: 1.34	[187]
	Poland	10	1.98	[194]
	Portugal	56	0.54	[195]
	Italy	18	Median: 0.95	[196]
	Italy (Sicily)	12	14,80	[197]
	Spain	44	4.17	[198]
	Spain	7	0.13	[199]
	Spain	5	0.11	[200]
	Netherlands	80	3.3 Median: 1,9	[201]
	Netherlands	35	Median: 0.9	[202]
	France	85	Median: 0.71	[203]
	Spain	37	Median:0.1-0.33	[204]

Table SI-9: Selection criteria for pan European terrestrial Hg monitoring.

	Distribution	Habitat	Migration
Advantageous	• Present in at least three countries within a main region	• Agricultural habitats • Forest patches • Urban habitats	• Resident
Limited	• Absence in three or more countries within a main region	• Avoidance of human settlements	
Exclusion	• Absent in a main region	• Natural/montane habitats	• Partial migration • Long-distance migration

Table SI-10: Median concentration of mercury (Hg) in livers of identified candidate species for pan-European monitoring. N is the number of animals tested for Hg residues.

Species	Countries	N	Median Hg liver (µg/g)	References
Northern Goshawk	Germany	61	0.13 Mean: 1.19	[205]
	Spain	15	0.18-0.35	[204]
	Belgium	2	5.04	[206]
	Norway	20	1.1	[207]
Tawny Owl	Belgium	8	0.36	[206]
	Norway	9	1.0	[207]
	Spain	34	0.26-0.61	[204]
	UK	25	Mean: 1.22	[208]

Table SI-11: Mean concentration of mercury (Hg) in feathers from juveniles/adults of identified candidate species for pan-European monitoring. N is the number of animals tested for Hg residues.

Species	Countries	N	Mean Hg feathers (μg/g)	References
Northern Goshawk	Spain	67	Median: 0.22-1.52	[209]
	Germany	26	3.51	[210]
	Sweden	3	5.1	[211]
Tawny Owl	Spain	130	Median 0.44-2.23	[209]
	Germany	96 adults 31 juveniles	4.09 2.55	[210]
	Sweden	3	7.03	[211]
	Norway	633	0.87	[212]
	Belgium	7	4.98	[213]

Table SI-12: Selection criteria for pan European ARs monitoring.

	Distribution	Foraging trait	Diet	Habitat	Migration
Advantageous	·Present in at least three countries within a main region	•Active hunter & facultative scavenger	·Mainly rodents •Small mammalian prey • Insects	•Agricultural habitats •Farmland •Farmland with patched forest •Urban habitats	·Resident
Limited	• Absence in three or more countries within a main region	•Obligate predator ·Obligate scavenger	·No preference for (small) mammalian prey	• Wilderness habitats	·Partial migration
Exclusion	·Absent in a main region		·Non-mammalian prey	•Natural/montane habitats	·Long-distance migration

Table SI-13: Frequency of detection and mean concentration of anticoagulant rodenticides (AR) in livers of identified candidate species for pan-European monitoring. N is the number of animals tested for liver residues. Table modified from López-Perea and Mateo, 2018.

Species	Countries	N	%	Mean ΣARs liver (µg/g)	References
Common Buzzard	Denmark	141	94	0.074	[214]
	France	43	95	0.318	[215-217]
	Spain	83	53	0.082	[218-221]
	UK	519	44	0.047	[222, 223]
	Estonia	18		0.032	[224]
Tawny Owl	Denmark	44	93	0.078	[214]
	France	5	40		[217]
	Spain	27	78	0.095	[218]
	UK	206	22	0.047	[222, 225]
	Estonia	10		0.039	[224]
	Finland	13	85	0.004	[226]

Table SI-14: Selection criteria for pan European monitoring of pesticides.

	Distribution	Foraging trait	Habitat	Migration
Advantageous	• Present in at least three countries within a main region	• Active hunter	• Agricultural habitats • Farmland with patched forest • Pastures	• Resident
Limited	• Absence in three or more countries within a main region	• Active hunter & facultative scavenger • Obligate scavenger	• Wilderness habitats	• Partial migration
Exclusion	• Absent in a main region		• Natural/montane habitats	• Long-distance migration

Table SI-15: Frequency of detection and mean concentration of the legacy pesticide dieldrin in livers of identified candidate species for pan-European monitoring. N refers to the number of animals tested for liver residues of dieldrin.

Species	Countries	N	Mean dieldrin liver (µg/g)	References
Tawny Owl	UK	55	0.15	[227]
	Norway	8	Median: < 0.01	[228]
	Italy (Cratere degli Astroni)	4	0.04	[229]

Table SI-16: Selection criteria for pan European monitoring of medicinal products.

	Distribution	Foraging trait	Habitat	Migration
Advantageous	•Present in at least three countries within a main region	•Active hunter& facultative scavenger •Obligate scavenger	•Agricultural habitats •Farmland with patched forest •Pastures	•Resident •Partial migration
Limited	•Absence in three or more countries within a main region	•Active hunter	•Wilderness habitats	•Long-distance migration
Exclusion	•Absent in a main region		•Natural/montane habitats	

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9.2 Supplementary information – Chapter 3

Linking landscape composition and biological factors with exposure levels of rodenticides and agrochemicals in avian apex predators from Germany

Supplementary information

Table SI-1: Metadata and necropsy results of the investigated birds of prey. **Id**: B = Berlin, Bra = Brandenburg, BW = Baden-Württemberg. HAM = Hamburg, MV = Mecklenburg-Western Pomerania, NRW: North Rhine-Westphalia, NS: Lower Saxony, RP: Rhineland-Palatinate, SA: Saxony-Anhalt, S: Saxony, SH: Schleswig-Holstein. State abbreviations are followed by continuous enumeration. **Species:** ACGE: *Accipiter gentilis*, ACNI: *Accipiter nisus*, HAAL: *Haliaeetus albicilla*, MIML: *Milvus milvus*, PAHA: *Pandion haliaetus*. **Sex:** m = male, f = female.

Id	Species	Sex	Age class	Year (found)	Latitude	Longitude	Nutrition condition	Cause of death	Found alive/unknown
B102	ACGE	f	adult	2002	52.6	13.3	bad	Other	
B103	ACGE	m	adult	2009	52.5	13.5	bad	Trauma	X
B109	ACGE	m	adult	2012	52.5	13.5	good	Trauma	X
B167	ACGE	f	adult	2016	52.6	13.4	good	Other Poisoning	
B169	ACGE	f	juvenile	2016	52.5	13.5	good	Infection	X
B170	ACGE	f	adult	2015	52.4	13.3	good	Trauma	X
B171	ACGE	m	adult	2015	52.2	13.4	bad	Infection	X
B172	ACGE	f	adult	2016	52.5	13.5	good	Trauma	X
B173	ACGE	m	juvenile	2016	52.5	13.5	moderate	Trauma	X
B178	ACGE	f	adult	2012	52.5	13.5	good	Trauma	
B181	ACGE	m	adult	2016	52.5	13.4	good	Trauma	X

B183	ACGE	f	juvenile	2015	52.5	13.3	bad	Infection	X
B186	ACGE	m	juvenile	2014	52.4	13.4	good	Trauma	
B188	ACGE	m	juvenile	2016	52.5	13.4	good	Other	
B191	ACGE	unknown	unknown	2015	52.4	13.4	unknown	Unclear	X
B193	ACGE	m	juvenile	2016	52.5	13.5	moderate	Trauma	X
B194	ACGE	m	juvenile	2014	52.5	13.4	good	Trauma	
B197	ACGE	m	adult	2017	52.5	13.3	good	Trauma	X
B198	ACGE	m	adult	2017	52.5	13.4	moderate	Trauma	X
B200	ACGE	f	juvenile	2017	52.5	13.4	bad	Trauma	
B206	ACGE	f	juvenile	2018	52.5	13.4	good	Other	
B207	ACGE	m	juvenile	2013	52.6	13.4	bad	Trauma	
B208	ACGE	m	adult	2018	52.5	13.4	moderate	Trauma	X
B38	ACGE	m	adult	1999	52.6	13.3	bad	Infection	X
B49	ACGE	f	adult	2000	52.4	13.2	bad	Unclear	X
B55	ACGE	m	adult	2000	52.5	13.6	bad	Trauma	X
B62	ACGE	f	adult	2001	52.4	13.7	good	Unclear	X
B68	ACGE	f	adult	2001	52.4	13.4	bad	Unclear	X
B79	ACGE	m	adult	2003	52.6	13.4	bad	Infection	
B80	ACGE	f	adult	2003	52.5	13.2	bad	Infection	X
B81	ACGE	f	adult	2003	52.5	13.4	moderate	Trauma	X
B82	ACGE	f	adult	2003	52.5	13.3	good	Trauma	

B83	ACGE	f	adult	2003	52.6	13.2	bad	Infection	X
B97	ACGE	m	adult	2004	52.6	13.6	bad	Trauma	
B98	ACGE	m	adult	2004	52.5	13.5	bad	Trauma	X
Bra152	ACGE	f	adult	2000	52.2	13.1	bad	Unclear	X
Bra328	ACGE	m	juvenile	2004	unknown	unknown	good	Trauma	
Bra382	ACGE	m	adult	2015	52.3	13.4	bad	Trauma	X
BW T9587	ACGE	m	adult	1998	48.2	9	bad	Other	X
HAM009	ACGE	f	adult	2002	53.6	10	moderate	Other	X
MV552	ACGE	f	juvenile	2000	unknown	unknown	good	Other	X
NRW68	ACGE	m	adult	2016	51.7	8	bad	Unclear	X
NS442	ACGE	m	adult	1999	52.4	10.5	moderate	Trauma	X
NS495	ACGE	f	adult	1999	52.9	9.7	good	Trauma	X
NS96	ACGE	f	adult	2010	52.5	10.4	moderate	Trauma	X
NS97	ACGE	m	juvenile	2017	53.8	9.2	good	Unclear	
NS98	ACGE	m	juvenile	2017	53.8	9.2	good	Unclear	
RP004	ACGE	f	adult	2016	51	6.9	bad	Infection	X
1590Q	ACNI	m	juvenile	2000	unknown	unknown	bad	Unclear	X
B100	ACNI	f	juvenile	2004	52.5	13.5	good	Trauma	X
B101	ACNI	f	juvenile	2005	52.5	13.5	moderate	Trauma	
B104	ACNI	m	juvenile	2009	52.5	13.5	moderate	Trauma	X
B157	ACNI	m	adult	2012	52.5	13.5	moderate	Trauma	X

Bra213	ACNI	f	adult	2002	52.5	13.4	good	Trauma	
Bra216	ACNI	m	adult	2002	52.3	12.7	bad	Trauma	X
Bra75	ACNI	m	adult	1998	52.9	12.1	bad	Other	X
Bra89	ACNI	m	juvenile	1996	52.2	12.7	bad	Unclear	X
Bra98	ACNI	m	adult	1998	52.8	13.2	good	Trauma	X
NS027	ACNI	f	adult	1998	52.5	10.8	bad	Trauma	X
NS21	ACNI	m	juvenile	1997	52.6	10.1	good	Trauma	X
NS22	ACNI	m	juvenile	2000	52.7	10.8	bad	Trauma	X
NS26	ACNI	m	juvenile	2000	52.3	10.3	bad	Trauma	X
NS31	ACNI	m	juvenile	1997	52.5	10.5	bad	Trauma	X
NS33	ACNI	m	juvenile	1997	52	10.6	bad	Trauma	X
NS34	ACNI	m	juvenile	1997	52.3	10.5	good	Trauma	X
NS340	ACNI	f	juvenile	1997	52.4	10.8	bad	Unclear	X
NS348	ACNI	f	adult	1997	52.4	10	good	Unclear	X
NS359	ACNI	m	juvenile	1997	52.4	10.7	bad	Unclear	X
NS390	ACNI	f	juvenile	1998	52.2	10.5	bad	Unclear	X
SA05	ACNI	f	juvenile	2003	51.5	12	good	Trauma	
SA06	ACNI	f	juvenile	2003	51.5	12	bad	Infection	X
MV145	HAAL	f	adult	2005	53.6	12.6	bad	Pb Poisoning	X
MV149	HAAL	f	adult	2005	53.9	12.8	good	Unclear	
MV150	HAAL	m	adult	2005	53.8	13.2	good	Pb Poisoning	

MV158	HAAL	m	adult	2005	54.5	13.5	bad	Pb Poisoning	X
MV159	HAAL	m	adult	2005	53.3	12.8	moderate	Other	
MV160	HAAL	m	adult	2005	54	13.9	good	Pb Poisoning	
MV165	HAAL	f	adult	2005	53.9	13.7	good	Other	
MV172	HAAL	m	adult	2005	53.4	13	bad	Other	
MV173	HAAL	m	adult	2005	53.8	11	good	Trauma	
MV174	HAAL	f	adult	2005	53.5	12.8	good	Trauma	
MV181	HAAL	f	adult	2005	53.6	12.4	bad	Unclear	
MV184	HAAL	f	adult	2005	53.7	11.4	moderate	Trauma	
MV189	HAAL	m	adult	2005	53.5	12.4	good	Trauma	
MV319	HAAL	m	adult	2010	53.6	12.2	good	Other	
MV324	HAAL	m	adult	2010	53.6	12.5	good	Trauma	
MV327	HAAL	f	adult	2010	53.5	13.5	good	Trauma	
MV333	HAAL	m	adult	2010	53.9	12.2	good	Other	
MV334	HAAL	m	adult	2010	53.5	14.2	good	Trauma	
MV343	HAAL	m	adult	2010	53.7	13.8	bad	Pb Poisoning	
MV346	HAAL	f	adult	2010	54.2	13.7	good	Other	
MV399	HAAL	m	adult	2010	53.8	12.5	bad	Trauma	X
MV401	HAAL	f	adult	2010	53.7	12	bad	Pb Poisoning	
MV460	HAAL	m	adult	2010	53.8	13.8	moderate	Other	X
MV479	HAAL	m	adult	2015	54	12.4	good	Pb Poisoning	

MV488	HAAL	f	adult	2015	54.1	13.8	moderate	Other	
MV502	HAAL	f	adult	2015	53.6	12	good	Pb Poisoning	
MV503	HAAL	m	adult	2015	54	14	good	Other	
MV504	HAAL	f	adult	2015	53.4	12.6	good	Other	
MV505	HAAL	f	adult	2015	54.3	13.1	good	Trauma	
MV506	HAAL	f	adult	2015	53.9	13.9	bad	Other	X
MV516	HAAL	f	adult	2015	53.7	12.8	good	Trauma	X
MV523	HAAL	m	adult	2015	53.3	12.6	unknown	Unclear	
MV524	HAAL	m	adult	2015	53.7	13.2	good	Trauma	
NS41	HAAL	f	adult	2005	53.2	11.1	moderate	Pb Poisoning	X
NS42	HAAL	f	adult	2006	53.8	9.1	good	Unclear	X
S10	HAAL	m	adult	2004	51.4	14.8	good	Trauma	
S12	HAAL	m	adult	2004	51.4	14	good	Unclear	
S14	HAAL	f	adult	2004	51.4	14.3	good	Trauma	X
S15	HAAL	m	adult	2004	51.2	13.7	good	Trauma	X
S23	HAAL	f	adult	2009	51.3	14.1	good	Pb Poisoning	
S24	HAAL	f	adult	2009	51.4	14.8	good	Pb Poisoning	X
S25	HAAL	f	adult	2009	51.5	14.6	good	Other	X
S27	HAAL	m	adult	2009	51.4	14.3	good	Pb Poisoning	X
S31	HAAL	m	adult	2009	51.4	13.3	good	Trauma	
S56	HAAL	f	adult	2014	51.3	14.7	good	Other	

S58	HAAL	f	adult	2014	51.3	14.8	bad	Trauma	X
S61	HAAL	m	adult	2014	51.3	14.1	good	Other	
S63	HAAL	m	adult	2015	51.4	15	moderate	Pb Poisoning	X
S71	HAAL	m	adult	2015	51.3	14.4	moderate	Trauma	X
SH134	HAAL	m	adult	2015	54.2	9.2	good	Other Poisoning	X
SH135	HAAL	f	adult	2015	54.2	10.7	good	Trauma	
SH143	HAAL	f	adult	2015	54	9.2	good	Other Poisoning	
SH150	HAAL	f	adult	2015	54.2	10.8	bad	Pb Poisoning	
SH151	HAAL	f	adult	2015	54.2	10.6	good	Pb Poisoning	
SH37	HAAL	f	adult	2006	54.6	9.9	good	Trauma	
SH57	HAAL	f	adult	2010	53.5	10.7	bad	Other Poisoning	
SH58	HAAL	f	adult	2010	53.6	10.8	good	Pb Poisoning	
SH60	HAAL	m	adult	2010	54.1	10.6	good	Other Poisoning	
SH62	HAAL	f	adult	2010	54.6	10	moderate	Infection	X
SH63	HAAL	f	adult	2011	53.6	10.8	good	Pb Poisoning	
B150	MIML	m	adult	1999	52.5	13.5	moderate	Trauma	X
Bra138	MIML	m	adult	2000	52.6	12.9	bad	Unclear	X
Bra305	MIML	f	adult	2004	53.1	12.9	good	Trauma	
Bra320	MIML	m	adult	2004	51.7	13.3	good	Trauma	
Bra321	MIML	f	adult	2004	51.5	13.4	good	Other	
Bra333	MIML	f	adult	2003	52.6	12.9	good	Trauma	X

Bra334	MIML	f	adult	2002	52.5	14.1	good	Trauma	X
Bra376	MIML	m	adult	2013	53.2	14.2	moderate	Infection	X
Bra391	MIML	m	adult	2019	53	12.5	moderate	Unclear	X
BW10187	MIML	m	adult	1999	48.6	8.7	good	Unclear	X
BW10225	MIML	f	adult	1999	47.8	8.9	good	Unclear	X
MV27	MIML	f	adult	1999	53.5	12.4	good	Trauma	X
MV29	MIML	f	adult	1999	53.9	12.9	good	Other	
MV307	MIML	m	adult	2009	53.6	13.9	good	Unclear	X
MV35	MIML	m	adult	2000	54	13.1	moderate	Unclear	X
MV467	MIML	f	adult	2014	unknown	unknown	moderate	Unclear	X
MV493	MIML	f	adult	2015	53.6	13.1	moderate	Unclear	
MV573	MIML	m	adult	2016	54.4	9.8	bad	Trauma	
NRW26	MIML	m	adult	2011	51.5	7.8	good	Trauma	
NRW42	MIML	f	adult	2010	51.5	8.3	unknown	Trauma	
NRW48	MIML	m	adult	2015	51.5	8.5	good	Trauma	X
NRW63	MIML	f	adult	2016	unknown	unknown	good	Other	X
NRW76	MIML	f	adult	2019	51.4	7.3	good	Trauma	X
NS13	MIML	m	adult	2003	53.1	11.1	moderate	Unclear	
NS56	MIML	f	adult	2009	53.1	11.2	good	Unclear	
NS57	MIML	f	adult	2009	53.3	10.8	good	Other	X
NS66	MIML	m	adult	2012	51.5	9.6	bad	Trauma	X

NS72	MIML	m	adult	2013	51.5	10.3	good	Other Poisoning	
NS73	MIML	m	adult	2013	52	10.1	moderate	Other	
S70	MIML	f	adult	2015	51	13.2	moderate	Trauma	X
SA040	MIML	m	adult	2013	51.8	11.1	bad	Infection	X
SA045	MIML	m	adult	2016	51.9	11.4	bad	Trauma	X
SA046	MIML	m	adult	2017	51.9	11.1	good	Trauma	
SA048	MIML	f	adult	2018	51.8	11.2	good	Trauma	
SA049	MIML	m	juvenile	2018	51.9	11.1	bad	Infection	
SA050	MIML	f	adult	2018	51.9	11.1	bad	Infection	
SA051	MIML	m	adult	2018	51.4	12	good	Unclear	
SA1	MIML	f	adult	1996	51.9	11.3	good	Trauma	X
SA2	MIML	m	adult	2000	51.9	11.3	good	Unclear	X
SA4	MIML	m	adult	2000	51.9	11.3	bad	Unclear	X
SH55	MIML	f	adult	2009	54.5	11.1	good	Trauma	
SH77	MIML	f	adult	2012	53.6	10.9	moderate	Other Poisoning	
Bra307	PAHA	unknown	adult	2004	51.8	14.4	good	Other	
MV168	PAHA	m	adult	2005	53.4	13.5	moderate	Other	
MV176	PAHA	unknown	juvenile	unknown	unknown	unknown	good	Trauma	X
MV178	PAHA	m	adult	2004	53.4	13.5	moderate	Trauma	
MV191	PAHA	f	juvenile	2003	53.5	12.2	moderate	Trauma	X
MV192	PAHA	m	adult	2005	53.3	11.5	bad	Other	

MV484	PAHA	m	adult	2014	53.7	11.8	good	Trauma	X
MV551	PAHA	f	adult	2015	53.4	11.5	moderate	Trauma	
MV559	PAHA	m	adult	2016	53.4	11.7	moderate	Unclear	X
MV563	PAHA	f	juvenile	unknown	unknown	unknown	bad	Trauma	X
MV566	PAHA	f	juvenile	2003	53.7	12.4	bad	Trauma	
NRW37	PAHA	f	juvenile	2014	51.5	8.1	bad	Unclear	
NS78	PAHA	m	adult	2013	53.5	9	good	Trauma	

Table SI-2: Validation - RECovery of analytes and surrogates (100 ng/g; n=5). No analytes were detected in control samples (n=2). RSD= relative standard deviation and Reporting Limit n.d. (not detected) = < RL (Reporting Limit). HMP=human medicinal product; VMP= veterinary medicinal product.

Analyte	Intended use	RL	REC	RSD
		ng/g	%	
Brodifacoum	Biocide	2	88	13
Bromadiolone	Biocide	2	82	22
Chlorophacinone	Biocide	10	90	6
Coumatetralyl	Biocide	0.4	89	11
Difenacoum	Biocide	1	88	9
Difethialone	Biocide	2	77	13
Flocoumafen	Biocide	1	97	9
Permethrin	Biocide	20	55	12
Warfarin	Biocide	0.4	96	4
Cypermethrin	Biocide/Insecticide	20	76	10
Cyprodinil	Fungicide	20	94	5
Difenoconazole	Fungicide	2	103	5
Dimoxystrobin	Fungicide	2	110	4
Epoxiconazole	Fungicide	10	115	7
Fenpropimorph	Fungicide	10	56	11
Fludioxonil	Fungicide	1	112	8
Isopyrazam	Fungicide	10	110	4
Metconazole	Fungicide	2	113	3
Prochloraz	Fungicide	2	102	9
Propiconazole	Fungicide	10	99	9
Quinoxyfen	Fungicide	10	87	6
Tebuconazole	Fungicide	10	113	3
Aclonifen	Herbicide	10	112	9
Chlortoluron	Herbicide	2	116	3
Diflufenican	Herbicide	10	106	6
Flufenacet	Herbicide	2	107	4
Isoproturon	Herbicide	0.2	116	5
Metribuzin	Herbicide	10	101	5
Nicosulfuron	Herbicide	10	51	10
Pendimethalin	Herbicide	20	92	4
Chlorpyrifos	Insecticide	10	89	9
Clothianidin	Insecticide	20	125	5
lambda-Chalothrin	Insecticide	4	73	16
Dimethoate	Insecticide	10	121	2
Omethoate	Dimethoate metabolite	10	112	5
Imidacloprid	Insecticide	10	120	2
Methiocarb	Insecticide	1	108	5
Pirimicarb	Insecticide	2	109	2
Thiacloprid	Insecticide	2	122	3
Ciprofloxacin	HMP	20	51	6
Diclofenac	HMP	10	90	11
Ibuprofen	HMP	10	94	6
Enrofloxacin	VMP	20	93	11

Marbofloxacin	VMP	10	82	9
Sulfamethazin	VMP	1	55	22
Surrogate (recovery)	**Method**		**REC**	**RSD**
			%	
Acenocoumarol	LC/A		104	7
Chlorpyrifos-methyl	GC/EI		87	7
Clothianidin D3	LC/C		131	5
Coumachlor	LC/A		95	6
trans-Cypermethrin D6	GC/NCI		79	13
Diclofenac D4	LC/A		85	9
Difenoconazole D6	LC/C		105	6
Diphacinone D4	LC/A		93	3
Enrofloxacin D5	LC/D		92	9
Tebuconazole D9	LC/C		111	3
Terbuthylazine D5	LC/B		111	4
Surrogate (samples)	**Method**		**REC**	**RSD**
			%	
Acenocoumarol	LC/A		98	22
Chlorpyrifos-methyl	GC/EI		100	20
Clothianidin D3	LC/C		126	19
Coumachlor	LC/A		107	23
trans-Cypermethrin D6	GC/NCI		94	33
Diclofenac D4	LC/A		62	28
Difenoconazole D6	LC/C		114	26
Diphacinone D4	LC/A		78	28
Enrofloxacin D5	LC/D		119	45
Tebuconazole D9	LC/C		110	19
Terbuthylazine D5	LC/B		74	23

Table SI-3: Sample preparation and extraction.

Defrosting of liver samples, cutting in small pieces and weigh in pp - tubes (50 mL)

⇩

Spike with surrogates

⇩

Addition of 20 mL methanol

⇩

Homogenisation (IKA Ultra-Turrax T25) 3 min

⇩

Addition of 10 ml water

⇩

Homogenisation (IKA Ultra-Turrax T25) 1 min

⇩

Centrifugation (Heraeus Megafuge 1.0) 5 min with 5.000 rpm at RT

⇩

Transfer an aliquot of supernatant (15 mL) in a new pp - tube

⇩

Addition of 5 mL sodium chloride - solution (20%)

⇩

Agitation for 4 min

⇩

Transfer of solution on ChemElut - column (Agilent 12198008) and wait at least 15 min

⇩

Elute with 100 mL dichloromethane (250 mL round bottom flask)

⇩

Transfer aliquots in conical flasks

⇙ ⇘

10 ml 50 ml

⇩ ⇩

Aliquots reduce to dryness (Büchi Rotavapor, 37 °C bath temp.)

⇩ ⇩

methanol / water **Redissolve** with 1 ml internal Standards acetonitrile

⇩ ⇩

Briefly vortex

⇩ ⇩

Filtration through syringe filter (0.2 µm PTFE)

⇙ ⇘

LC-MS/MS GC-MS/MS

Storage at -20 °C until to measurement

Table SI-4: Configuration of LC-MS/MS.

LIQUID CHROMATOGRAPHY													**Agilent 1290 Infinity II**
METHOD	**A**			**B**			**C**			**D**			
Autosampler temperature	10 °C												
Injection volume	5 µL												
Syringe rinse	100 µL												
Analytical column	Agilent Zorbax Eclipse C18 (1.8 µm, 50 mm, 2.1 mm i.d.)			Agilent Zorbax Eclipse C18 (1.8 µm, 50 mm, 2.1 mm i.d.)			Phenomenex Kinetex C18 EVO (2.6 µm, 50 mm, 2.1 mm i.d.)			Phenomenex Kinetex C18 PS (2.6 µm, 50 mm, 2.1 mm i.d.)			
Column temperature	40 °C												
Mobile phase A	H2O +1mmol NH4F			H2O +5mmol NH4formate + 0.5% formic acid			H2O +1mmol NH4F			H2O + 0.1% Formic acid			
Mobile phase B	Methanol /Acetonitrile (65/35)			Methanol + 5mmol NH4formate+ 0.5% Formic acid			Methanol /Acetonitrile (65/35)			Methanol + 0.1% Formic acid			
Gradient program	Time (min)	A (%)	B (%)	Time (min)	A (%)	B (%)	Time (min)	A (%)	B (%)	Time (min)	A (%)	B (%)	
	0.0	98	2	0.0	98	2	0.0	98	2	0.0	97	3	
	3.0	2	98	3.0	2	98	3.0	2	98	0.5	97	3	
	5.0	2	98	5.0	2	98	5.0	2	98	4.0	0	100	
	5.1	98	2	5.1	98	2	5.1	98	2	5.0	0	100	
	6.0	98	2	6.0	98	2	6.0	98	2	5.1	97	3	
										6.0	97	3	
Flow rate	500 µL/min												
MASS SPECTROMETRY													**QTRAP 6500+ (SCIEX)**
Mode	negative ESI			positive ESI									
Ion spray potential	-4500 V			5500 V									
Source temperature	550 °C												
Dwell time	10 ms			20 ms			10 ms			20 ms			
Scan type	Multiple Reaction Monitoring												
Confirmation	Enhanced Product Ion spectra in the sample agree with > 80% with standards in the same sequence (response > 500 cps)												
Software	Analyst 1.7.1												
Quantification	Relative peak area												

Table SI-5: LC-MS/MS – MRM- and EPI-conditions (precursor (Q1) and product ions (Q3) in m/z and declustering potential (DP), entrance potential (EP), collision energy (CE) and cell exit potential (CXP) in V).

Q1	Q3	Analyte	DP	EP	CE	CXP
Method A						
520.9	78.8	Brodifacoum	-20	-10	-128	-11
526.9	249.9	Bromadiolone	-30	-10	-50	-19
373.1	201.0	Chlorophacinone	-75	-10	-30	-13
291.0	140.9	Coumatetralyl	-125	-10	-38	-13
293.9	250.0	Diclofenac	-55	-10	-10	-16
443.1	135.0	Difenacoum	-55	-10	-46	-15
538.9	80.8	Difethialone	-20	-10	-92	-13
541.0	382.0	Flocoumafen	-65	-10	-36	-29
307.0	161.0	Warfarin	-45	-10	-26	-19
247.0	180.0	Fludioxonil	-35	-10	-40	-9
205.0	161.0	Ibuprofen	-45	-10	-10	-9
351.9	265.0	Acenocoumarol (Surr)	-70	-10	-40	-13
340.9	160.8	Coumachlor (Surr)	-60	-10	-30	-21
298.1	254.0	Diclofenac D4 (Surr)	-55	-10	-16	-19
343.1	167.0	Diphacinone D4 (Surr)	-115	-10	-32	-15
377.1	200.9	Chlorophacinone D4 (IS)	-120	-10	-32	-15
312.1	161.0	Warfarin D5 (IS)	-95	-10	-28	-9
Method B						
265.0	182.1	Aclonifen	36	12	39	10
350.0	96.7	Chlorpyrifos	51	10	55	10
395.1	265.8	Diflufenican	34	11	33	10
304.3	147.1	Fenpropimorph	34	11.5	39	10
207.1	72.1	Isoproturon	1	10	21	6
226.1	121.0	Methiocarb	41	10.5	25	10
215.1	187.2	Metribuzin	29	10.5	25	10
282.1	212.2	Pendimethalin	17	7.5	15	10
307.9	162.0	Quinoxyfen	21	12	57	10
235.0	179.0	Terbuthylazine D5 (Surr)	76	10	25	10
221.1	179.1	Atrazine D5 (IS)	21	10	25	10
213.2	78.0	Isoproturon D6 (IS)	1	10	21	6
229.2	168.9	Methiocarb D3 (IS)	51	10	13	10
Method C						
213.1	72.0	Chlortoluron	34	11.5	33	10
250.1	169.0	Clothianidin	41	10	17	10
226.1	77.0	Cyprodinil	96	10	63	10
406.1	250.9	Difenoconazole	76	10	33	10
230.0	125.0	Dimethoate	14	10	29	10
327.2	205.1	Dimoxystrobin	41	10.	13	10
330.1	121.0	Epoxiconazole	39	11.	27	10
364.1	194.2	Flufenacet	11	10	17	10
256.1	175.0	Imidacloprid	86	10	23	10
360.2	244.0	Isopyrazam	56	10	31	10
320.1	70.1	Metconazole	31	10	59	10
411.1	182.1	Nicosulfuron	41	9	25	10
214.1	182.9	Omethoate	36	10	15	10

239.1	72.1	Pirimicarb	16	7	31	10
376.0	308.0	Prochloraz	31	10	15	10
342.1	69.1	Propiconazole	46	10.5	33	10
308.1	70.0	Tebuconazole	55	10	25	10
253.0	126.0	Thiacloprid	71	10	27	10
253.1	172.0	Clothianidin D3 (Surr)	42	10	19	10
412.1	250.9	Difenoconazole D6	41	9	37	10
317.2	70.0	Tebuconazole D9 (Surr)	81	10	61	10
226.0	126.0	Acetamiprid D3 (IS)	56	10	31	10
221.1	179.1	Atrazine D5 (IS)	21	10	25	10
295.0	70.0	Cyproconazole D3 (IS)	16	10	35	10
260.0	213.0	Imidacloprid D4 (IS)	86	10	23	10
213.2	78.0	Isoproturon D6 (IS)	71	10	10	10
147.9	97.0	Methamidiohos D6 (IS)	56	10	23	10
229.2	168.9	Methiocarb D3 (IS)	51	10	13	10
Method D						
332.2	314.0	Ciprofloxacin	101	10	29	20
360.3	316.2	Enrofloxacin	41	10	27	26
363.0	319.9	Marbofloxacin	106	10	21	16
279.3	186.0	Sulfamethazin	71	10	15	14
365.2	321.1	Enrofloxacin D5 (Surr)	41	10	27	26
221.1	179.1	Atrazine D5 (IS)	21	10	25	10
EPI (enhanced product ion spectra)						
Mass range			**DP**	**EP**	**CE**	
50 – 450 m/z			-	-	-30/+30 (± 15)	

Matrix matched standard: 0.01 - 50 pg/µl

Table SI-6: Configuration of GC-MS/MS.

GAS CHROMATOGRAPHY	**Trace GC Ultra (Thermo Scientific)**	
METHOD	**EI (electron impact ionisation)**	**NCI (negative ion chemical ionisation)**
Autosampler temperature	10 °C	
Injector type	Split/Splitless	
Injection volume	1 µL	
Injection technique	Splitless (0-3 min) wSurge (200 kPa, 1.5 min)	
Injector temperature	210 °C	
Analytical column	Phenomenex ZB-5-plus (0.25 µm, 30 m, 0.25 mm i.d.)	
Carrier gas	He 5.0 / 1.2 ml/min (const. flow)	
Column temperature	70°C (2') > 20°C/min > 320°C (3')	70°C (2') >10°C/min > 320°C (5')
MASS SPECTROMETER	**TSQ Quantum GC XLS (Thermo Scientific)**	
Reactant gas	-	Methane 5.5 / 3 ml/min
Source temperature	240°C	
Transfer line temperature	275 °C	
Collision gas	Argon 5.0 / 1.5 mTorr	
Scan type	Selected Reaction Monitoring	
Confirmation	Ion-ratio in a sample within ± 30% of the average of the standard from the same sequence	
Software	Xcalibur 3.1.66.10	
Quantification	relative peak area	

Table SI-7: GC-MS/MS - SRM-conditions (precursor (Q1) and product ions (Q3) in m/z and collision energy (CE)).

Q1	Q3	Analyte	CE
EI (electron impact ionisation)			
183	153	Permethrin	15
183	168		15
292	274	Chlorpyrifos-methyl D6 (Surr)	25
294	276		25
324	260	Chlorpyrifos D10 (IS)	15
326	262		12
NCI (negative ion chemical ionisation)			
205	121	lambda-Cyhalothrin	20
241	205		10
207	207	Cypermethrin	5
209	209		5
213	213	trans-Cypermethrin D6 (Surr)	5
215	215		5
211	126	Bifenthrin D6 (IS)	20
211	147		15

Matrix matched standard: 1 - 100 pg/µl

Table SI-8: Proportion of the five main land cover classes [%] within a buffer of 10 km of the location where an individual was found. All data were extracted from the Corine landcover data set 2018 using QuantumGIS software. **Species:** ACGE: *Accipiter gentilis* (n=48), ACNI: *Accipiter nisus* (n=23), HAAL: *Haliaeetus albicilla* (n=60), MIML: *Milvus milvus* (n=42), PAHA: *Pandion haliaetus* (n=13). n.d. = no data available.

Id	Species	Artificial surfaces [%]	Agriculture [%]	Forest and semi natural areas [%]	Water bodies [%]	Wetlands [%]
B102	ACGE	75.0	3.1	18.0	3.5	0.4
B103	ACGE	84.0	8.0	6.2	1.8	0.1
B109	ACGE	82.5	6.2	8.3	3.1	0.0
B167	ACGE	82.5	9.5	6.2	1.5	0.4
B169	ACGE	84.0	6.0	7.4	2.6	0.0
B170	ACGE	48.7	25.2	23.1	3.0	0.0
B171	ACGE	9.4	28.5	58.1	2.3	1.6
B172	ACGE	85.0	9.5	4.2	1.2	0.1
B173	ACGE	93.7	3.0	2.1	1.2	0.0
B178	ACGE	84.3	9.3	5.0	1.3	0.1
B181	ACGE	95.2	3.3	0.8	0.7	0.0
B183	ACGE	76.5	6.2	13.4	3.9	0.0
B186	ACGE	83.4	13.3	2.1	1.3	0.0
B188	ACGE	96.5	1.7	1.1	0.8	0.0
B191	ACGE	80.2	15.6	3.5	0.7	0.0
B193	ACGE	84.0	8.0	6.2	1.8	0.1
B194	ACGE	95.3	0.2	3.8	0.7	0.0
B197	ACGE	84.4	2.0	10.5	2.7	0.4
B198	ACGE	97.2	1.4	0.7	0.8	0.0
B200	ACGE	96.8	1.5	0.8	0.9	0.0
B206	ACGE	90.3	4.3	4.8	0.7	0.0
B207	ACGE	84.0	10.6	4.1	0.9	0.4
B208	ACGE	97.4	1.1	0.6	0.8	0.0
B38	ACGE	84.1	3.5	9.6	2.5	0.4
B49	ACGE	54.8	11.7	27	6.5	0.0

B55	ACGE	64.8	19.4	11.9	3.8	0.1
B62	ACGE	25.7	10.7	55.1	8.4	0.1
B68	ACGE	74.2	17.6	8.1	0.1	0.0
B79	ACGE	60.9	22	16	0.8	0.4
B80	ACGE	54.8	7.9	30.1	7.2	0.0
B81	ACGE	96.0	2.4	0.6	1.0	0.0
B82	ACGE	90.6	0.8	7.9	0.7	0.0
B83	ACGE	61.4	10.3	23.9	4.2	0.2
B97	ACGE	62.8	31.2	5.3	0.6	0.2
B98	ACGE	84.0	8.0	6.2	1.8	0.1
Bra152	ACGE	6.5	51.4	38.8	2.7	0.7
Bra328	ACGE	n.d.	n.d.	n.d.	n.d.	n.d.
Bra382	ACGE	23.1	58.4	17.6	0.8	0.1
BW T9587	ACGE	9.7	31.5	58.8	0.0	0.0
HAM009	ACGE	82.1	8.3	1.0	8.4	0.3
MV552	ACGE	n.d.	n.d.	n.d.	n.d.	n.d.
NRW68	ACGE	6.0	84.9	9.0	0.0	0.0
NS442	ACGE	16.4	67.8	15.5	0.4	0.0
NS495	ACGE	7.8	35.8	56.1	0.0	0.3
NS96	ACGE	11.7	61.3	26.3	0.6	0.0
NS97	ACGE	3.8	88.5	0.4	1.4	5.9
NS98	ACGE	3.8	88.5	0.4	1.4	5.9
RP004	ACGE	47.6	35.6	7.2	4.3	0.0
1590 Q	ACNI	n.d.	n.d.	n.d.	n.d.	n.d.
B100	ACNI	84.0	8.0	6.2	1.8	0.1
B101	ACNI	84.0	8.0	6.2	1.8	0.1
B104	ACNI	84.0	8.0	6.2	1.8	0.1
B157	ACNI	84.0	8.0	6.2	1.8	0.1
Bra213	ACNI	94.9	0.5	3.8	0.7	0.0

Bra216	ACNI	6.2	40.4	50.4	2.0	1.0
Bra75	ACNI	2.1	65	32	0.9	0.0
Bra89	ACNI	4.4	48.3	47.2	0.1	0.0
Bra98	ACNI	15.9	35	48.6	0.6	0.0
NS027	ACNI	17.6	56.2	25.5	0.2	0.5
NS21	ACNI	16.3	46.5	36.9	0.1	0.2
NS22	ACNI	3.1	66.8	30.1	0.0	0.0
NS26	ACNI	15.7	72.5	10.7	1.2	0.0
NS31	ACNI	11.3	51.9	35.7	0.1	1.0
NS33	ACNI	10.7	70.8	17.3	1.2	0.0
NS34	ACNI	19.4	66.2	13.6	0.8	0.0
NS340	ACNI	20.7	56.9	21.6	0.4	0.5
NS348	ACNI	17.8	62.2	19.6	0.4	0.0
NS359	ACNI	19.1	55.7	23.9	0.8	0.5
NS390	ACNI	21.3	64.6	13.8	0.3	0.0
SA05	ACNI	29.6	60.0	9.5	0.9	0.0
SA06	ACNI	28.7	62.2	8.6	0.5	0.0
MV145	HAAL	1.6	73.0	20.1	5.0	0.3
MV149	HAAL	1.7	70.8	15.7	8.3	3.5
MV150	HAAL	2.6	85.7	11.7	0.0	0.0
MV158	HAAL	3.4	48.4	12.5	34.6	1.1
MV159	HAAL	2.2	37.2	50.5	9.6	0.4
MV160	HAAL	5.4	42.5	6.2	43.7	2.2
MV165	HAAL	3.7	66.4	11.7	8.9	9.2
MV172	HAAL	4.6	30.1	56.2	8.5	0.6
MV173	HAAL	1.9	88.5	8.0	0.9	0.8
MV174	HAAL	4.6	40.3	33.4	19.1	2.7
MV181	HAAL	2.8	32.6	52.5	11.9	0.2
MV184	HAAL	10.1	55.3	11.9	22.7	0.1

MV189	HAAL	5.5	37.8	37.4	19.0	0.3
MV319	HAAL	2.3	47.2	37.6	11.4	1.5
MV324	HAAL	2.8	64.0	28.2	4.7	0.3
MV327	HAAL	2.2	82.6	13.4	1.8	0.0
MV333	HAAL	5.4	80.2	12.8	1.2	0.5
MV334	HAAL	3.0	73.8	21.2	1.1	0.9
MV343	HAAL	2.6	65.4	29.4	1.1	1.4
MV346	HAAL	4.0	19.6	10.6	64.1	1.8
MV399	HAAL	2.7	79.5	14.9	2.6	0.2
MV401	HAAL	1.1	70.3	23.3	4.3	1.0
MV460	HAAL	1.8	53.9	19.0	18	7.4
MV479	HAAL	4.5	78.8	15.5	0.4	0.9
MV488	HAAL	6.0	28.7	13.1	50.1	2.1
MV502	HAAL	2.0	75.8	17.0	4.8	0.3
MV503	HAAL	2.2	38.1	16.6	41.9	1.2
MV504	HAAL	2.0	52.1	11.0	33.9	1.0
MV505	HAAL	10.7	62.3	8.1	18.3	0.6
MV506	HAAL	1.0	50.2	17.9	25.1	5.8
MV516	HAAL	3.9	70.3	20.2	5.2	0.5
MV523	HAAL	2.2	61.1	30.9	5.4	0.5
MV524	HAAL	3.5	86.7	9.6	0.0	0.3
NS41	HAAL	2.9	61.0	33.0	2.9	0.2
NS42	HAAL	3.3	67.8	2.2	14.3	12.4
S10	HAAL	8.9	20.5	66.5	3.8	0.2
S12	HAAL	4.5	29.2	64.7	1.4	0.3
S14	HAAL	9.6	28.2	51.1	9.5	1.6
S15	HAAL	19.3	47.8	30.7	2.2	0.0
S23	HAAL	6.8	44.0	45.4	2.7	1.0
S24	HAAL	3.2	21.5	72.8	2.2	0.3

S25	HAAL	22.1	12.8	61.6	3.3	0.2
S27	HAAL	9.9	35.6	41.6	11.3	1.6
S31	HAAL	11.0	67.8	18.1	3.1	0.0
S56	HAAL	3.3	58.5	34.0	4.0	0.3
S58	HAAL	5.8	42.2	47.1	4.9	0.0
S61	HAAL	6.1	58.6	33.5	1.8	0.0
S63	HAAL	3.5	26.9	64.5	2.0	0.5
S71	HAAL	5.4	50.5	36.8	7.2	0.1
SH134	HAAL	9.6	81.1	7.8	0.3	1.2
SH135	HAAL	4.1	72.3	20.2	3.3	0.0
SH143	HAAL	6.4	85.3	6.8	1.0	0.5
SH150	HAAL	3.6	77.1	15.4	3.2	0.7
SH151	HAAL	5.4	67.4	21.1	6.1	0.0
SH37	HAAL	2.9	85.4	4.3	6.9	0.5
SH57	HAAL	4.7	58.5	35.5	1.3	0.0
SH58	HAAL	7.1	57.1	28.8	7.0	0.0
SH60	HAAL	6.4	76.8	12.5	4.3	0.0
SH62	HAAL	2.4	42.7	2.7	49.4	0.0
SH63	HAAL	7.2	57.3	28.8	6.7	0.0
B150	MIML	84.0	8.0	6.2	1.8	0.1
Bra138	MIML	8.2	65.4	26.4	0.0	0.0
Bra305	MIML	3.0	20.5	67.6	9.0	0.0
Bra320	MIML	5.4	61.2	33.2	0.2	0.0
Bra321	MIML	8.4	64.8	25.4	1.4	0.0
Bra333	MIML	15.0	63.5	20.5	0.5	0.4
Bra334	MIML	4.5	58.6	35.3	1.4	0.1
Bra376	MIML	2.8	85.9	10.7	0.7	0.0
Bra391	MIML	1.3	46.0	51.1	1.5	0.2
BW10187	MIML	10.4	47.0	42.6	0.0	0.0

BW10225	MIML	14.2	51.0	22.7	2.7	0.7
MV27	MIML	5.2	39.5	36.3	18.7	0.3
MV29	MIML	1.5	70.0	17.3	3.6	7.5
MV307	MIML	4.2	60.1	35.5	0.0	0.1
MV35	MIML	3.6	76.3	15.2	0.3	4.5
MV467	MIML	n.d.	n.d.	n.d.	n.d.	n.d.
MV493	MIML	1.2	85.8	12.2	0.4	0.5
MV573	MIML	6.4	77.9	9.9	5.5	0.4
NRW26	MIML	20.6	68.9	10.5	0.0	0.0
NRW42	MIML	9.4	65.8	24.2	0.5	0.0
NRW48	MIML	5.1	53.8	41.2	0.0	0.0
NRW63	MIML	n.d.	n.d.	n.d.	n.d.	n.d.
NRW76	MIML	31.7	44.2	23.4	0.6	0.0
NS13	MIML	4.6	68.5	23.9	2.9	0.2
NS56	MIML	3.9	69.5	24.4	2.0	0.2
NS57	MIML	3.7	72.1	21.6	2.3	0.3
NS66	MIML	3.7	29.5	66.9	0.0	0.0
NS72	MIML	7.7	67.9	24.1	0.2	0.0
NS73	MIML	4.7	60.5	34.8	0.0	0.0
S70	MIML	9.3	71.8	18.8	0.0	0.0
SA040	MIML	11.3	45.6	43.0	0.0	0.0
SA045	MIML	7.0	89.0	3.3	0.7	0.0
SA046	MIML	8.7	88.0	2.6	0.7	0.0
SA048	MIML	10.0	83.8	5.7	0.4	0.0
SA049	MIML	8.4	79.0	12.1	0.5	0.0
SA050	MIML	8.5	81.3	9.6	0.6	0.0
SA051	MIML	23.2	61.4	11.7	3.2	0.6
SA1	MIML	5.8	85.2	7.0	2.1	0.0
SA2	MIML	5.8	85.2	7.0	2.1	0.0

SA4	MIML	5.8	85.2	7.0	2.1	0.0
SH55	MIML	1.5	39.0	2.7	56.6	0.2
SH77	MIML	3.5	63.7	24.2	8.7	0.0
Bra307	PAHA	30.8	39.8	25.1	4.2	0.0
MV168	PAHA	2.1	69.8	21.4	6.7	0.0
MV176	PAHA	n.d.	n.d.	n.d.	n.d.	n.d.
MV178	PAHA	2.1	69.8	21.4	6.7	0.0
MV191	PAHA	2.4	61.3	21.9	13.3	1.0
MV192	PAHA	5.8	58.6	35.7	0.0	0.0
MV484	PAHA	2.1	59.9	33.7	4.0	0.3
MV551	PAHA	3.4	60.1	33.3	2.9	0.3
MV559	PAHA	6.3	65	25.8	2.6	0.3
MV563	PAHA	n.d.	n.d.	n.d.	n.d.	n.d.
MV566	PAHA	3.7	68.2	23.4	4.3	0.4
NRW37	PAHA	8.4	29.6	58.6	3.4	0.0
NS78	PAHA	4.4	77.8	15.5	0.3	2.0

Table SI-9: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} wet wt and detection rate (%) of investigated anticoagulant rodenticides in livers from five species of birds of prey from Germany. ACGE: *Accipiter gentilis*; MIML: *Milvus milvus*; HAAL: *Haliaeetus albicilla*; ACNI: *Accipiter nisus*; PAHA: *Pandion haliaetus*; n.d. = not detected. One MIML (Bra305; brodifacoum: 4853.47 ng g^{-1}; difenacoum: 69.41 ng g^{-1}) was excluded due to deliberate poisoning.

	ACGE n=48	**MIML** n=41	**HAAL** n=60	**ACNI** n=23	**PAHA** n=13	**Overall** n=185
Brodifacoum	34.9 (17.07-106.92)	37.38 (22.69-71.84)	5.85 (4.67-14.89)	n.d.	n.d.	26.22 (12.87-75.3)
Detection rate [%]	60.42	46.34	18.33	0	0	31.89
Bromadiolone	15.01 (8.44-37.31)	42.88 (30.98-56.24)	9.28 (6.54-9.7)	10.71 (7.52-40.81)	n.d	20.85 (9.8-44.05)
Detection rate [%]	37.5	29.27	5.0	13.04	0	19.46
Chlorophacinone	n.d	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Coumatetralyl	5.37 (1.27-9.91)	n.d.	n.d.	n.d.	n.d	5.37 (1.27-9.91)
Detection rate [%]	16.67	0	0	0	0	4.32
Difenacoum	37.03 (16.32-83.11)	18.35 (10.88-57.34)	18.04 (5.41-28.49)	n.d.	n.d	27.94 (7.64-61.19)
Detection rate [%]	66.67	46.34	21.67	0	0	34.59
Difethialone	25.73 (10.8-119.31)	20.99 (10.39-37.17)	8.03 (7.58-8.47)	n.d.	n.d	18.49 (8.47-39.19)
Detection rate [%]	16.67	19.51	3.33	0	0	9.73

Flocoumafen	10.87 (8.08-13.66)	59.44 (31.2-87.69)	n.d.	n.d.	n.d	10.87 (4.71-41.32)
Detection rate [%]	4.17	4.88	0	0	0	2.16
Warfarin	n.d.	n.d.	n.d.	n.d.	n.d	n.d.
Detection rate [%]	0	0	0	0	0	0

Table SI-10: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} wet wt and detection rate (%) of investigated medicinal products in livers from five species of birds of prey from Germany. Analysis only comprises individuals that were found dead to exclude potential deliberate treatments prior to death. ACGE: *Accipiter gentilis*, MIML: *Milvus milvus*; HAAL: *Haliaeetus albicilla*; ACNI: *Accipiter nisus*; PAHA: *Pandion haliaetus*. n.d. = not detected.

	ACGE n=15	**MIML** n=19	**HAAL** n=42	**ACNI** n=3	**PAHA** n=8	**Overall** n=87
Ciprofloxacin	n.d.	135.34 (n=1)	257.3 (n=1)	n.d.	n.d.	196.32 (165.83-226.81)
Detection rate [%]	0	5.26	2.38	0	0	2.3
Diclofenac	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Enrofloxacin	21.12 (n=1)	1655.35 (n=1)	n.d.	n.d.	n.d.	838.24 (429.68-1246.79)
Detection rate [%]	6.67	5.26	0	0	0	2.3
Ibuprofen	18.55 (16.69-20.42)	55.45 (n=1)	33.6 (21.53-74.59)	n.d.	n.d.	30.49 (21.15-74.57)
Detection rate [%]	13.33	5.26	23.81	0	0	14.94
Marbofloxacin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Permethrin	35.0 (n=1)	n.d.	n.d.	n.d.	n.d.	35.0 (n=1)
Detection rate [%]	6.67	0	0	0	0	1.15
Sulfamethazin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0

Table SI-11: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} wet wt and detection rate (%) of investigated plant protection products in livers from five species of birds of prey from Germany. ACGE: *Accipiter gentilis*, MIML: *Milvus milvus*; HAAL: *Haliaeetus albicilla*; ACNI: *Accipiter nisus*; PAHA: *Pandion haliaetus*. n.d. = not detected.

	ACGE n=48	**MIML** n=42	**HAAL** n=60	**ACNI** n=23	**PAHA** n=13	**Overall** n=186
Aclonifen	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Chlorpyrifos	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Chlortoluron	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Clothianidin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Cypermethrin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Cyprodinil	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Difenoconazole	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Diflufenican	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0

Dimethoate	n.d.	21042.21 (15701.05-26383.38)	n.d.	n.d.	n.d.	21042.21 (15701.05-26383.38)
Detection rate [%]	0	4.76	0	0	0	1.08
Dimoxystrobin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Epoxiconazole	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Fenpropimorph	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Fludioxonil	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Flufenacet	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Imidacloprid	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Isoproturon	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Isopyrazam	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
L-Cyhalothrin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

Detection rate [%]	0	0	0	0	0	0
Metconazole	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Methiocarb	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Metribuzin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Nicosulfuron	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Omethoate	n.d.	4077.85 (2252.92-5902.78)	n.d.	n.d.	n.d.	4077.85 (2252.92-5902.78)
Detection rate [%]	0	4.76	0	0	0	1.08
Pendimethalin	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Pirimicarb	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Prochloraz	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Propiconazole	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0

Quinoxyfen	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Tebuconazol	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Detection rate [%]	0	0	0	0	0	0
Thiacloprid	n.d.	99.95 (76.74-123.17)	n.d.	n.d.	n.d.	99.95 (76.74-123.17)
Detection rate [%]	0	4.76	0	0	0	1.08

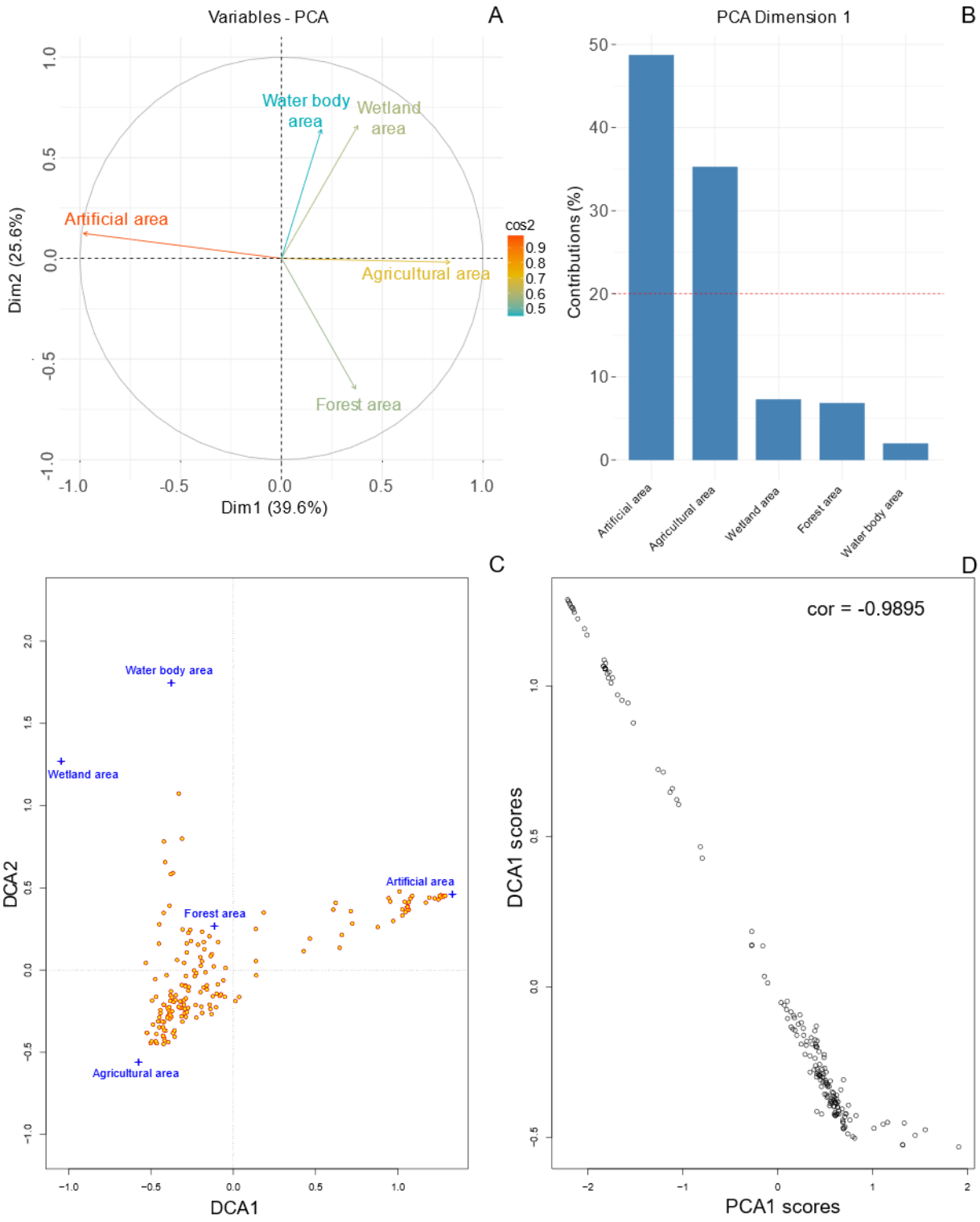

Figure SI-1: Principal component analysis (PCA) (A) and contribution of land cover classes to the first dimension (B). The red horizontal dashed represents the expected contribution of each variable if they all contributed equally. Detrended correspondence analysis (DCA) (C) and correlation between PCA1 and DCA1 scores (D). Both PCA and DCA analysis were based on quantification of land cover classes around a 10 km radius where an individual was found.

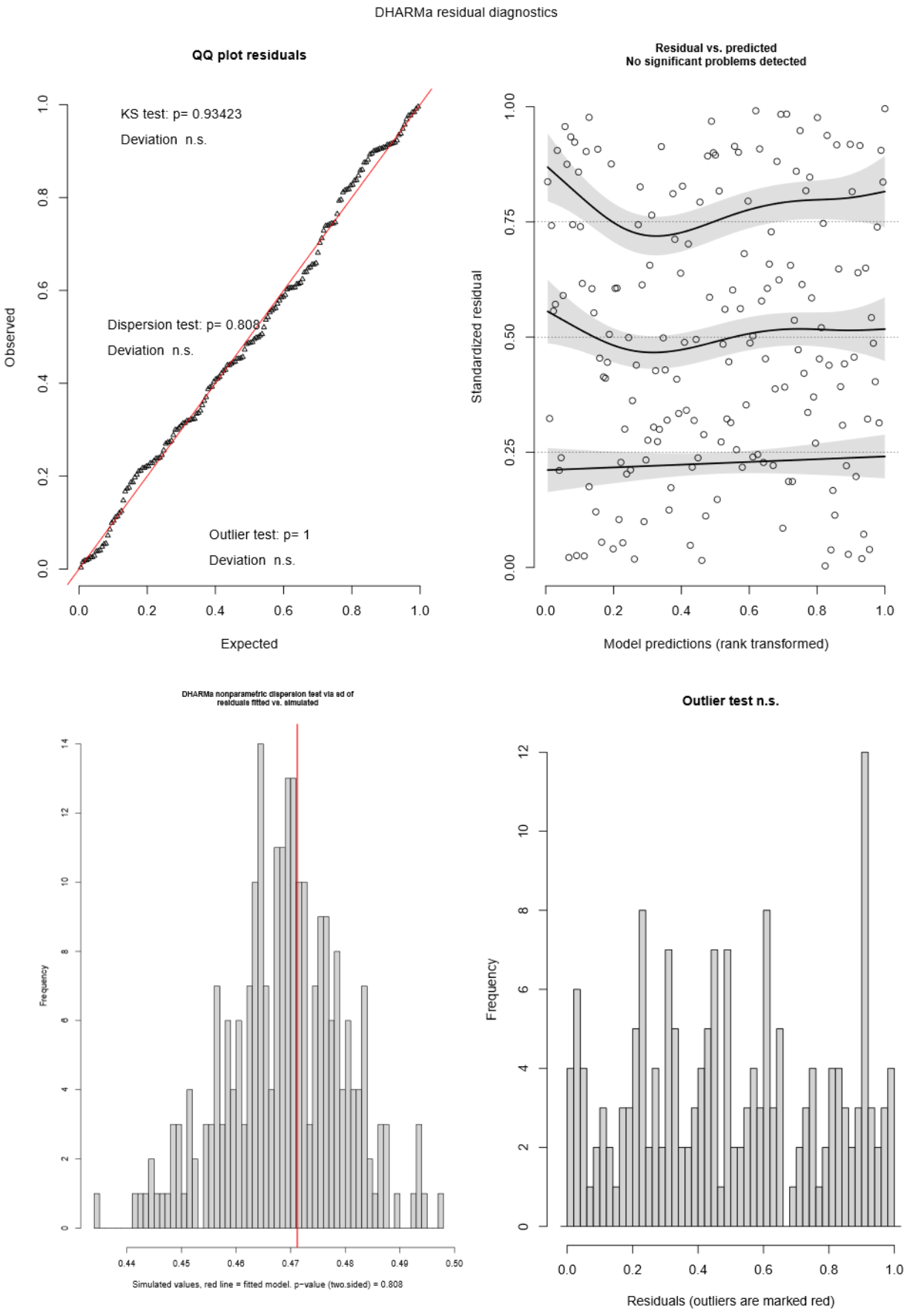

Figure SI-2: Verification of model assumptions for binomial GLM (logit link) on anticoagulant rodenticides (n=176). Number of simulations = 250.

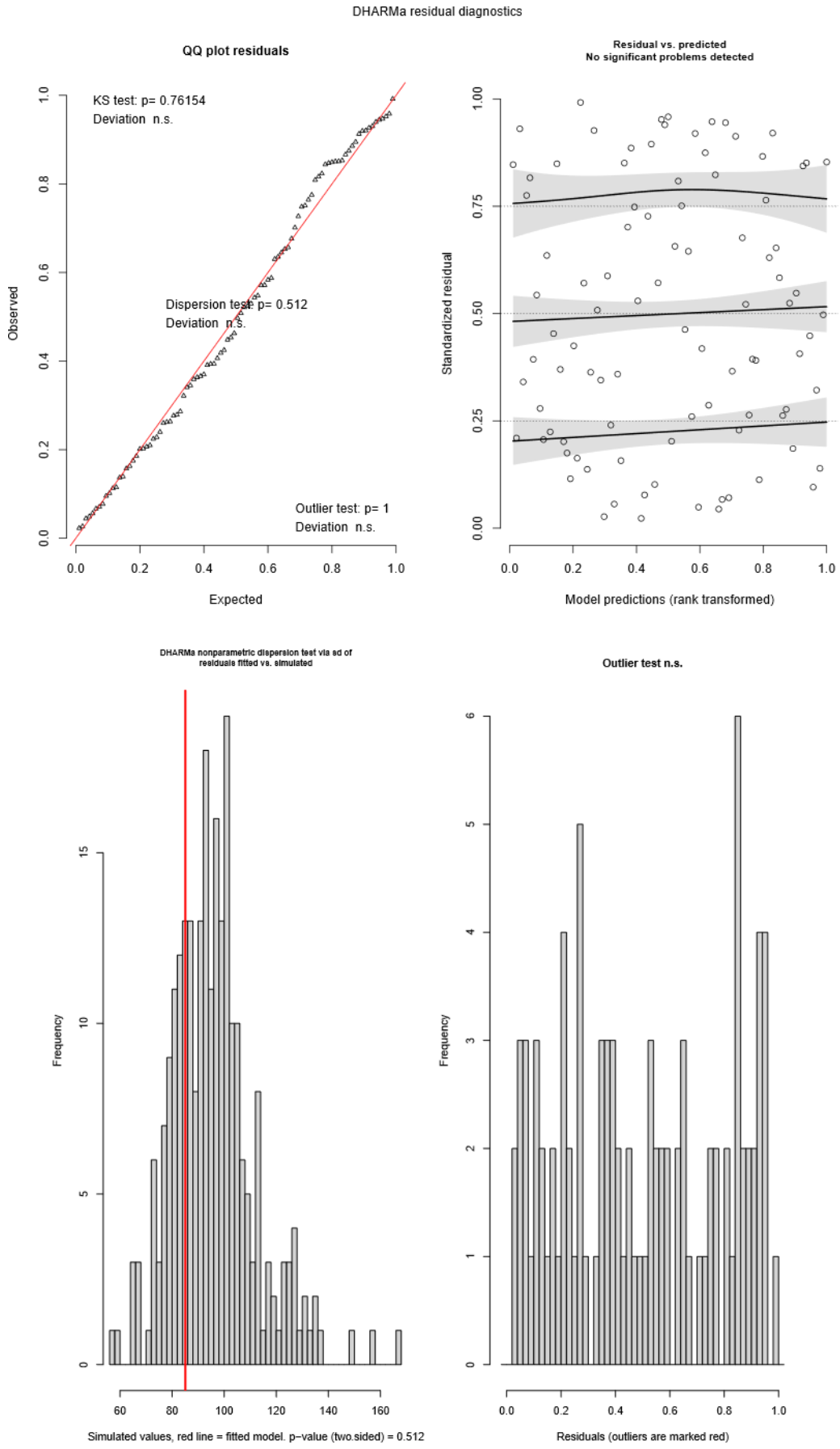

Figure SI-3: Verification of model assumptions for gamma GLM (log link) on anticoagulant rodenticides (n=94). Number of simulations = 250.

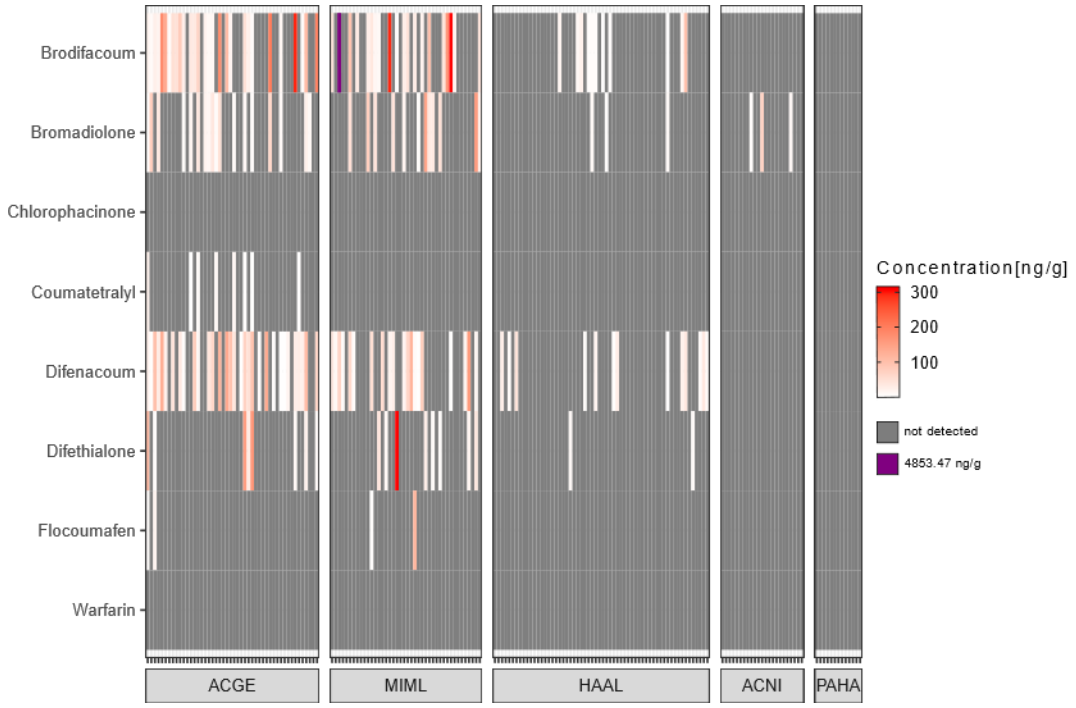

Figure SI-4: Heat map of anticoagulant rodenticides concentrations among individuals. ACGE: *Accipiter gentilis* (ACGE = 48); MIML: *Milvus milvus* (n=42); HAAL: *Haliaeetus albicilla* (n=60); ACNI: *Accipiter nisus* (n=23); PAHA: *Pandion haliaetus* (n=13). Not detected = concentration below reporting limit (Table SI-2).

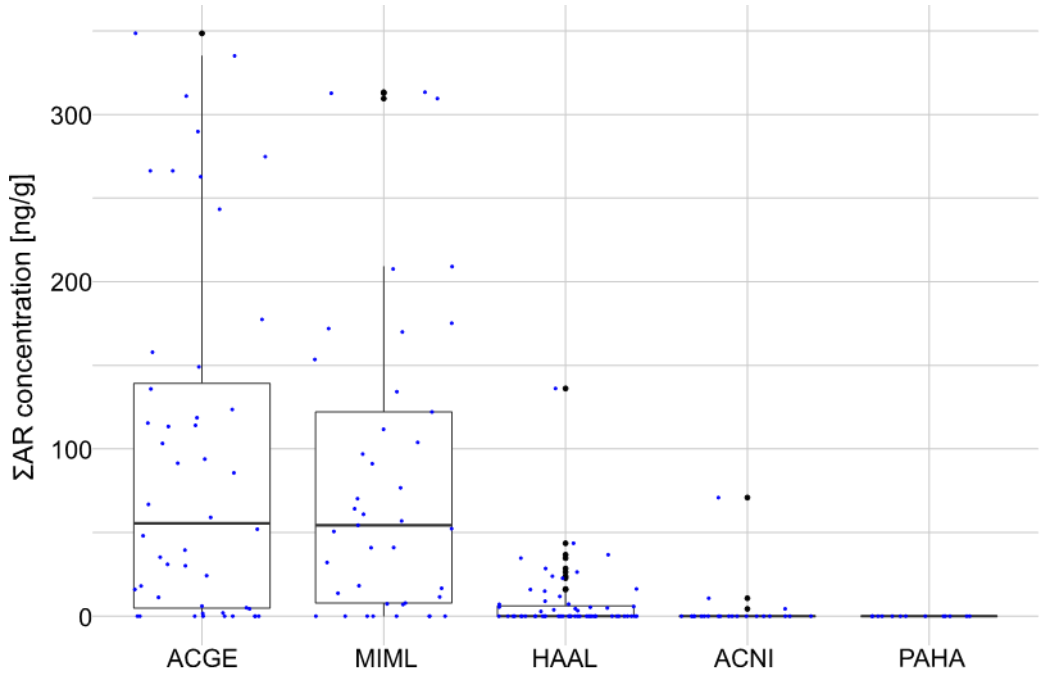

Figure SI-5: Box plots of ΣAR concentration among the different species. The lower and upper hinges of the box correspond to the 25th and 75th percentile. The upper whisker extends from the hinge to the largest value no further than 1.5*IQR from the hinge. The lower whisker extends from the hinge to the smallest value at most 1.5*IQR of the hinge. Data points beyond are plotted individually by black dots. Raw data points are given by blue dots. ACGE: *Accipiter gentilis*, MIML: *Milvus milvus*; HAAL: *Haliaeetus albicilla*; ACNI: *Accipiter nisus*; PAHA: *Pandion haliaetus*. One MIML (Bra305; brodifacoum: 4853.47 ng g^{-1}; difenacoum: 69.41 ng g^{-1}) was excluded due to deliberate poisoning.

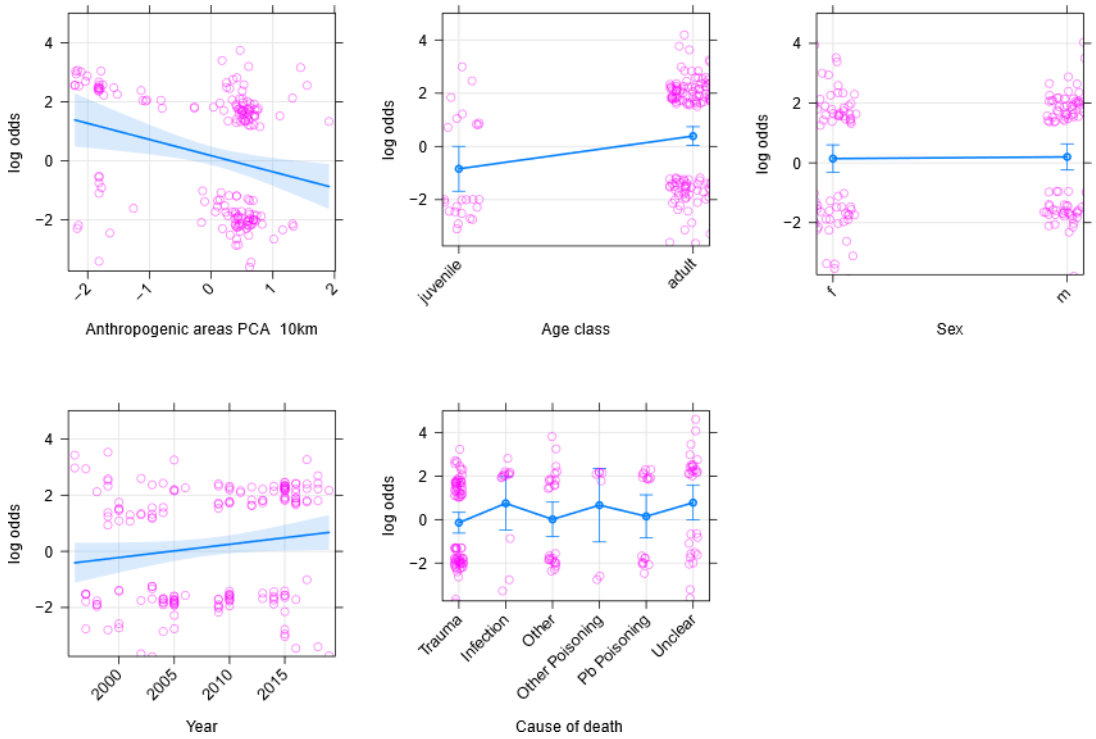

Figure SI-6: Predictor effect plot with partial residuals (magenta dots) for the binomial model with 95% confidence intervals and error bars. The fitted blue lines represent the partial regression line. A predictor effect plot summarizes the role of a focal predictor when the other numerical predictors are held constant at their median. For factorial predictors, a weighted average of within-level fitted values, with weights proportional to the number of observations at each level of the factor were used.

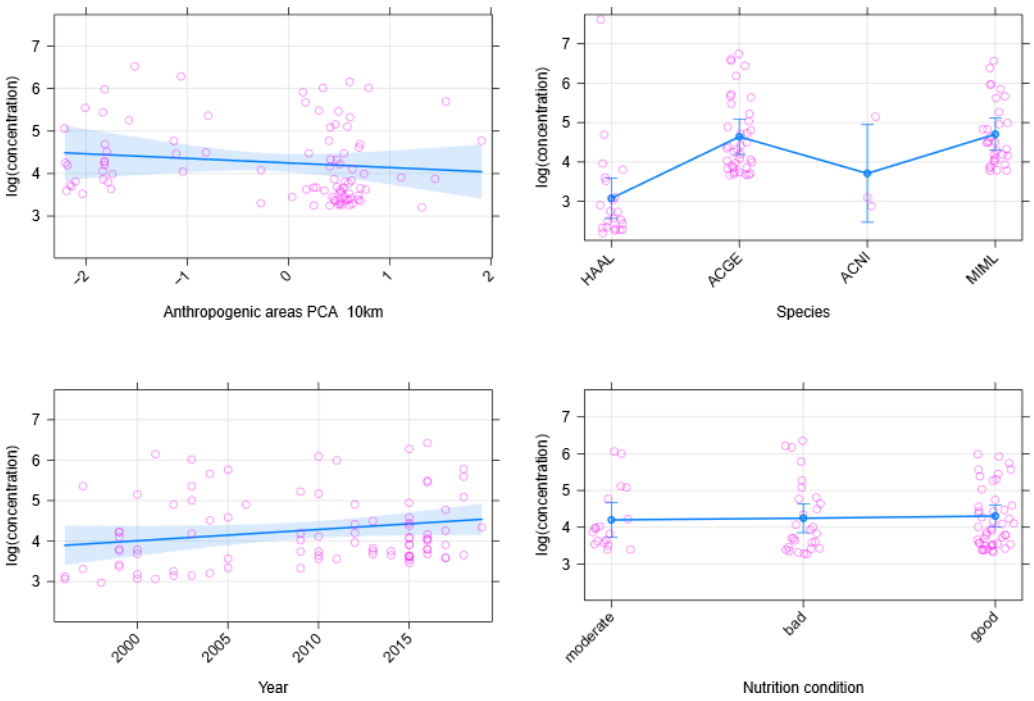

Figure SI-7: Predictor effect plot with partial residuals (magenta dots) for the gamma model with 95% confidence intervals and error bars. The fitted blue lines represent the partial regression line. A predictor effect plot summarizes the role of a focal predictor when the other numerical predictors are held constant at their median. For factorial predictors, a weighted average of within-level fitted values, with weights proportional to the number of observations at each level of the factor were used.

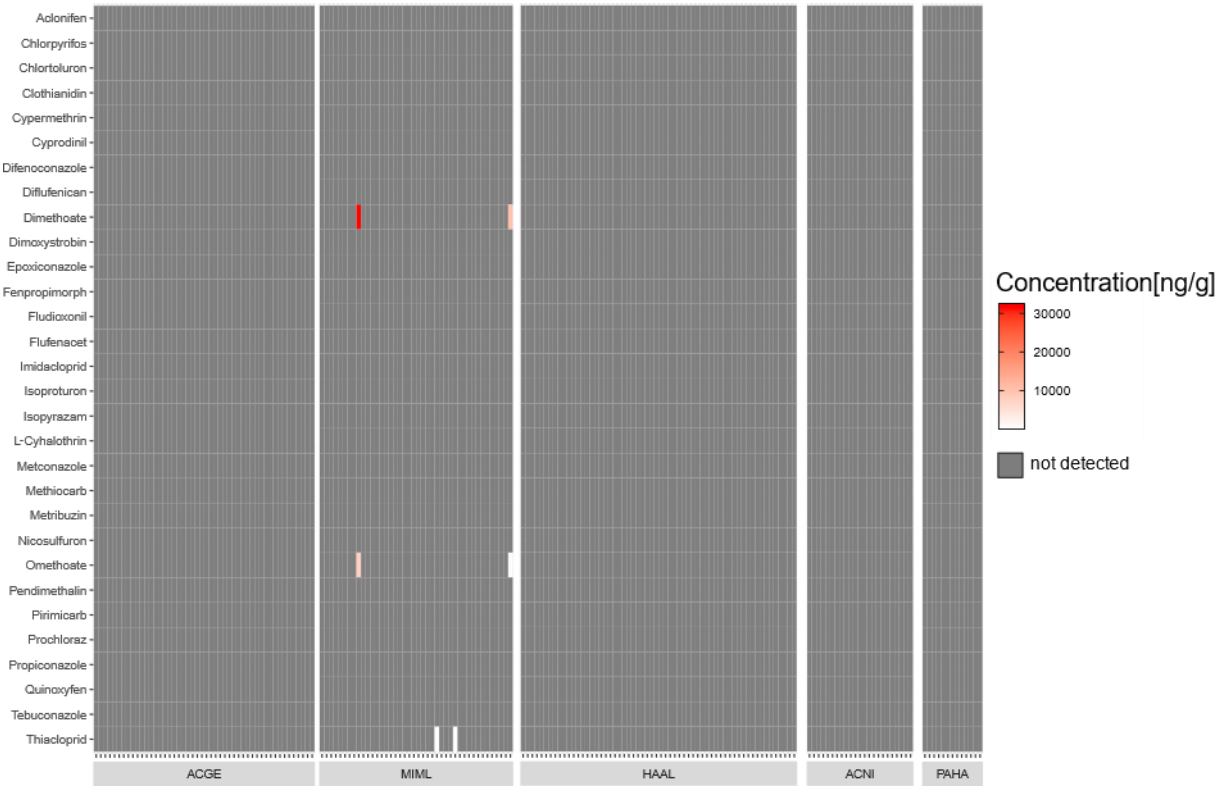

Figure SI-8: Heat map of plant protection products among individuals. ACGE: *Accipiter gentilis* (ACGE = 48); MIML: *Milvus milvus* (n=42); HAAL: *Haliaeetus albicilla* (n=60); ACNI: *Accipiter nisus* (n=23); PAHA: *Pandion haliaetus* (n=13). Not detected = concentration below reporting limit (Table SI-2).

9.3 Supplementary information – Chapter 4

Ecological and spatial variations of legacy and emerging contaminants in white-tailed sea eagles from Germany: Implications for prioritisation and future risk management

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1. Methods

1.1 Extraction of LC-amenable contaminants

ASE was used for the extraction of contaminants from HAAL livers, followed by a clean-up step using in-house mixed-mode SPE cartridges. Individual steps of the sample preparation protocol are presented in Figure SI-1 and described as follows: 0.2g of lyophilised liver was weighed and mixed with 0.8g of samples' dispersant Sodium Sulfate (Na_2SO_4). Then, a mix of isotopically labelled internal standards was spiked in each sample and left in contact with the matrix for at least 30 min prior to the extraction. Representative compounds from different classes of the LC target list were selected. After spiking, the samples were placed in extraction cells (Figure SI-2) and the analytes were extracted by ASE (Dionex™ ASE™ 350, Thermo Fisher Scientific) using the conditions given in Table SI-2. After ASE, the extracts were filtered through filter paper and pre-concentrated using a rotary evaporator (at 40°C) until reaching a final volume of 3-4 mL. Milli-Q water was added to adjust the final volume to 15 mL and 5 mL of n-hexane was added as a defatting step. After vortex stirring, the hexane layer was discarded, and 50 mL water was adjusted for the final volume. The samples were then cleaned up by solid-phase extraction (SPE). Layered 'mixed bed' cartridges (depicted in Figure SI-3) consisted of Oasis HLB (200 mg) and a mixture of Strata-X-AW (weak anion exchanger), Strata-X-CW (weak cation exchanger) and Isolute ENV+ (300 mg of the total mixture). Conditioning of the cartridges was performed with 3 mL of methanol and 3 mL of Milli-Q water. After conditioning, the samples were loaded in the SPE cartridges. The cartridges were dried and the elution of analytes from the adsorbent material was performed by a basic solution (6 mL of ethylacetate/methanol (50/50 v/v) containing 2% ammonia hydroxide (v/v)), followed by an acidic solution (4 mL of ethylacetate/methanol (50/50, v/v) containing 1.7% formic acid (v/v)). The extract was evaporated using a nitrogen stream at 40-45°C till dryness and 250 µL of methanol (LC-MS grade)/ Milli-Q water (50/50 v/v) were used for the final reconstitution of the extract. During the sample preparation, the 4-fold sample enrichment was achieved. The final extract was filtered through Regenerated Cellulose (RC) filter (Chromafil - pore size: 0,2 µm; filter diameter: 15 mm) into a 2 mL glass vial for RPLC-ESI-QToF MS analysis.

1.2 Extraction of GC-amenable contaminants

Individual steps of the sample preparation for the determination of GC-amenable compounds are presented in Figure SI-4 and described as follows. After weighting and adding isotopic labelled internal standards (similar to the procedure for LC), the analytes were extracted by ASE using the conditions giving in Table SI-2. After ASE, 50 µL of isooctane were added as keeper and the extract was pre-concentrated by rotary evaporation (max. temp. 30°C) until 10 mL. The samples were then cleaned up by SPE. Strata® FL-PR Florisil ((170 µm, 80 Å), 5 g/ 20 mL, Giga Tubes, Phenomenex) cartridges. The conditioning of the cartridges was performed using 20 mL of 10% Isopropanol in dichloromethane followed by 30 mL of hexane. Then, the samples were loaded in the SPE cartridges and the eluent was collected. The elution of the analytes from the adsorbent material was performed using 20 mL of dichloromethane: hexane (50/50 v/v), followed by 20 mL of hexane. The extract was placed into an evaporation flask. 50 µL of isooctane were added and the extract was pre-concentrated 50 µL of hexane. During the sample preparation, 4-fold enrichment of the extracts was achieved. The final extract was filtered through the Regenerated Cellulose (RC) filter (Chromafil - pore size: 0,2 µm; filter diameter: 15 mm) into a 2 mL glass vial for GC-APCI-QToF MS analysis.

1.3 Quantification in wide-scope target screening

The equation used for the calculation of the concentration is presented below:

$$\text{Concentration (ng g}^{-1}\text{ ww)} = \frac{Relative\ Peak\ Area_{sample} - b}{a} * \frac{100 - \%\ water\ content}{100}$$

where b refers to the intercept and a refers to the slope of the spiked calibration curve. The relative peak area is calculated by diving the analyte chromatographic peak area with the Internal Standard (IS) chromatographic peak area.

The SDL is calculated from spiked samples; specifically, the lowest concentration level for which the identification of the 95% of the analytes, included in the target list, is reliable (Gago-Ferrero et al., 2020). The experiment was performed using dry matrix (liver) and the SDL was calculated to be 6.25 ng g^{-1} dw. Since the results were expressed in wet weight, a water content of 70.7% was considered (mean value of the tested samples) and the method SDL was provided as 1.83 ng g^{-1} ww.

2. Discussion

2.1 Wide-scope target screening vs. multi-target analysis

Seven individuals were previously analysed by a multi-target method by Badry et al. (2021) for a subset of the 2441 target compounds analysed in this study (Table SI-15). For six individuals, brodifacoum exposure was previously reported at concentrations ranging from 4.46 ng g^{-1} to 99.75 ng g^{-1} ww (Table SI-16), whereas the current study detected residues only in the individual with previously reported highest residues. This is expected to be related to different sensitivities for SGAR of both methods, which is indicated by the different LOQs (2 ng g^{-1} vs. 8.85 ng g^{-1}). The analysis of anticoagulant rodenticide may therefore require compound-specific extraction and analysis protocols. The other detected overlapping compound between both studies was ibuprofen in SH150 (Table SI-16). However, whereas the previous analysis detected the parent compound (30.49 ng g^{-1} ww; Badry et al. (2021) without considering the metabolite, the current study only detected the metabolite 2-hydroxy-ibuprofen (8.87 ng g^{-1} (LOQ/2); this study) but not ibuprofen (<SDL 1.83 ng g^{-1} ww). Taken together, the comparison shows that both methods show consistent results for the majority of the overlapping compounds (< LOD), whereas for some compound classes specific extraction and analysis protocols may be necessary.

3 Supplementary tables (SI 1-16)

Table SI-1: Metadata and necropsy results of the investigated white-tailed sea eagles (HAALs). **Id**: Letters indicate the federal state followed by continuous enumeration: MV = Mecklenburg-Western Pomerania, NS: Lower Saxony, SH: Schleswig-Holstein. **Sex:** m = male, f = female. Except MV542, all individuals were found dead.

Id	Liver water content [%]	Age class	Sex	Year (found)	Latitude	Longitude	Nutrition condition
MV479	72.40	adult	m	2015	54.0	12.4	good
MV488	72.23	adult	f	2015	54.1	13.8	moderate
MV503	69.66	adult	m	2015	54.0	14.0	good
MV522	70.04	immature	f	2015	53.4	10.9	moderate
MV524	69.78	adult	m	2015	53.7	13.2	good
MV527	68.63	immature	m	2016	53.8	11.8	good
MV530	72.69	immature	m	2015	53.2	11.8	good
MV533	71.30	adult	f	2016	53.5	13.1	moderate
MV535	71.57	adult	f	2015	53.9	13.8	good
MV536	68.36	(sub-)adult	m	2016	53.6	12.5	good
MV542	68.00	adult	m	2016	53.8	11.6	moderate
MV543	70.28	adult	f	2016	53.6	12.4	good
MV545	73.15	adult	f	2016	53.8	13.8	good
MV549	73.22	adult	m	2016	53.5	11.6	moderate
MV564	72.60	adult	m	2016	53.8	12.7	moderate
MV571	68.74	adult	f	2016	53.7	13.1	good

MV580	71.44	adult	f	2017	53.9	13.9	good
MV586	67.46	adult	m	2017	53.5	13.8	good
NS101	69.54	adult	m	2018	53.4	7.1	good
NS102	68.33	adult	f	2018	53.3	10.9	moderate
NS89	71.63	adult	m	2016	53.8	9.1	good
NS90	71.12	immature	m	2016	52.8	9.6	good
NS93	70.65	adult	f	2017	53.0	11.5	good
SH135	67.23	adult	f	2015	54.2	10.7	good
SH145	71.91	immature	f	2015	54.5	8.6	bad
SH149	73.15	adult	f	2016	54.4	9.9	moderate
SH150	71.22	adult	f	2015	54.2	10.8	bad
SH151	71.86	adult	f	2015	54.2	10.6	good
SH154	68.30	immature	f	2016	54.3	10.4	good
SH157	74.11	adult	m	2016	53.6	10.8	bad

Table SI-2: Accelerated Solvent Extraction (ASE) conditions for LC and GC-amenable compounds.

Time (min)	LC	GC
Temperature (°C)	50	100
Pressure (psi)	1500	1500
Heating Time (s)	300	300
Static Time (s)	420	300
Number of Static Cycles	3	3
Flush Volume [%]	60	60
Purge Time (s)	180	180
Extraction Solvent ratio	Methanol: Acetonitrile (2:1)	Hexane: Dichloromethane (2:1)
Total volume of extraction solvents (mL)	60	70

Table SI-3: Reversed phase-LC gradient elution programme. In positive ionization mode, the aqueous solvent consisted of H_2O/Methanol 90/10 (v/v), 5 mM HCOONH4, 0.01% formic acid and the organic solvent of methanol, 5 mM $HCOONH_4$, 0.01% formic acid. In negative ionization mode, the aqueous solvent consisted of H_2O/Methanol 90/10 v/v, 5 mM CH3COONH4 and the organic solvent of methanol, 5 mM CH_3COONH_4.

Time [min]	Flow rate [mL min^{-1}]	Aqueous solvent [%]	Organic solvent [%]
0	0.2	99.0	1.0
1	0.2	99.0	1.0
3	0.2	61.0	39.0
14	0.4	0.1	99.9
16	0.48	0.1	99.9
16.1	0.48	99.0	1.0
19.1	0.2	99.0	1.0
20.0	0.2	99.0	1.0

Table SI-4: Wide-scope target screening validation **(REC** (Recovery + relative standard deviation (**RSD**). **LOD** (Limit of detection)). **LOQ** (Limit of quantification). LOD and LOQ are given in dry weight (dw) and wet weight (ww). HMP: human medicinal product; VMP: veterinary medicinal product, TPs: transformation products.

Analyte	Intended (former) use	LOD	LOQ	LOD	LOQ	REC	RSD
Stockholm Convention*		ng/g dw		ng/g ww		%	
PCB 28	Industrial	0.41	1.22	0.12	0.36	76.5	8.56
PCB 52	Industrial	1.17	3.50	0.34	1.03	85.9	5.95
PCB 101	Industrial	2.08	6.23	0.61	1.83	82.1	6.79
PCB 138	Industrial	2.93	8.79	0.86	2.58	81.4	10.0
PCB 153	Industrial	2.46	7.38	0.72	2.16	80.9	9.60
PCB 180	Industrial	7.20	21.60	2.11	6.33	114	13.6
PCB 209	Industrial	4.01	12.00	1.18	3.52	75.2	12.5
DDD	Insecticide	0.55	1.65	0.16	0.48	56.3	15.7
DDE	Insecticide	0.61	1.83	0.18	0.54	112	9.78
β-HCH	Industrial	3.10	9.31	0.91	2.73	68.1	15.4
cis-Chlordane	Insecticide	0.66	1.97	0.19	0.58	71.2	13.1
trans-Chlordane	Insecticide	1.64	4.92	0.48	1.44	70.7	12.2
Dicofol	Miticide	0.37	1.12	0.11	0.33	78.1	7.89
4,4´-Dichlorobenzophenone	Metabolite (dicofol)	0.41	1.23	0.12	0.36	66.7	6.00
Pentachlorobenzene	Industrial	0.54	1.63	0.16	0.48	111	8.78
Hexachlorobenzene	Fungicide	0.29	0.86	0.08	0.25	91.3	13.5
Heptachlor expoxide	Insecticide (metabolite)	0.78	2.35	0.23	0.69	95.2	5.15
Industrial chemicals regulated under REACH**							
2-OH-benzothiazole	Industrial	21.80	65.40	6.39	19.17	87.5	9.46
Benzenesulfonamide	Industrial	24.30	72.90	7.12	21.37	69.5	4.06
Didecyldimethylammonium (DADMAC (C10:C10))	Industrial	19.1	57.3	5.60	16.8	69.2	9.68
Galaxolide	Synthetic musk (personal care product)	10.8	32.5	3.17	9.53	79.4	5.95
Lauric isopropanolamide	Surfactant	3.64	10.9	1.07	3.20	62.2	21.6
Methylparaben	Various	3.40	10.2	0.997	2.99	86.6	7.47
Phenanthrene	Synthesis of dyes	1.87	5.60	0.548	1.64	119	13.1
Tributylamine	Industrial	6.15	18.50	1.80	5.42	33.1	22.9
PFAS – PFSAs**							

PFHxS	Industrial	0.12	0.35	0.03	0.10	118	6.61
PFHpS	Industrial	0.49	1.45	0.14	0.43	99.4	8.80
PFOS (branched)	Industrial	1.68	5.05	0.49	1.48	95.1	7.89
PFOS (linear)	Industrial	3.12	9.37	0.91	2.75	94.8	5.77
PFAS – PFCAs**							
PFOA	Industrial	1.52	4.55	0.45	1.33	88.1	12.5
PFNA	Industrial	2.12	6.37	0.62	1.87	87.2	7.56
PFDeA	Industrial	1.82	5.45	0.53	1.60	64.6	8.59
PFUnA	Industrial	1.74	5.21	0.51	1.53	56.1	9.85
PFDoA	Industrial	1.35	4.06	0.40	1.19	113	12.6
PFTrDA	Industrial	1.54	4.62	0.45	1.35	106	9.23
Plant protection products – approved & TPs**							
Bromoxynil	Herbicide	5.11	15.30	1.50	4.49	75.0	13.7
Dimethachlor-ESA	Herbicide	20.70	62.00	6.07	18.17	71.4	14.3
Dimethachlor-OXA	Herbicide	65.00	195.00	19.05	57.16	69.5	10.0
Dichlorobenzamide (fluopicolide/dichlobenil)	Fungicide	2.36	7.08	0.69	2.08	78.7	9.14
Metalaxyl	Fungicide	1.15	3.46	0.34	1.01	73.2	14.0
Myclobutanil	Fungicide	4.98	15.00	1.46	4.40	82.0	12.4
Napropamide	Herbicide	3.97	11.90	1.16	3.49	63.9	14.6
Propamocarb	Fungicide	1.62	4.85	0.47	1.42	76.6	5.12
Pymetrozine	Insecticide	17.50	52.60	5.13	15.42	61.2	9.96
Pyrethrin I	Insecticide	5.26	15.80	1.54	4.63	59.9	7.55
Spiroxamine	Fungicide	0.28	0.85	0.08	0.25	82.3	39.9
Plant protection products – not approved & TPs**							
Alachlor-OXA	Herbicide	35.40	106.00	10.38	31.07	73.5	9.82
Carbofuran	Acaricide, Insecticide, Nematicide	13.10	39.20	3.84	11.49	85.8	13.5
Dikegulac	Plant growth regulator/industrial	52.80	158.00	15.48	46.32	126	15.2
Ethiofencarb-sulfone	Insecticide	4.31	12.90	1.26	3.78	94.1	8.60
Propachlor	Herbicide	5.60	16.80	1.64	4.92	79.1	4.13
Simazine	Herbicide	0.79	2.38	0.23	0.70	67.6	9.92

Human medicinal products**							
Cinoxacin	Antibacterial agent	15.90	47.70	4.66	13.98	68.4	9.22
Cytarabin	Chemotherapy	4.43	13.30	1.30	3.90	71.9	5.47
D L-N N Didesmethyl-Venlafaxine	Antidepressant	3.94	11.80	1.15	3.46	73.2	10.0
D L-N O Didesmethyl-Venlafaxine	Antidepressant	0.80	2.39	0.23	0.70	68.4	10.1
Desethylhydroxy-Chloroquine	Metabolite of hydroxychloroquine (used against Malaria)	5.95	17.80	1.74	5.22	56.1	13.9
Dorzolamide	Glaucoma and ocular hypertension	8.50	25.50	2.49	7.48	77.6	8.34
Meptazinol	Opioid analgesic	11.40	34.10	3.34	10.00	69.8	14.7
N-Desmethyl-Tapentadol	Metabolite of Tapentadol (opioid analgesic)	6.36	19.10	1.86	5.60	59.5	9.82
Pindolol	Beta blocker	11.80	35.40	3.46	10.38	82.6	16.5
Salicylamide	Analgesic and antipyretic	36.70	110	10.76	32.25	60.4	31.4
2-Hydroxy-Ibuprofen	Metabolite of Ibuprofen (nonsteroidal anti-inflammatory drug)	20.20	60.50	5.92	17.73	65.49	13.13
Veterinary medicinal products**							
Oxfendazole	Anthelmintic	11.40	34.10	3.34	10.00	87.6	5.57
Sulfadoxine	Antibacterial agent	20.00	60.00	5.86	17.59	77.7	18.9
Human and veterinary medicinal products**							
Deprenyl/Selegiline	Antidepressant/Canine cognitive dysfunction	19.30	57.90	5.66	16.97	81.7	6.60
Lidocaine	Anaesthetic	4.00	12.00	1.17	3.52	86.5	6.21
Lidocaine-N-oxide	Metabolite Lidocaine	3.33	10.00	0.98	2.93	82.1	6.60
Nalidixic acid	Antibacterial agents	10.10	30.30	2.96	8.88	103	8.64
N-bisdesmethyl-Tramadol	Metabolite Tramadol (opioid analgesic)	10.60	31.80	3.11	9.32	98.1	7.61
Nor Tramadol (Tramadol-N-Desmethyl)	Metabolite Tramadol (opioid analgesic)	10.10	30.30	2.96	8.88	100	11.8
O-Desmethyldinor-Tramadol	Metabolite Tramadol (opioid analgesic)	6.73	20.20	1.97	5.92	103	8.23
O-Desmethylnor-Tramadol	Metabolite Tramadol (opioid analgesic)	9.09	27.30	2.66	8.00	92.3	9.45

Tramadol	Opioid analgesic	6.06	18.20	1.78	5.34	81.8	10.2
Paracetamol	Analgesic and antipyretic HMP/VMP	11.40	34.20	3.34	10.03	105	16.5
Stimulants & TPs**							
Nicotine	Tobacco	26.40	79.30	7.74	23.25	83.49	7.65
Nor-Nicotine	Tobacco	29.40	88.10	8.62	25.83	80.39	7.49
Cotinine	Tobacco	13.60	40.90	3.99	11.99	58.96	8.68
Hydroxy-Cotinine	Tobacco	25.90	77.80	7.59	22.81	56.45	8.59
Harman	Tobacco smoke/plant metabolite	4.39	13.20	1.29	3.87	68.85	7.77
Methyl-Amphetamine (methamphetamine)	Drug of abuse	14.80	44.30	4.34	12.99	71.06	6.59
Others							
1,2-Benzisothiazolinone	REACH/Biocide	10.9	32.7	3.20	9.59	73.5	6.98
Aspartame	Artificial sweetener	33.8	101	9.91	29.6	82.2	13.5
Brodifacoum	Biocide (anticoagulant rodenticide)	10.1	30.2	2.96	8.85	53.0	13.5
Fluorene	Polyaromatic hydrocarbon (combustion by-product)	2.13	6.40	0.624	1.88	95.6	7.45

*** compounds determined by GC-APCI-QToF MS**

**** compounds determined by LC-ESI-QToF MS**

Table SI-5: Results from the JANUS calculations on P, B and T properties as well as regulation status, CAS number, and used tonnage (if available), and toxicity thresholds (if available) of detected compounds. Sources were PUBCHEM (https://pubchem.ncbi.nlm.nih.gov/), ECHA database (https://echa.europa.eu/information-on-chemicals), and EFSA database (https://www.efsa.europa.eu/en/publications). Table SI-5 is given as separate Excel-file for better accessibility here: https://doi.org/10.1016/j.envint.2021.106934

Chemical class	Compounds	CAS	Chemical regulation	FoA [%]	Median [ng/g ww]	Mean [ng/g ww]	Effect data in birds (NOAEL; NOEL; LC10, LD50)	Tonnage (EU) or (DE)	Use/ application in EU	Dossier	Substa	classified ED	classified PBT/vPvB	CLH classified	Candidate list	classified as	Risk	Restriction in force or	POP	Time of Authorisation	End of Authorisation	P	Score P	Score B	Score T	PBT	PB
REACH	2-OH-benzothiazol	934-34-9	pre-registered REACH, Annex III (likely metabolite of benzothiazol)	3.3	9.6	9.6	n.a.	no information	Toys (EPA), food additive, frangracne, animicrobila agent (Pubchem);														**P/vP**	**0.712**	0.246	0.422	0.419	0.419
	Lauric isopropanolamide	142-54-1	pre-registered REACH	3.3	1.6	1.6	n.a.	no information	no information														nP	0.31	0.285	0.418	0.318	0.297
	Perfluoroundecanoic acid (PFUnA)	2058-94-8	pre-registered REACH	60.0	2.0	2.1	n.a.	no information	Used in products to resist heat, stains, oil, grease, water				vPvB			x	1	on-going				**P/vP**	**0.785**	0.309	0.5	0.494	0.493
	Perfluorodecanoic acid (PFDeA)	335-76-2	pre-registered REACH	96.7	1.8	3.1	n.a.	no information	Flame retardant				PBT		x	x	1	on-going				**P/vP**	**0.785**	0.343	0.5	0.515	0.519
	Perfluorohexanesulfonic acid (PFHxS)	355-46-4	pre-registered REACH	23.3	0.1	0.1	n.a.	no information	Flame retardant				vPvB		x	x	1	on-going	on-going			**P/vP**	**0.785**	**0.769**	0.5	**0.711**	**0.777**
	Perfluoroheptanesulfonic acid (PFHpS)	375-92-8	pre-registered REACH	30.0	0.2	0.3	n.a.	no information	Used in products to resist heat, stains, oil, grease, water								1	on-going				**P/vP**	**0.785**	**0.724**	0.5	**0.694**	**0.754**
	Perfluorononanoic acid (PFNA)	375-95-1	pre-registered REACH	90.0	4.0	4.8	n.a.	no information	Used in products to resist heat, stains, oil, grease, water								1	on-going				**P/vP**	**0.785**	0.383	0.5	0.538	0.548
	Perfluorotridecanoic acid (PFTrDA)	72629-94-8	pre-registered REACH	20.0	0.7	1.5	n.a.	no information	Used in products to resist heat, stains, oil, grease, water				vPvB		x	x	1	on-going				**P/vP**	**0.785**	0.289	0.5	0.481	0.476
	Perfluorododecanoic acid (PFDoA)	307-55-1	pre-registered REACH	20.0	0.6	0.8	n.a.	no information	Byproduct of stain- and greaseproof coatings on food				vPvB			x	1	on-going				**P/vP**	**0.785**	0.297	0.5	0.486	0.483
	Galaxolide	1222-05-5	full registered REACH, biocide	30.0	11.3	24.9	n.a.	1000-10.000 t (EU)	Washing & cleaning products, air care products, polishes and waxes,	3	1	1					1			2011		nP	0.5	**0.669**	**0.61**	0.585	0.578
	Tributylamine	102-82-9	full-registered REACH	20.0	2.7	2.7	n.a.	100-1000t (EU)	Chemical production or refinery in closed process without likelihood	1										2011		nP	0.359	0.168	0.43	0.275	0.245
	Methylparaben	99-76-3	full-registered REACH	3.3	8.0	8.0	n.a.	1000-10.000 (EU)	Cosmetics and personal care products, plant protection products	2	1	1								2011		nP	0.333	0.117	0.265	0.209	0.197
	Phenanthrene	85-01-8	Intermediate REACH	20.0	1.7	3.2	n.a.	no information	Syntheses of dyes				vPvB		x	x	2					**vP**	1	**0.69**	0.469	**0.741**	**0.881**
	Didecyldimethylammonium (DADMAC (C10:C10))	20256-56-8	full-registered under REACH	6.7	8.4	8.4	n.a.	100-1000 t (REACH)	Antimicrobial agent											2013		nP	0.5	0.245	**0.62**	0.392	0.35
	Benzenesulfonamide	98-10-2	Intermediate REACH	6.7	10.7	10.7	n.a.	intermediate	Closed batch processing in synthesis or formulation and											2013		**P/vP**	**0.712**	0.089	0.285	0.259	0.252
Medicinal products	Paracetamol	103-90-2	HMP/VMP, full-registered REACH Intermediate	3.5	19.9	19.9	n.a.	10-100 (REACH; EU)	Human & veterinary analgetic (pigs)											2012		nP/P	0.571	0.102	0.133	0.214	0.242
	Pindolol	13523-86-9	HMP, pre-registered REACh	13.8	5.2	5.2	n.a.	confidential	Beta blocker													**P/vP**	**0.712**	0.141	0.376	0.328	0.317
	Dorzolamide	120279-96-1	HMP	3.5	3.7	3.7	n.a.	confidential	Eye treatment													nP	0.359	0.261	0.5	0.338	0.306
	Lidocaine	137-58-6	HMP/VMP, Intermediate REACH	3.5	1.8	1.8	n.a.	confidential	Local anestaticum											2018		P/vP	**0.712**	0.15	0.413	0.342	0.327
	Lidocaine-N-oxide	2903-45-9	HMP/VMP Metabolite	6.9	6.1	6.1	n.a.	confidential	Human & veterinary analgetics													P/vP	**0.712**	0.231	0.453	0.415	0.406
	Cytarabin	147-94-4	HMP, pre-registered REACH	6.9	2.0	2.0	n.a.	confidential	Cytostatic agent Virostatic agent													nP	0.288	0.245	0.376	0.314	0.312
	Deprenyl / Selegiline	2323-36-6	HMP/VMP	10.3	8.5	12.7	n.a.	confidential	Parkison treatment & veterinary drug													nP/P	0.571	0.145	0.42	0.31	0.288
	Tramadol	27203-92-5	HMP/VMP, Intermediate REACH	10.3	2.7	6.8	n.a.	confidential	Human & veterinary opeoid (dogs)											2018		nP/P	0.584	0.282	0.45	0.414	0.406
	Cinoxacin	28657-80-9	HMP, pre-registered REACH	3.5	7.0	7.0	n.a.	confidential	Antibiotic agent													nP	0.216	0.198	0.345	0.295	0.265
	Desethylhydroxy-Chloroquine	4298-15-1	HMP Metabolite	3.5	9.4	9.4	n.a.	confidential	Metabolite of Chloroquine													P/vP	**0.712**	0.274	0.5	0.453	0.442
	N-bisdesmethyl-Tramadol (dinor-tramadol)	73806-40-3	HMP/VMP Metabolite	10.3	4.7	4.6	n.a.	confidential	Metabolite of Tramadol													nP	0.359	0.2	0.424	0.294	0.268
	Nor-Tramadol (Tramadol-N-desmethyl)	1261398-09-7(	HMP/VMP Metabolite	3.5	11.2	11.2	n.a.	confidential	Metabolite of Tramadol													nP	0.216	0.198	0.345	0.295	0.277
	O-Desmethyldinor-Tramadol	144830-18-2	HMP/VMP Metabolite	20.7	19.9	22.5	n.a.	confidential	Metabolite													nP	0.359	0.205	0.523	0.309	0.271
	O-Desmethylnor-Tramadol	73986-53-5	HMP/VMP Metabolite	58.6	19.0	31.3	n.a.	confidential	Metabolite of Tramadol													nP/P	0.584	0.291	0.524	0.432	0.412
	N-Desmethyl-tapentadol	1300037-83-5(	HMP Metabolite	17.2	17.2	14.9	n.a.	confidential	Metabolite of Tapendatol (Opioid)													nP/P	0.571	0.214	0.5	0.375	0.349
	D L-N N-Didesmethyl-Venlafaxine	93413-77-5	HMP metabolite, pre-registered REACH	37.9	5.4	6.4	n.a.	confidential	Metabolite of Venlafaxine													nP	0.359	0.203	0.506	0.306	0.27
	D L-N O-Didesmethyl-Venlafaxine	135308-74-6	HMP metabolite, pre-registered REACH	10.3	7.8	8.5	n.a.	confidential	Metabolite of Venlafaxine													nP	0.31	0.208	0.5	0.291	0.254
	2-Hydroxy-Ibuprofen	51146-55-5	HMP	3.5	8.9	8.9	n.a.	confidential	Metabolite of Ibuprofen Nonsteroidal and anti-inflammatory													nP/P	0.584	0.123	0.406	0.291	0.268

	Meptazinol	54340-58-8	HMP, pre-registered REACH	55.2	25.3	32.4	n.a.	confidential	Opioid														nP/P	0.584	0.364	0.598	0.486	0.461
	Salicylamide	65-45-2	HMP, pre-registered REACH	72.4	36.5	34.9	n.a.	confidential	Analgetic											2011			nP	0.333	0.106	0.138	0.176	0.188
	Sulfadoxine (antibiotic)	2447-57-6	VMP, pre-registered REACH	6.9	8.8	8.8	n.a.	confidential	Human & veterinary antibiotic														vP	**0.854**	0.092	0.521	0.318	0.281
	Nalidixic acid (antibiotic)	389-08-2	HMP/VMP, full registered REACH	6.9	4.4	4.4	n.a.	confidential	Antimicrobial agent														nP	0.423	0.22	0.56	0.321	0.332
	Oxfendazole	53716-50-0	VMP, pre-registered REACH	100.0	40.6	39.8	n.a.	confidential	Antelmintic agent														**P/vP**	**0.712**	0.289	0.5	0.332	0.454
PPPs	Alachlor-OXA	171262-17-2	PPP	30.0	15.5	19.8	long-term NOAEL: 5.4 mg a.s./kg bw/day acute LD50 = 477 mg a.s./kg bw/day		Metabolite of Alachlor												2006		**P/vP**	**0.712**	0.142	0.459	0.342	0.318
	Spiroxamine	118134-30-8	PPP, pre-registered REACH	100.0	3.0	3.3	long-term NOEL = 82 mg/kg bw/d	250 - 1000 t in 2019 in DE	Fungicide					2					1999, renewal 01.01.2012	31/12/2023		**P/vP**	**0.712**	0.262	0.371	0.419	0.432
	Pyrethrin I	121-21-1	PPP, pre-registered REACH	6.7	4.1	4.1	n.a.	< 1 t in 2019 in DE	Insecticide														nP	0.359	0.345	0.486	0.375	0.352
	Simazine	122-34-9	PPP, pre-registered REACH	93.3	4.7	5.6	long-term LC10 (Anas platyrhynchos, 14 d) = 0.64 mg a.s./kg bw/d (Note : The reproductive endpoint for birds is based on a short-term dietary study (14 d) with Anas platyrhynchos ducklings, acute LD50 (male, Anas platyrhynchos) = 0.71 mg a.s./kg bw/d.	not in use	Herbicide Use as on-site isolated intermediate registered according to REACH Article 17(3)											2018	EU 2003: DE 1998	**vP**	**0.854**	0.15	0.392	0.364	0.358
	Carbofuran	1563-66-2	PPP, pre-registered REACH	6.7	1333.7	1333.7	long-term NOAEL: 15.9 mg a.s./kg bw/d, acute LD50 = 153 mg a.s./kg bw/d	not in use	Insecticide												2007	nP	0.595	0.147	0.518	0.331	0.296
	Bromoxynil	1689-84-5	PPP, pre-registered REACH	3.3	2.1	2.1	n.a.	25 - 100 t in 2019 in DE	Herbicide												March 2021		**P/vP**	**0.712**	0.123	0.326	0.302	0.296
	Dikegulac	18467-77-1	PPP, pre-registered REACH	6.7	23.2	23.2	n.a.	not in use	Growth inhibitor												2002		nP	0.333	0.099	0.42	0.215	0.182
	Propachlor	1918-16-7	PPP, pre-registered REACH	6.7	2.5	2.5	long-term NOEL= 105 mg a.s./kg b.w./day, acute LD50 >1842 mg a.s./kg b.w./day	not in use	Herbicide												2008		**P/vP**	**0.712**	0.209	0.311	0.369	0.385
	Propamocarb	24579-73-5	PPP, pre-registered REACH	10.0	0.7	0.7	n.a.	100 - 250 t in 2019 in DE	Fungicide												31/07/2021		nP	0.571	0.234	0.299	0.351	0.365
	Ethiofencarb-sulfone	5427-28-1	PPP, pre-registered REACH	33.3	2.9	6.6	n.a.	not in use	Insecticide											1977	1999		nP	0.31	0.133	0.379	0.23	0.203
	Metalaxyl	57837-19-1	PPP, pre-registered REACH	3.3	9.6	9.6	1466 mg a.s./kg bw/d Metalaxyl-M: long-term nEOL= 84 mg a.s./kg bw/d, acute LD50 = 981 mg a.s./kg bw/d, BCF = 3.7	10 - 25 t in 2019 (Metalaxyl-M), <1 t in 2019 (Metalaxyl) in DE	Fungicide proteomics research											2010 (Metalaxyl)	30/06/2023		nP	0.333	0.124	0.454	0.239	0.203
	Fluorene	86-73-7	PPP, intermediate REACH	6.7	4.0	4.0	n.a.	not in use	Pesticide production of chemicals											2016			**vP**	**1**	0.453	0.566	**0.65**	**0.673**
	Pymetrozine	123312-89-0	PPP, full-registered REACH	13.3	7.7	13.0	long-term NOEL = 21.8 mg a.s./kg bw per day , acute LD50 ≥ 2000 (extrapolated 3776) mg a.s./kg bw per day.	10 - 25 t in 2019 für	Insecticide					1						2002	April 2019		**vP**	**0.854**	0.227	0.284	0.403	0.44
	Napropamide	15299-99-7	PPP, full-registered REACH	16.7	1.7	1.7	long-term NOEL 3000 ppm = 309 mg a.s./kg bw /day (mallard duck), acute LD50 > 2250 mg a.s./kg bw	25 - 100 t in 2019 in DE	Herbicide											2011	31/12/2023		**P/vP**	**0.712**	0.279	0.441	0.445	0.446
	Dimethachlor-OXA	1086384-49-7	PPP	10.0	28.6	45.4	n.a.	Dimethachlor: 10 - 25 t in 2019 in DE	Transformation product of Fluopicolide (approved) and Dichlobenil (not approved)												31/12/2021		nP	0.333	0.126	0.369	0.23	0.204
	Dichlorobenzamide	2447-79-2	pre-registered REACH, PPP	6.7	1.0	1.0	n.a.	Fluopicolide: 10 - 25 t in 2019 in DE	Microbial metabolite of Dichlobenil												31/05/2023		nP/P	0.571	0.087	0.2	0.219	0.223
	Myclobutanil	88671-89-0	PPP, full-registered REACH	3.3	2.2	2.2	long-term NOEL = 24.2 mg a.s./kg bw/d bzw. NOEC = 260 mg a.s./kg feed, acute LD50 = 510 mg a.s./kg bw/d	2,5 - 10 t in 2019 in DE)	Fungicide											1992 (UK)	31/05/2021	**P/vP**	**0.8**	0.255	0.414	0.444	0.451
POPs	Heptachlor Epoxide	1024-57-3	PPP, pre-registered REACH	16.7	0.9	2.4	n.a.	not in use	not in use										x	1971 (Heptachlor)	1981 PPP: 1981 POP: 2004		**vP**	**0.854**	**0.85**	**0.741**	**0.828**	**0.852**
	Dicofol	115-32-2	PPP, pre-registered REACH	70.0	0.8	2.7	n.a.	not in use	not in use										x	1955	2008		**vP**	**0.854**	**0.829**	0.59	**0.784**	**0.841**
	4,4'-Dichlorobenzophenone	90-98-2	pre-registered REACH	60.0	0.5	1.7	n.a.	not in use	not in use										(x)				**vP**	**0.854**	**0.831**	0.37	**0.714**	**0.842**
	Hexachlorobenzene	118-74-1	PPP, pre-registered REACH	6.7	44.9	44.9	n.a.	not in use	not in use										x				**vP**	**1**	**0.935**	**0.687**	**0.889**	**0.907**
	trans Chlordane	5103-74-2	PPP, pre-registered REACH	6.7	11.9	11.9	n.a.	not in use	not in use										x	2001	2001		**vP**	**1**	**0.93**	**0.726**	**0.911**	**0.964**
	cis Chlordane	5103-71-9	pre-registered REACH, biocide	6.7	4.4	4.4	n.a.	not in use	not in use										x		since 1981 restricted in EU		**vP**	**1**	**0.93**	**0.726**	**0.911**	**0.964**
	Pentachlorobenzene	608-93-5	PPP, pre-registered ECHA	10.0	0.2	0.4	n.a.	not in use	not in use										x	2009	1992: POP: 2009		**vP**	**1**	**0.866**	**0.651**	**0.867**	**0.931**
	PCB 209	2051-24-3	full registered REACH (before 2010)	16.7	1.8	8.5	n.a.	not in use	not in use										x				**vP**	**1**	**0.901**	**0.626**	**0.873**	**0.949**
	PCB 153	35065-27-1	full registered REACH (before 2010)	80.0	90.1	297.6	n.a.	not in use	not in use										x				**vP**	**0.918**	**0.995**	0.591	**0.868**	**0.956**
	PCB 138	35065-28-2	full registered REACH (before 2010)	100.0	238.1	395.9	n.a.	not in use	not in use										x				**vP**	**0.918**	**0.995**	0.591	**0.836**	**0.912**
	PCB 180	35065-29-3	full registered REACH (before 2010)	100.0	112.7	383.8	n.a.	not in use	not in use										x				**vP**	**1**	**0.766**	0.594	**0.81**	**0.875**
	PCB 52	35693-99-3	full registered REACH (before 2010)	43.3	0.5	8.6	n.a.	not in use	not in use										x				**vP**	**1**	**0.964**	**0.681**	**0.912**	**0.982**
	PCB 101	37680-73-2	full registered REACH (before 2010)	93.3	6.9	30.6	n.a.	not in use	not in use										x				**vP**	**1**	**0.968**	**0.736**	**0.928**	**0.984**
	PCB 28	7012-37-5	full registered REACH (before 2010)	53.3	0.6	13.9	n.a.	not in use	not in use										x				**vP**	**1**	**0.935**	0.594	**0.877**	**0.967**

	beta-1,2,3,4,5,6-Hexachlorocyclohexane (b-HCH)	319-85-7	pre-registered REACH	33.3	4.4	8.1	n.a.	not in use	not in use									x			**vP**	**0.816**	0.53	**0.705**	**0.667**	**0.658**
	4,4-DDE , Metabolite DDT	72-55-9	pre-registered REACH	100.0	168.8	166.7	n.a.	not in use	not in use									x			**vP**	**0.854**	0.427	0.549	**0.592**	**0.603**
	4,4-DDD, Metabolite DDT	72-54-8	PPP, pre-registered REACH	100.0	2.2	8.2	n.a.	not in use	not in use									x			**vP**	**1**	**0.953**	0.54	**0.867**	**0.976**
	Perfluorooctanoic acid (PFOA)	335-67-1	pre-registered REACH	23.3	0.7	0.7	n.a.	not in use	not in use					1		1		x	POP: 2020		**P/vP**	**0.785**	**0.56**	0.5	**0.626**	**0.663**
	Perfluorooctanesulfonic acid (PFOS)	1763-23-1	pre-registered REACH	100.0	479.7	614.8	n.a.	not in use	not in use									x	2009	POP: 2009	**P/vP**	**0.785**	**0.812**	0.5	**0.727**	**0.798**
Biocides	1,2-Benzisothiazolinone	2634-33-5	full registered REACH, biocide	3.3	13.3	13.3	n.a.	100-1000 t (EU)	1) Biocidal application: Preservative for products during storage					1					2018		nP	0.321	0.231	0.22	0.27	0.28
	Brodifacoum	56073-10-0	Biocide, full-registered under REACH	3.3	11.9	11.9	acute toxicity: LD50(mallard duck)=0.31 mg/kg bw avian reproduction toxicity: read-across from Difenacoum: NOEC=0.0038 mg/kg food	no information	Rodenticide				1	1					2012	2024	nP	0.359	0.377	0.551	0.399	0.368
Stimulants&others	Methyl-Amphetamine (methamphetamine)	537-46-2	Intermediate REACH, drug of abuse	10.0	6.5	6.5	n.a.	no information	Drug of abuse										2018		nP/P	0.571	0.139	0.337	0.292	0.282
	Nicotine	54-11-5	full registered REACH	20.0	92.6	107.8	n.a.	1000-10.000 t/a	Tobacco products					1					2015		nP/P	0.571	0.09	0.414	0.256	0.227
	Nor-Nicotine	5746-86-1	pre-registered REACH	83.3	194.0	226.9	n.a.	no information	Metabolite of nicotin												nP/P	0.571	0.095	0.346	0.252	0.233
	Hydroxy-Cotinine	34834-67-8		6.7	388.4	388.4	n.a.	no information	Metabolite of nicotin												**vP**	**0.854**	0.154	0.343	0.358	0.362
	Harman	486-84-0	pre-registered REACH, pharmaceutical	10.0	1.9	5.3	n.a.	confidential	a putative endogenous imidazoline ligand for imidazoline binding sites												nP	0.359	0.238	0.474	0.322	0.292
	Aspartame	22839-47-0	pre-registered REACH	40.0	14.8	26.7	n.a.	15000 t/a (BMBP)	Food additive: artifical sweetener												nP/P	0.571	0.175	0.42	0.334	0.316
	Cotinine	486-56-6	pre-registered REACH	3.3	58.9	58.9	n.a.	no information	Metabolite of nicotin												nP	0.359	0.155	0.341	0.253	0.235

Table SI-6: Proportion of the five main land cover classes [%] within a circular buffer of 5 km around the location where an individual was found. Data was extracted from the Corine landcover data set 2018.

Id	Artificial (urban) areas [%]	Agricultural areas [%]	Forest and seminatural areas [%]	Wetlands [%]	Water bodies [%]
MV479	2.84	77.94	18.27	0.95	0.00
MV488	9.95	23.02	29.37	6.67	30.98
MV503	2.08	34.51	4.16	2.19	57.06
MV522	3.36	82.44	14.2	0.00	0.00
MV524	4.95	89.36	4.54	1.15	0.00
MV527	0.57	68.36	28.33	0.00	2.74
MV530	2.29	93.79	3.91	0.00	0.00
MV533	2.71	82.58	11.48	0.6	2.63
MV535	1.23	39.29	26.69	16.69	16.09
MV536	4.6	70.88	21.53	0.00	2.99
MV542	2.03	73.54	21.11	1.52	1.8
MV543	0.13	14.09	76.41	0.00	9.37
MV545	2.32	50.93	22.63	15.62	8.51
MV549	1.44	58.2	37.14	1.35	1.88
MV564	0.34	89.01	10.65	0.00	0.00
MV571	1.3	91.02	7.3	0.00	0.38
MV580	1.22	44.15	16.71	1.93	35.99
MV586	4.45	89.36	5.74	0.09	0.36
NS101	5.49	93.86	0.48	0.17	0.00
NS102	3.39	70.01	26.6	0.00	0.00
NS89	1.56	83.04	0.00	11.28	4.12
NS90	8.38	51.61	40.01	0.00	0.00
NS93	2.83	62.34	30.15	0.00	4.69
SH135	2.16	61.27	35.51	0.00	1.06
SH145	0.49	44.17	0.00	49.41	5.93
SH149	2.16	84.71	11.34	0.00	1.8
SH150	1.67	80.99	17.34	0.00	0.00
SH151	6.32	64.04	21.85	0.00	7.8
SH154	2.47	82.86	13.29	0.00	1.39
SH157	3.92	66.21	26.6	0.00	3.26

Table SI-7: Stable isotope values: mean ± 2*SE (range) for $\delta^{13}C$ and $\delta^{15}N$ in [‰] for white-tailed sea eagles (liver) and prey species (muscle; taken from Nadjafzadeh et al. (2016)). **P** = piscivore, **O** = omnivore, **H** = herbivore, **C** = carnivore.

	$\delta^{13}C$ [‰]	**$\delta^{15}N$ [‰]**
White-tailed sea eagle (P/C) *Haliaeetus albicilla*	-24.7±0.5 (-27.9-(-21.4)) 30	12.4±0.7 (7.7-17.3) n=30
Fish		
European Perch (P) *Perca fluviatilis*	-26.8±0.4 (-27.3-(-26.2)) n=5	14.4±1.5 (13.1-17.0) n=5
Northern Pike (P) *Esox lucius*	-25.2±0.4 (-25.7-(-24.2)) n=6	15.1±0.3 (14.6-15.5) n=6
Common Bream (O) *Abramis brama*	-27.7±0.4 (-28.4-(-27.0)) n=6	11.8±1.9 (8.5-14.9) n=6
Common Roach (O) *Rutilus rutilus*	-26.1±0.5 (-26.7-(-25.2)) n=6	13.7±0.4 (13.3-14.7) n=6
Common Rudd (O/H) *Scardinius erythrophthalmus*	-24.2±1.7 (-26.9-(-21.5)) n=6	12.3±1.0 (10.3-13.4) n=6
Waterfowl/Seabirds		
Great Cormorant (P) *Phalacrocorax carbo*	-26.2±2.5 (-28.6-(-20.5)) n=6	15.8±1.3 (13.8-17.8) n=6
Great Crested Grebe (P) *Podiceps cristatus*	-22.9 n=1	16.2 n=1
Black-headed Gull (P/O) *Chroicocephalus ridibundus*	-24.3±0.5 (-24.8-(-23.1)) n=6	10.6±0.4 (10.1-11.3) n=6
Mallard (O) *Anas platyrhynchos*	-27.0±1.4 (-28.5-(-25.0)) n=5	9.9±1.3 (8.1-11.5) n=5
Eurasian Coot (H/O) *Fulica atra*	-30.1±1.2 (-31.6-(-27.4))	11.3±2.7 (6.6-16.5)

	n=6	n=6
Goose sp. (H) *Anser sp.*	-28.6±1.0 (-30.6-(-27.1))	7.7±0.5 (6.8-8.8)
	n=7	n=7
Game mammals		
Red fox (C/O) *Vulpes vulpes*	-24.6±0.6 (-25.8-(-23.7))	9.0±1.8 (4.7-10.8)
	n=6	n=6
Racoon Dog (C/O) *Nyctereutes procyonoides*	-24.4±0.5 (-25.3-(-23.7))	10.6±1.5 (8.0-13.4)
	n=6	n=6
Wild Boar (O) *Sus scrofa*	-23.1±1.7 (-24.9-(-19.2))	1.9±1.7 (-1.7-4.5)
	n=6	n=6
Fallow Deer (H) *Dama dama*	-27.7±0.3 (-28.3-(-27.2))	1.9±1.1 (-0.3-3.5)
	n=6	n=6
Roe Deer (H) *Capreolus capreolus*	-27.4±0.5 (-28.5-(-26.5))	-0.5±1.0 (-2.1-1.5)
	n=6	n=6

Table SI-8: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of chemicals regulated by the Stockholm Convention in livers of white-tailed sea eagles from Germany. Polychlorinated biphenyls (PCBs), *4,4'*-Dichlorodiphenyldichloroethane (*4,4'*-DDD), *4,4'*-Dichlorodiphenyldichloroethylene (*4,4'*-DDE). n = 30.

PCBs		DDTs		Others	
PCB 28	0.6 (0.29-1.82)	***4,4'*-DDD**	2.18 (0.79-6.2)	**β-Hexachlorocyclohexane (HCH)**	4.35 (1.37-14.55)
Detection rate [%]	53.33	Detection rate [%]	100	Detection rate [%]	33.33
PCB 52	0.52 (0.52-5.68)	***4,4'*-DDE**	168.76 (62.8-222.01)	**cis-Chlordane**	4.4 (3.43-5.38)
Detection rate [%]	43.33	Detection rate [%]	100	Detection rate [%]	6.67
PCB 101	6.91 (2.95-15.94)			**trans-Chlordane**	11.9 (11.25-12.55)
Detection rate [%]	93.33			Detection rate [%]	6.67
PCB 138	238.13 (118.71-502.98)			**Dicofol**	0.77 (0.56-1.66)
Detection rate [%]	100			Detection rate [%]	70.0
PCB 153	90.12 (24.48-241.61)			**4,4'-Dichlorobenzophenone**	0.51 (0.22-1.48)
Detection rate [%]	80.0			Detection rate [%]	60.0
PCB 180	112.69 (42.49-363.68)			**Pentachlorobenzene**	0.24 (0.24-0.45)
Detection rate [%]	100			Detection rate [%]	10.0
PCB 209	1.76 (1.17-13.72)			**Hexachlorobenzene**	44.93 (32.08-57.78)
Detection rate [%]	16.67			Detection rate [%]	6.67

		Heptachlor expoxide	0.87 (0.82-2.27)
		Detection rate [%]	16.67

Table SI-9: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of industrial chemicals regulated under REACH (other than PFAS) in livers of white-tailed sea eagles from Germany. n^+ = samples with detectable residues.

REACH chemicals (n=30)			
2-OH-benzothiazole	9.59 (9.59-9.59)	**Lauric isopropanolamide**	1.6 (1.6-1.6)
Detection rate [%]	3.33 (n=1)	Detection rate [%]	3.33 (n=1)
Benzenesulfonamide	10.69 (10.69-10.69)	**Methylparaben**	7.95 (7.95-7.95)
Detection rate [%]	6.67	Detection rate [%]	3.33 (n^+=1)
DADMAC (C10:C10)	8.4 (8.4-8.4)	**Phenanthrene**	1.74 (0.82-3.47)
Detection rate [%]	6.67	Detection rate [%]	20.0
Galaxolide	11.28 (4.77-20.13)	**Tributylamine**	2.71 (2.71-2.71)
Detection rate [%]	30.0	Detection rate [%]	20.0

Table SI-10: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of per- and polyfluoroalkyl substances (PFAS) in livers of white-tailed sea eagles from Germany. Perfluorohexane-1-sulphonic acid (PFHxS), Perfluoroheptane sulfonic acid (PFHpS), Perfluorooctane sulfonic acid (PFOS), Perfluorooctanoic acid (PFOA), Perfluorononanoic acid (PFNA), Perfluorodecanoic acid (PFDeA), Perfluoroundecanoic acid (PFUnA), Perfluorododecanoic acid (PFDoA), Perfluorotridecanoic acid (PFTrDA). n=30. "C" denotes the carbon chain length.

PFAS (n=30)			
PFSAs		**PFCAs**	
PFHxS **C_6**	0.05 (0.05-0.17)	**PFOA** **C_8**	0.67 (0.67-0.67)
Detection rate [%]	23.33	Detection rate [%]	23.33
PFHpS **C_7**	0.22 (0.22-0.5)	**PFNA** **C_9**	3.97 (2.47-4.7)
Detection rate [%]	30.0	Detection rate [%]	90.0
PFOS (linear) **C_8**	479.74 (255.17-773.48)	**PFDeA** **C_{10}**	1.78 (0.8-3.3)
Detection rate [%]	100	Detection rate [%]	96.67
PFOS (branched) **C_8**	8.41 (3.73-16.43)	**PFUnA** **C_{11}**	1.98 (0.77-2.33)
Detection rate [%]	100	Detection rate [%]	60.0
		PFDoA **C_{12}**	0.6 (0.6-0.6)
		Detection rate [%]	20.0
		PFTrDA **C_{13}**	0.68 (0.68-2.06)
		Detection rate [%]	20.0

Table SI-11: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of plant protection products in livers of white-tailed sea eagles from Germany. Approved: currently (June 2021) authorised active substances in the Germany. Not approved: withdrawn authorisation of active substances before 31.12.2018. n^+ = samples with detectable residues.

Approved PPPs (EU/Germany) n=30					
Bromoxynil (withdrawal 2021)	2.09 (2.09-2.09)	**Metalaxyl**	9.62 (9.62-9.62)	**Pymetrozine** (withdrawal 2019)	7.71 (7.71-13.04)
Detection rate [%]	3.33 (n^+=1)	Detection rate [%]	3.33 (n^+=1)	Detection rate [%]	13.33
Dimethachlor-ESA	9.09 (9.09-9.09)	**Myclobutanil** (withdrawal 2021)	2.2 (2.2-2.2)	**Pyrethrin I**	4.14 (3.23-5.05)
Detection rate [%]	6.67	Detection rate [%]	3.33 (n^+=1)	Detection rate [%]	6.67
Dimethachlor-OXA	28.58 (28.58-53.74)	**Napropamide**	1.75 (1.75-1.75)	**Spiroxamine**	3.03 (2.28-4.07)
Detection rate [%]	10.0	Detection rate [%]	16.67	Detection rate [%]	100
Dichlorobenzamide (parent compound: Fluopicolide)	1.04 (1.04-1.04)	**Propamocarb**	0.71 (0.71-0.71)		
Detection rate [%]	6.67	Detection rate [%]	10.0		
Not approved PPPs (EU/Germany) n=30					
Alachlor-OXA (withdrawal 1992)	15.54 (15.54-15.54)	**Ethiofencarb-sulfone** (withdrawal 1999)	2.85 (1.89-4.41)		
Detection rate [%]	30.0	Detection rate [%]	33.33		
Carbofuran (withdrawal 2005)	1333.7 (762.16-1905.25)	**Propachlor** (withdrawal 1994)	2.46 (2.46-2.46)		
Detection rate [%]	6.67	Detection rate [%]	6.67		

Dikegulac (withdrawal 2004)	23.16 (23.16-23.16)	**Simazine** (withdrawal 1998)	4.67 (2.78-6.99)
Detection rate [%]	6.67	Detection rate [%]	93.33

Table SI-12: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of medicinal products in livers of white-tailed sea eagles from Germany. n^+ = samples with detectable residues. MV542 was excluded due to potential deliberate treatments.

Human medicinal products (n=29)					
Cinoxacin	6.99 (6.99-6.99)	**Desethylhydroxy-Chloroquine**	9.36 (9.36-9.36)	**Pindolol**	5.19 (5.19-5.19)
Detection rate [%]	3.45 (n^+=1)	Detection rate [%]	3.45 (n^+=1)	Detection rate [%]	13.79
Cytarabin	1.95 (1.95-1.95)	**Dorzolamide**	3.74 (3.74-3.74)	**Salicylamide**	36.47 (16.13-49.89)
Detection rate [%]	6.9	Detection rate [%]	3.45 (n=1)	Detection rate [%]	72.41
D L-N N Didesmethyl-Venlafaxine	5.38 (4.51-8.96)	**Meptazinol**	25.3 (11.14-38.19)	**2-Hydroxy-Ibuprofen**	2.61 (2.61-2.61)
Detection rate [%]	37.93	Detection rate [%]	55.17	Detection rate [%]	3.45 (n^+=1)
D L-N O Didesmethyl-Venlafaxine	7.77 (6.46-10.18)	**N-Desmethyl-Tapentadol**	17.21 (10.15-19.23)		
Detection rate [%]	10.34	Detection rate [%]	17.24		
Veterinary medicinal products (n=29)					
Oxfendazole	40.61 (36.89-46.1)		**Sulfadoxine**	8.8 (8.8-8.8)	
Detection rate [%]	100		Detection rate [%]	6.9	

Human&Veterinary medicinal products (n=29)					
Deprenyl/Selegiline	8.49 (8.49-14.82)	**N-bisdesmethyl-Tramadol**	4.66 (4.66-4.66)	**Tramadol**	2.67 (2.67-8.89)
Detection rate [%]	10.34	Detection rate [%]	10.34	Detection rate [%]	10.34
Lidocaine	1.76 (1.76-1.76)	**Nor Tramadol (Tramadol-N-Desmethyl)**	11.17 (11.17-11.17)	**Paracetamol**	19.93 (19.93-19.93)
Detection rate [%]	3.45 (n^+=1)	Detection rate [%]	3.45 (n^+=1)	Detection rate [%]	3.45 (n^+=1)
Lidocaine-N-oxide	6.13 (3.80-8.47)	**O-Desmethyldinor-Tramadol**	19.88 (17.69-27.53)		
Detection rate [%]	6.9	Detection rate [%]	20.69		
Nalidixic acid	4.44 (4.44-4.44)	**O-Desmethylnor-Tramadol**	18.98 (12.01-37.21)		
Detection rate [%]	6.9	Detection rate [%]	58.62		

Table SI-13: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of stimulants in livers of white-tailed sea eagles from Germany. n^+ = samples with detectable residues.

Stimulants n=30			
Nicotine	92.61 (82.85-109.02)	**Hydroxy-Cotinine**	388.44 (371.12-405.76)
Detection rate [%]	20.0	Detection rate [%]	6.67
Nor-Nicotine	194.03 (110.85-239.36)	**Harman**	1.94 (1.94-6.91)
Detection rate [%]	83.33	Detection rate [%]	10.0
Cotinine	58.87 (58.87-58.87)	**Methyl-Amphetamine**	6.49 (6.49-6.49)
Detection rate [%]	3.33 (n^+=1)	Detection rate [%]	10.0

Table SI-14: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng g^{-1} ww for samples with detectable residues and detection rate [%] of various origins in livers of white-tailed sea eagles from Germany. n^+ = samples with detectable residues.

Others n=30	
1,2-Benzisothiazolinone	13.25 (13.25-13.25)
Detection rate [%]	3.33 (n^+=1)
Aspartame	14.8 (14.8-37.12)
Detection rate [%]	40.0
Brodifacoum	11.9 (11.9-11.9)
Detection rate [%]	3.33 (n^+=1)
Fluorene	4.0 (3.06-4.94)
Detection rate [%]	6.67

Table SI-15: Overlapping target analytes between this study (wide-scope target screening) and a multi-target method (Badry et al., 2021). HMP: human medicinal product. VMP: veterinary medicinal product.

Biocides	**Plant protection products**	**Medicinal products**
Brodifacoum (Rodenticide)	Cyprodinil (Fungicide)	Ciprofloxacin (HMP)
Bromadiolone (Rodenticide)	Difenoconazole (Fungicide)	Diclofenac (HMP)
Chlorophacinone (Rodenticide)	Dimoxystrobin (Fungicide)	Ibuprofen (HMP)
Flocoumafen (Rodenticide)	Epoxiconazole (Fungicide)	Enrofloxacin (VMP)
Warfarin (Rodenticide)	Fenpropimorph (Fungicide)	Marbofloxacin (VMP)
Permethrin (Pyrethroide)	Fludioxonil (Fungicide)	Sulfamethazin (VMP)
Cypermethrin (Biocide/Insecticide)	Metconazole (Fungicide)	
	Prochloraz (Fungicide)	
	Propiconazole (Fungicide)	
	Quinoxyfen (Fungicide)	
	Tebuconazole (Fungicide)	
	Aclonifen (Herbicide)	
	Chlorotoluron (Herbicide)	
	Diflufenican (Herbicide)	
	Flufenacet (Herbicide)	
	Isoproturon (Herbicide)	
	Metribuzin (Herbicide)	
	Nicosulfuron (Herbicide)	
	Pendimethalin (Herbicide)	
	Chlorpyriphos (Insecticide)	
	Clothiandin (Insecticide)	
	Lambda-Cyhalothrin (Insecticide)	
	Dimethoate (Insecticide)	
	Omethoate (Dimethoate metabolite)	
	Imidacloprid (Insecticide)	
	Methiocarb (Insecticide)	
	Pirimicarb (Insecticide)	
	Thiacloprid (Insecticide)	

Table SI-16: Detection of overlapping target analytes between the current wide-scope target screening (brodifacoum LOQ: 8.85 ng g^{-1} wet weight; this study) and a multi-target method for seven individuals (brodifacoum LOQ: 2 ng g^{-1} wet weight; Badry et al. (2021)).

Id (overlapping individuals)		**Detection (wet weight)** (this study)	**Detection (wet weight)** (Badry et al., 2021)
MV479	Brodifacoum	<LOD	11.74 ng g^{-1}
MV488	Brodifacoum	<LOD	22.67 ng g^{-1}
MV503	Brodifacoum	<LOD	4.87 ng g^{-1}
MV524	Brodifacoum	<LOD	4.46 ng g^{-1}
SH135	No overlap	No overlap	No overlap
SH150	Brodifacoum		13.55 ng g^{-1}
	Ibuprofen	Ibuprofen: <LOD 2-hydroxy-ibuprofen: 8.87 ng g^{-1}	30.49 ng g^{-1}
SH151	Brodifacoum	11.9 ng g^{-1}	99.75 ng g^{-1}

4 Supplementary figures (SI 1-5)

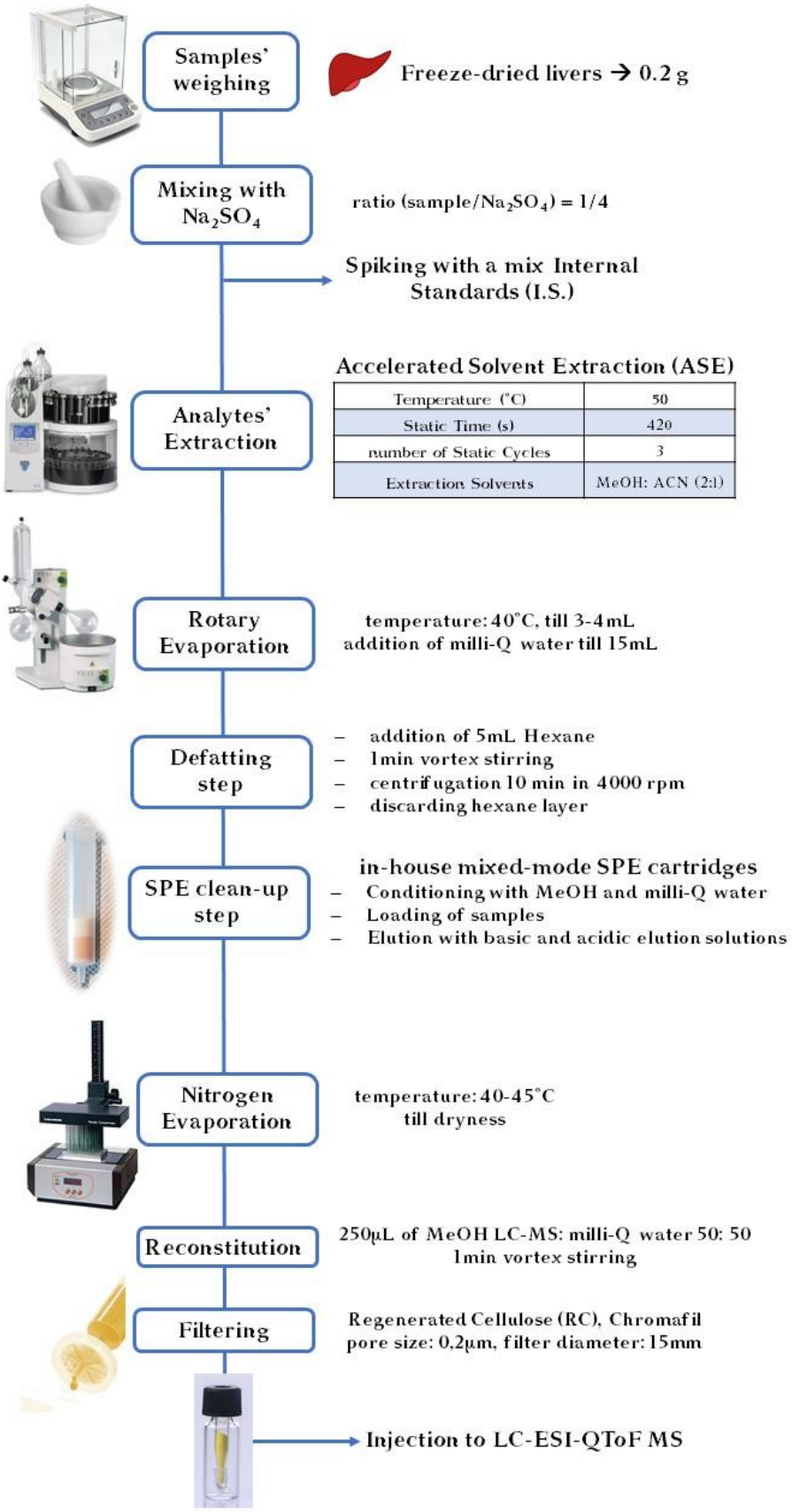

Figure SI-1: Sample preparation protocol for the LC-amenable compounds.

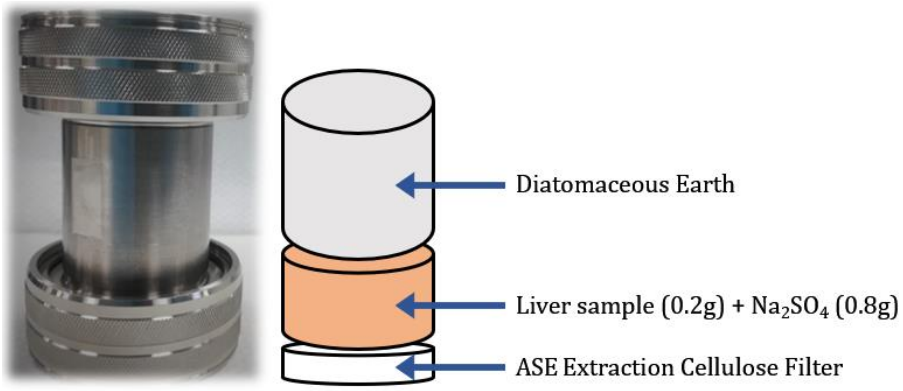

Figure SI-2: Samples' loading in the Accelerated Solvent Extraction (ASE) extraction cell.

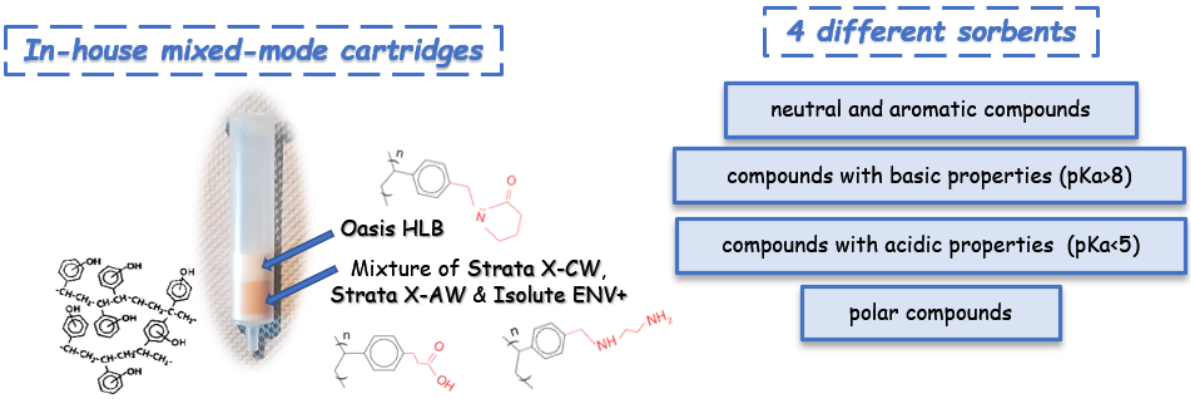

Figure SI-3: Mixed-mode solid-phase extraction (SPE) cartridges.

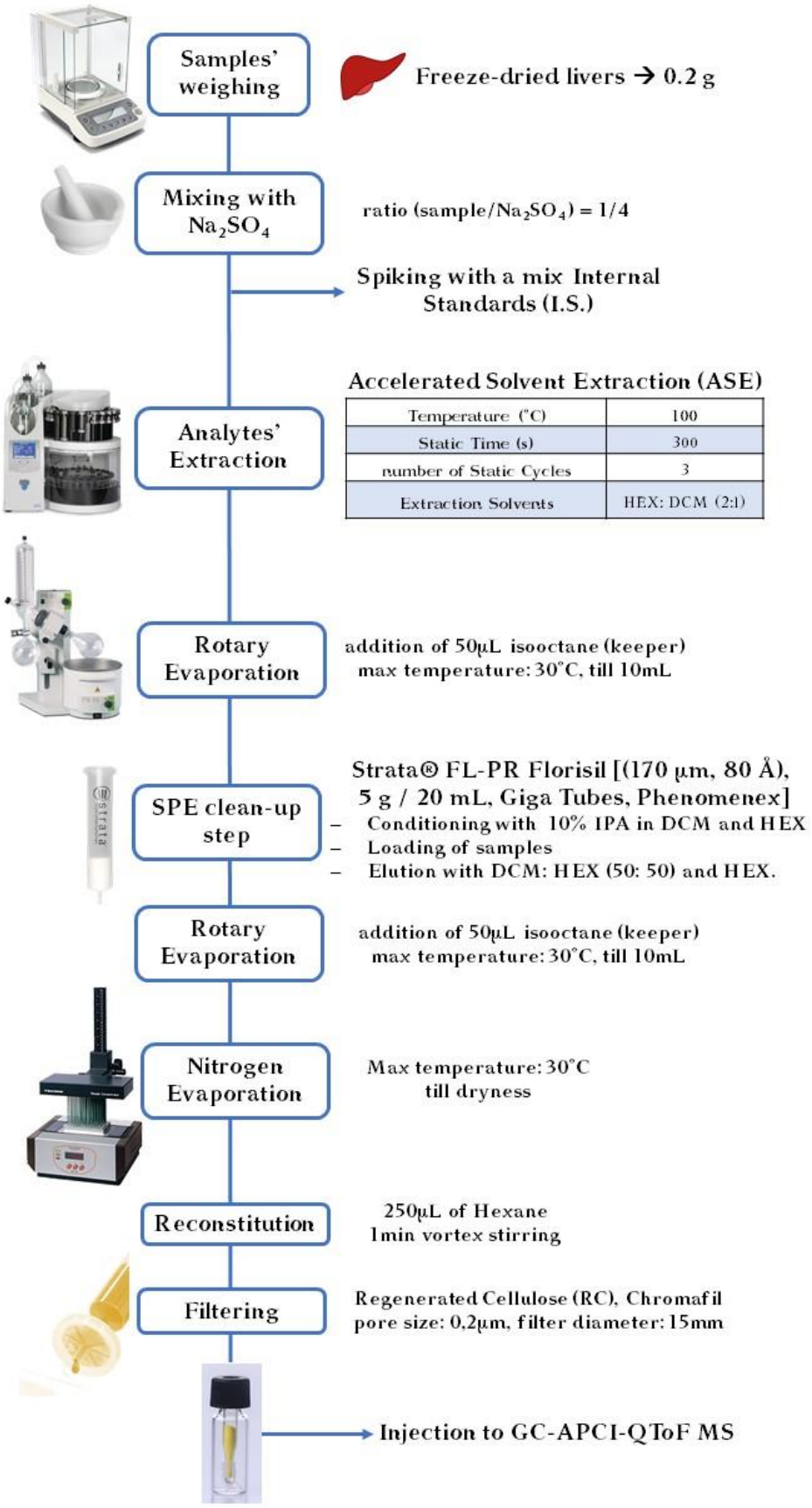

Figure SI-4: Sample preparation protocol for the GC-amenable compounds.

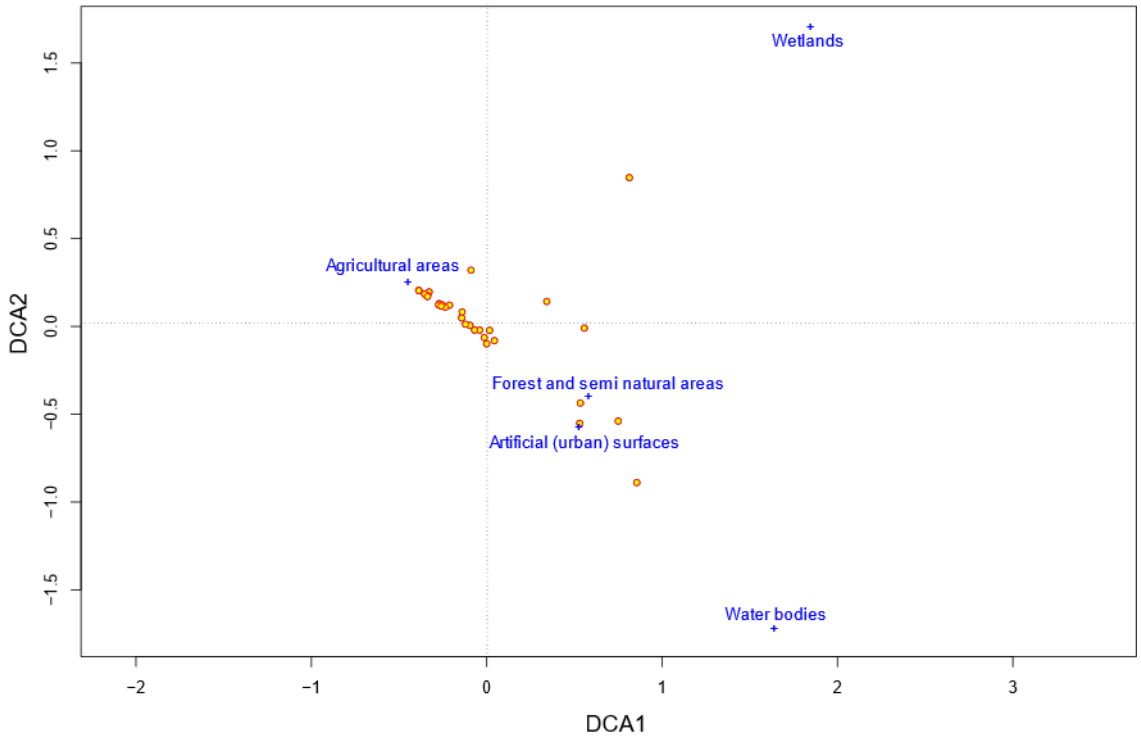

Figure SI-5: Detrended correspondence analysis (DCA) for the 5 main land cover types with scores for each individual. The analysis was based on a quantification of land cover classes around a 5 km radius where an individual was found using the Corine landcover data set 2018.

5 References

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9.4 Supplementary information – Chapter 5

Spatial variation of rodenticides and emerging contaminants in blood of raptor nestlings from Germany

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Tables SI-1-7

Table SI-1: Biometric data of the investigated species. Common buzzards (*Buteo buteo*, BUBT), Montagu's harriers (*Circus pygargus*, CIPY), white-tailed sea eagles (*Haliaeetus albicilla*, HAAL), red kites (*Milvus milvus*, MIML), and ospreys (*Pandion haliaetus*, PAHA). NA = no data available

Id	Species	Year	Wing length	Weight	No of nestlings per nest
1	BUBT	2019	92	420	3
2	BUBT	2019	200	660	2
3	BUBT	2019	143	575	2
4	BUBT	2019	149	715	1
5	BUBT	2019	191	725	3
6	BUBT	2019	158	620	3
7	BUBT	2019	275	820	3
47	BUBT	2019	222	690	NA
48	BUBT	2019	235	940	1
49	BUBT	2019	232	880	2
84	BUBT	2020	243	840	1
85	BUBT	2020	241	925	3
86	BUBT	2020	211	835	1
87	BUBT	2020	317	920	2
102	BUBT	2020	246	745	2
103	BUBT	2020	197	830	2
104	BUBT	2020	173	860	2
105	BUBT	2020	159	530	3
106	BUBT	2020	129	600	2
107	BUBT	2020	146	645	1
108	BUBT	2020	187	695	3
109	BUBT	2020	183	700	1
110	BUBT	2020	279	815	2
111	BUBT	2020	184	680	3
112	BUBT	2020	151	660	2

122	BUBT	2020	244	870	1
128	BUBT	2020	NA	NA	NA
129	BUBT	2020	NA	NA	1
130	BUBT	2020	NA	NA	1
131	BUBT	2020	NA	NA	3
132	BUBT	2020	NA	NA	2
133	BUBT	2020	NA	NA	2
134	BUBT	2020	NA	NA	2
135	BUBT	2020	NA	NA	2
161	BUBT	2020	112	560	NA
32	CIPY	2019	230	335	7
33	CIPY	2019	282	337	3
34	CIPY	2019	289	333	3
35	CIPY	2019	218	388	5
36	CIPY	2019	266	378	1
37	CIPY	2019	216	375	4
38	CIPY	2019	161	315	3
39	CIPY	2019	243	372	4
40	CIPY	2019	266	358	3
41	CIPY	2019	236	308	4
42	CIPY	2019	191	343	2
43	CIPY	2019	249	314	3
44	CIPY	2019	192	336	4
45	CIPY	2019	230	327	4
46	CIPY	2019	221	262	2
88	CIPY	2020	189	340	4
89	CIPY	2020	200	330	5
90	CIPY	2020	266	310	4
91	CIPY	2020	189	330	4
92	CIPY	2020	280	320	4
93	CIPY	2020	230	398	4

94	CIPY	2020	228	315	4
95	CIPY	2020	188	387	3
96	CIPY	2020	229	358	3
97	CIPY	2020	204	393	5
98	CIPY	2020	254	336	4
99	CIPY	2020	251	337	5
100	CIPY	2020	274	310	3
101	CIPY	2020	191	400	2
136	HAAL	2019	NA	NA	NA
137	HAAL	2019	NA	NA	1
138	HAAL	2019	NA	NA	1
139	HAAL	2019	NA	NA	2
140	HAAL	2019	NA	NA	1
141	HAAL	2019	NA	NA	1
142	HAAL	2019	NA	NA	2
143	HAAL	2019	NA	NA	1
144	HAAL	2019	NA	NA	3
145	HAAL	2019	NA	NA	1
146	HAAL	2019	NA	NA	3
147	HAAL	2019	NA	NA	1
148	HAAL	2019	NA	NA	2
149	HAAL	2019	NA	NA	2
162	HAAL	2019	292	3920	2
163	HAAL	2019	343	3810	2
164	HAAL	2019	318	3880	1
165	HAAL	2019	232	3610	2
166	HAAL	2019	336	3330	1
167	HAAL	2019	325	3870	1
168	HAAL	2019	178	2300	1
169	HAAL	2019	211	2890	2
170	HAAL	2019	303	3970	1

171	HAAL	2019	159	2630	1
172	HAAL	2019	396	5320	2
173	HAAL	2019	312	4400	2
174	HAAL	2019	331	4090	2
175	HAAL	2019	345	4500	2
176	HAAL	2019	436	4220	2
177	HAAL	2019	502	5450	2
178	HAAL	2019	451	4310	2
179	HAAL	2019	489	5620	2
180	HAAL	2019	406	3780	2
181	HAAL	2019	484	3990	2
150	HAAL	2020	NA	NA	2
151	HAAL	2020	NA	NA	2
152	HAAL	2020	NA	NA	2
153	HAAL	2020	NA	NA	2
154	HAAL	2020	NA	NA	1
155	HAAL	2020	NA	NA	2
156	HAAL	2020	NA	NA	2
157	HAAL	2020	NA	NA	1
158	HAAL	2020	NA	NA	1
159	HAAL	2020	NA	NA	1
160	HAAL	2020	NA	NA	2
182	HAAL	2020	352	5060	2
183	HAAL	2020	213	3540	1
184	HAAL	2020	233	3150	2
185	HAAL	2020	415	3510	1
186	HAAL	2020	273	3310	2
187	HAAL	2020	271	3800	2
188	HAAL	2020	407	5100	1
189	HAAL	2020	352	4650	1
190	HAAL	2020	497	5170	1

191	HAAL	2020	336	3610	1
192	HAAL	2020	346	3670	1
193	HAAL	2020	296	4340	1
194	HAAL	2020	383	4430	2
195	HAAL	2020	514	5360	1
196	HAAL	2020	355	3820	2
197	HAAL	2020	381	3880	1
198	HAAL	2020	285	4290	1
199	HAAL	2020	245	3670	1
200	HAAL	2020	254	3540	2
8	MIML	2019	259	920	2
9	MIML	2019	217	630	1
10	MIML	2019	204	660	2
11	MIML	2019	287	880	1
12	MIML	2019	255	900	1
13	MIML	2019	254	860	3
14	MIML	2019	184	720	2
15	MIML	2019	240	810	3
16	MIML	2019	242	790	2
17	MIML	2019	317	950	2
18	MIML	2019	305	990	2
19	MIML	2019	170	630	2
20	MIML	2019	350	910	2
21	MIML	2019	304	910	1
22	MIML	2019	338	1100	2
23	MIML	2019	356	1250	3
50	MIML	2019	335	1035	NA
51	MIML	2019	203	840	3
52	MIML	2019	368	1020	NA
53	MIML	2019	194	780	NA
54	MIML	2019	258	900	1

55	MIML	2019	350	1040	2
56	MIML	2019	206	840	NA
57	MIML	2019	199	895	NA
58	MIML	2020	263	870	1
59	MIML	2020	329	1010	3
60	MIML	2020	285	940	1
61	MIML	2020	296	870	3
62	MIML	2020	334	910	2
63	MIML	2020	218	880	1
64	MIML	2020	295	980	2
65	MIML	2020	325	1010	3
66	MIML	2020	331	950	2
67	MIML	2020	250	790	2
68	MIML	2020	301	890	2
69	MIML	2020	359	895	3
70	MIML	2020	345	1020	3
71	MIML	2020	340	1000	1
72	MIML	2020	323	920	3
73	MIML	2020	353	950	2
74	MIML	2020	356	885	3
75	MIML	2020	351	1000	NA
76	MIML	2020	330	1045	2
113	MIML	2020	323	990	3
114	MIML	2020	269	905	3
115	MIML	2020	241	905	2
116	MIML	2020	192	815	1
117	MIML	2020	319	NA	1
118	MIML	2020	344	1030	3
119	MIML	2020	35	970	3
120	MIML	2020	281	1010	2
121	MIML	2020	152	710	2

123	MIML	2020	284	1050	3
24	PAHA	2019	315	1250	2
25	PAHA	2019	320	1150	2
26	PAHA	2019	289	1150	3
27	PAHA	2019	271	1040	3
28	PAHA	2019	303	1460	3
29	PAHA	2019	338	1600	3
30	PAHA	2019	323	1230	3
31	PAHA	2019	330	1700	4
201	PAHA	2019	308	1720	3
202	PAHA	2019	218	1270	3
203	PAHA	2019	245	1290	2
204	PAHA	2019	361	1370	2
205	PAHA	2019	364	1500	1
77	PAHA	2020	225	1340	1
78	PAHA	2020	204	820	2
79	PAHA	2020	352	1280	2
80	PAHA	2020	208	1000	2
81	PAHA	2020	213	1080	2
82	PAHA	2020	251	1400	2
83	PAHA	2020	226	1030	3
206	PAHA	2020	352	1460 (wet)	2
207	PAHA	2020	NA	1830 (wet)	2
208	PAHA	2020	364	1660	2

Table SI-2: Tonnages of plant protection products based on the inland sales (Germany) of active substances in 2019 (BVL, 2020). Dates of withdrawn plant protection products during the sampling period (until 01/08/2021) are indicated in bold. Further information can be found here: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=search.as. Sales of veterinary medicinal products in 2019 were based on Wallmann et al. (2020). HMP: Human Medicinal Product. VMP: Veterinary Medicinal Product.

Name	Intended use	CAS	Detected	End of Authorisation	Tonnage (2019)
Brodifacoum	Biocide	56073-10-0			
Bromadiolone	Biocide	28772-56-7			
Chlorophacinone	Biocide	3691-35-8			
Coumatetralyl	Biocide	5836-29-3			
Difenacoum	Biocide	56073-07-5			
Difethialone	Biocide	104653-34-1			
Flocoumafen	Biocide	90035-08-8			
Warfarin	Biocide	81-81-2			
2,4-D	Herbicide	94-75-7		31/12/2030	25-100
Acetamiprid	Insecticide	135410-20-7		28/02/2033	10-25
Aclonifen	Herbicide	74070-46-5		31/07/2022	250-1000
Amisulbrom	Fungicide	348635-87-0		30/09/2024	<1
Azoxystrobin	Fungicide	131860-33-8		31/12/2024	250-1000
Bentazone	Herbicide	25057-89-0		31/05/2025	/
Bixafen	Fungicide	581809-46-3		31/05/2025	25-100
Boscalid	Fungicide	188425-85-6		31/07/2022	100-250
Bromoxynil	Herbicide	1689-84-5	X	**31/07/2021**	25-100
Chlorantraniliprole	Insecticide	500008-45-7		31/12/2024	2.5-10
Chloridazon	Herbicide	1698-60-8		**31/12/2018**	1.0-2.5
Chlorotoluron	Herbicide	15545-48-9		31/10/2021	250-1000
Chlorpyrifos	Insecticide	2921-88-2		**16/01/2020**	/
Clothianidin	Insecticide	210880-92-5		**31/01/2019**	/export
Cyazofamid	Fungicide	120116-88-3		31/07/2036	10-25
Cyprodinil	Fungicide	121552-61-2		30/04/2022	25-100
Dichlorprop-P	Herbicide	15165-67-0		30/04/2022	25-100
Difenoconazole	Fungicide	119446-68-3		31/12/2021	100-250
Diflufenican	Herbicide	83164-33-4		31/12/2021	250-1000
Dimethachlor	Herbicide	50563-36-5		31/12/2021	10-25
Dimethenamid-P	Herbicide	163515-14-8		31/08/2034	250-1000
Dimethoate	Insecticide	60-51-5		**31/07/2019**	100-250
Dimethomorph	Fungicide	110488-70-5		31/07/2022	25-100
Dimoxystrobin	Fungicide	149961-52-4		31/01/2022	10-25
Epoxiconazole	Fungicide	106325-08-0		**30/04/2020**	100-250

Ethofumesate	Herbicide	26225-79-6		31/10/2031	250-1000
Famoxadone	Fungicide	131807-57-3		30/06/2022	2.5-10
Fenpropidin	Fungicide	67306-00-7	X	31/12/2021	100-250
Fenpropimorph	Fungicide	67564-91-4	X	**30/04/2019**	100-250
Fipronil	Insecticide/Biocide	120068-37-3		**30/09/2017**	/
Florasulam	Herbicide	145701-23-1		31/12/2030	10-25
Fludioxonil	Fungicide	131341-86-1		31/10/2021	25-100
Flufenacet	Herbicide	142459-58-3		31/10/2021	250-1000
Flumioxazin	Herbicide	103361-09-7		30/06/2022	2.5-10
Fluopicolide	Fungicide	239110-15-7		31/05/2023	10-25
Flupyrsulfuron-methyl	Herbicide	144740-53-4		**31/12/2017**	/
Fluroxypyr	Herbicide	69377-81-7		31/12/2024	100-250
Flurtamone	Herbicide	96525-23-4		**31/10/2019**	25-100
Fluxapyroxad	Fungicide	907204-31-3		31/05/2025	25-100
Foramsulfuron	Herbicide	173159-57-4		31/05/2035	25-100
Imazosulfuron	Herbicide	122548-33-8		**31/07/2017**	/
Imidacloprid	Insecticide	138261-41-3		01/12/2020	<1
Iodosulfuron-methyl	Herbicide	144550-06-1		31/03/2032	2.5-10
Isoproturon	Herbicide	34123-59-6		**31/12/2015**	/
Isopyrazam	Fungicide	881685-58-1		31/03/2023	25-100
Lenacil	Herbicide	2164-08-1		31/12/2021	25-100
MCPA	Herbicide	94-74-6	X	31/10/2021	250-1000
Mecoprop-P	Herbicide	16484-77-8		31/01/2021	25-100
Mesosulfuron-methyl	Herbicide	208465-21-8		30/06/2032	2.5-10
Mesotrione	Herbicide	104206-82-8		31/05/2032	100-250
Metamitron	Herbicide	41394-05-2		31/08/2022	1000-2500
Metazachlor	Herbicide	67129-08-2		31/07/2022	250-1000
Metconazole	Fungicide	125116-23-6		30/04/2022	25-100
Methiocarb	Insecticide	2032-65-7		**03/10/2019**	25-100
Metosulam	Herbicide	139528-85-1		30/04/2021	<1
Metrafenone	Fungicide	220899-03-6		07/04/2022	25-100
Metribuzin	Herbicide	21087-64-9		31/07/2022	25-100
Metsulfuron-methyl	Herbicide	74223-64-6		31/03/2023	2.5-10
Napropamide	Herbicide	15299-99-7		31/12/2023	25-100
Nicosulfuron	Herbicide	111991-09-4		31/12/2021	10-25

Omethoate	Dimethoate metab.	1113-02-6			/
Pendimethalin	Herbicide	40487-42-1		30/11/2024	250-1000
Pethoxamid	Herbicide	106700-29-2		30/11/2033	100-250
Picolinafen	Herbicide	137641-05-5		30/06/2031	1.0-2.5
Picoxystrobin	Fungicide	117428-22-5		**31/10/2017**	/
Pirimicarb	Insecticide	23103-98-2		30/04/2022	25-100
Prochloraz	Fungicide	67747-09-5		31/12/2023	100-250
Propiconazole	Fungicide	60207-90-1		19/12/2018	25-100
Propyzamide	Herbicide	23950-58-5		30/06/2025	100-250
Proquinazid	Fungicide	189278-12-4		31/07/2022	2.5-10
Prosulfuron	Herbicide	94125-34-5		31/07/2024	1.0-2.5
Pymetrozine	Insecticide	123312-89-0		**30/04/2019**	10-25
Pyraclostrobin	Fungicide	175013-18-0		31/01/2022	25-100
Pyroxsulam	Herbicide	422556-08-9		30/04/2025	10-25
Quinmerac	Herbicide	90717-03-6		31/07/2024	25-100
Quinoxyfen	Fungicide	124495-18-7		**30/04/2019**	2.5-10
S-Metolachlor	Herbicide	87392-12-9		31/07/2022	250-1000
Spinosyn A	Insecticide	131929-60-7		30/04/2022 (Spinosad)	2.5-10 (Spinosad)
Spiroxamine	Fungicide	118134-30-8	X	31/12/2023	250-1000
Sulcotrione	Fungicide	99105-77-8		31/08/2022	/
Tebuconazole	Fungicide	107534-96-3		31/08/2022	250-1000
Terbuthylazine	Herbicide	5915-41-3	X	31/12/2024	250-1000
Thiacloprid	Insecticide	111988-49-9		**03/02/2020**	25-100
Thiamethoxam	Insecticide	153719-23-4		**30/04/2019**	/
Thifensulfuron-methyl	Herbicide	79277-27-3		31/10/2031	10-25
Triadimenol	Fungicide	55219-65-3		**31/08/2019**	25-100
Triasulfuron	Herbicide	82097-50-5		**31/12/2015**	/
Trifloxystrobin	Fungicide	141517-21-7		31/07/2033	10-25
Tritosulfuron	Herbicide	142469-14-5		30/11/2021	10-25
Zoxamide	Fungicide	156052-68-5		30/06/2033	2.5-10
Ciprofloxacin	HMP	85721-33-1			
Diclofenac	HMP	15307-86-5			
Ibuprofen	HMP	15687-27-1			
Sulfadiazine	HMP	68-35-9			
Enrofloxacin	VMP	93106-60-6			4,770
Marbofloxacin	VMP	115550-35-1			1,155
Sulfamethazine	VMP	57-68-1			/

Table SI-3: Sample preparation and extraction.

Defrosting of blood samples, pipetting 200 µl in pp - tubes (15 mL)

⇩

Spike with surrogates (20 µl with 1 ng/µL)

⇩

Addition of 1.98 mL acetonitrile

⇩

Vortex with steel ball (30 sec)

⇩

Ultrasound 5 min

⇩

Centrifugation (Heraeus Megafuge 16 R) 10 min with 5,000 rpm at RT

⇩

Transfer an aliquot of supernatant in a new pp - tube

⇩

Repeat extraction with 2 mL acetonitrile

⇩

Combine the supernatants

⇩

Reduce aliquots (200 µL) to dryness with nitrogen

⇩

Resuspend the residue with 0.5 ml internal standards
in methanol/water for Method A, B, C, E
in acetonitrile/water for Method D

⇩

Briefly ultrasound

⇩

Filtration through syringe filter (0.2 µm PTFE)

⇩

Storage at -20°C until analysis

⇩

LC-MS/MS

Table SI-4: Configuration of LC-MS/MS for five methods (A-E).

Method A

LIQUID CHROMATOGRAPHY	**Agilent Infinity 1290 II**		
Autosampler temperature	10 °C		
Injection volume	10 µL		
Analytical column	Agilent Zorbax Eclipse C18 (1.8 µm, 50 mm, 2.1 mm i.d.)		
Column temperature	40 °C		
Mobile phase A	H_2O +1 mmol NH_4F		
Mobile phase B	Methanol / Acetonitrile (65/35)		
Gradient program	Time (min)	A (%)	B (%)
	0.0	98	2
	2.5	2	98
	4.0	2	98
	4.1	98	2
	6.0	98	2
Flow rate	500 µL/min		
MASS SPECTROMETER	**QTRAP 6500+ (SCIEX)**		
Mode	negative ESI		
Ion spray potential	-4500 V		
Source temperature	550 °C		
Scan type	Multiple Reaction Monitoring / Enhanced Product Ion		

Method B

LIQUID CHROMATOGRAPHY	**Agilent Infinity 1290 II**		
Autosampler temperature	10 °C		
Injection volume	5 µL		
Analytical column	Agilent Zorbax Eclipse C18 (1,8 µm, 50 mm, 2.1 mm i.d.)		
Column temperature	40 °C		
Mobile phase A	H_2O +5 mmol NH_4formate + 0.5% formic acid		
Mobile phase B	Methanol +5 mmol NH_4formate +0.5% formic acid		
Gradient program	Time (min)	A (%)	B (%)
	0.0	98	2
	2.5	2	98
	5.0	2	98
	5.1	98	2
	6.0	98	2
Flow rate	500 µL/min		
MASS SPECTROMETER	**QTRAP 6500+ (SCIEX)**		
Mode	positive ESI		
Ion spray potential	5500 V		
Source temperature	550 °C		
Scan type	Multiple Reaction Monitoring / Enhanced Product Ion		

Method C

LIQUID CHROMATOGRAPHY	**Agilent Infinity 1290 II**		
Autosampler temperature	10 °C		
Injection volume	5 µL		
Analytical column	Agilent Zorbax Eclipse C18 (1.8 µm, 50 mm, 2.1 mm i.d.)		
Column temperature	40 °C		
Mobile phase A	H_2O +1 mmol NH_4F		
Mobile phase B	Methanol / Acetonitrile (65/35)		
Gradient program	Time (min)	A (%)	B (%)
	0.00	98	2
	3.00	2	98
	4.50	2	98
	4.51	98	2
	6.00	98	2
Flow rate	500 µL/min		
MASS SPECTROMETER	**QTRAP 6500 (SCIEX)**		
Mode	positive ESI		
Ion spray potential	5500 V		
Source temperature	550 °C		
Scan type	Multiple Reaction Monitoring / Enhanced Product Ion		

Method D

LIQUID CHROMATOGRAPHY	**Agilent Infinity 1290 II**		
Autosampler temperature	10 °C		
Injection volume	10 µL		
Analytical column	Agilent Zorbax Eclipse (1.8 µm, 50 mm, 2.1 mm i.d.)		
Column temperature	40 °C		
Mobile phase A	H_2O +1 mmol NH_4F + 0.1% formic acid		
Mobile phase B	Acetonitrile + 0.1% formic acid		
Gradient program	Time (min)	A (%)	B (%)
	0.0	98	2
	0.5	98	2
	3.0	2	98
	4.0	2	98
	4.1	98	2
	5.0	98	2
Flow rate	500 µL/min		
MASS SPECTROMETER	**QTRAP 6500+ (SCIEX)**		
Mode	positive ESI		
Ion spray potential	5500 V		
Source temperature	500 °C		
Scan type	Multiple Reaction Monitoring / Enhanced Product Ion		

Method E

LIQUID CHROMATOGRAPHY	**Agilent Infinity 1290 II**		
Autosampler temperature	10 °C		
Injection volume	10 µL		
Analytical column	Agilent Zorbax Eclipse C18 (1.8 µm, 50 mm, 2.1 mm i.d.)		
Column temperature	40 °C		
Mobile phase A	H_2O +1 mmol NH_4F		
Mobile phase B	Methanol / Acetonitrile (65/35)		
Gradient program	Time (min)	A (%)	B (%)
	0.0	98	2
	2.5	2	98
	4.0	2	98
	4.1	98	2
	5.0	98	2
Flow rate	500 µL/min		
MASS SPECTROMETER	**QTRAP 6500+(SCIEX)**		
Mode	negative ESI		
Ion spray potential	-4500 V		
Source temperature	500 °C		
Scan type	Multiple Reaction Monitoring / Enhanced Product Ion		

Table SI-5: LC-MS/MS – MRM- and EPI-conditions (precursor (Q1) and product ions (Q3) in m/z and declustering potential (DP), entrance potential (EP), collision energy (CE) and cell exit potential (CXP) in V).

Q1	Q3	Analyte	DP	EP	CE	CXP
Method A						
520.9	78.8	Brodifacoum	-20	-10	-128	-11
526.9	249.9	Bromadiolone	-30	-10	-50.	-19
373.1	201.0	Chlorophacinone	-75	-10	-30	-13
291.0	140.9	Coumatetralyl	-125	-10	-38	-13
443.1	135.0	Difenacoum	-55	-10	-46	-15
538.9	80.8	Difethialone	-20	-10	-92	-13
541.0	382.0	Flocoumafen	-65	-10	-36	-29
307.0	161.0	Warfarin	-45	-10	-26	-19
351.9	265.0	Acenocoumarol (Surr)	-70	-10	-40	-13
532.0	255	Bromadiolone D5 (Surr)	-30	-10	-50	-19
340.9	160.8	Coumachlor (Surr)	-60	-10	-30	-21
343.1	167.0	Diphacinone D4 (Surr)	-115	-10	-32	-15
278.9	250.0	Phenprocoumon (Surr)	-55	-10	-32	-17
377.1	200.9	Chlorophacinone D4 (IS)	-120	-10	-32	-15
312.1	161.0	Warfarin D5 (IS)	-95	-10	-28	-9
Method B						
223.1	125.9	Acetamiprid	101	10	33	8
265.0	182.1	Aclonifen	36	10	39	2.6
403.9	372.0	Azoxystrobin	51	10	17	24
414.1	394.0	Bixafen	76	10	21	24
343.0	307.0	Boscalid	54	10	27	3.6
222.0	92.2	Chloridazon	39	10	35	1.8
213.1	72.0	Chlorotoluron	34	10	33	1.6
350.0	96.7	Chlorpyrifos	51	10	55	11
250.1	169.0	Clothianidin	42	10	19	12

226.1	108.0	Cyprodinil	106	10	35	8
406.1	250.9	Difenoconazole	41	10	37	3.3
395.1	266.1	Diflufenican	81	10	35	22
256.1	224.2	Dimethachlor	24	10	19	3
276.1	244.1	Dimethenamid-P	86	10	19	12
230.0	125.0	Dimethoate	14	10	29	2.1
388.1	301.1	Dimethomorph	41	10	27	3.6
329.9	121.0	Epoxiconazole	66	10	29	12
392.0	331.0	Famoxadone	26	10	13	15
274.2	147.1	Fenpropidin	31	10	37	2.3
304.3	147.1	Fenpropimorph	34	10	39	2.3
360.0	128.9	Florasulam	21	10	31	16
383.1	172.8	Fluopicolide	31	10	27	20
466.0	182.0	Flupyrsulfuron-methyl	91	10	29	10
255.0	209.1	Fluroxypyr	49	10	21	2.9
334.2	247.2	Flurtamone	86	10	35	20
381.8	342.0	Fluxapyroxad	50	10	30	10
453.1	182.2	Foramsulfuron	31	10	27	10
413.0	156.0	Imazosulfuron	25	10	20	20
256.1	175.0	Imidacloprid	49	10	25	10
507.8	167.0	Iodosulfuron-methyl	71	10	25	10
207.1	72.0	Isoproturon	46	10	19	10
360.2	244.0	Isopyrazam	56	10	31	22
235.1	153.1	Lenacil	34	10	21	10
504.0	182.0	Mesosulfuron-methyl	81	10	31	10
203.1	175.0	Metamitron	49	10	29	2.5
278.1	210.1	Metazachlor	15	10	15	20
417.9	175.0	Metosulam	61	10	35	14
215.1	187.2	Metribuzin	29	10	25	2.6
382.1	198.9	Metsulfuron-methyl	34	10	27	10
272.1	129.1	Napropamid	46	10	21	10
282.0	212.0	Pendimethalin	50	10	15	25
296.1	131.1	Pethoxamid	39	10	27	2.1
377.1	237.9	Picolinafen	46	10	39	14
239.2	182.3	Pirimicarb	66	10	21	10
342.1	69.1	Propiconazole	15	10	25	15
256.0	173.1	Propyzamide	39	10	31	2.5
372.9	331.0	Proquinazid	66	10	19	24
420.0	141.0	Prosulfuron	76	10	27	16
218.1	104.9	Pymetrozine	61	10	29	12
435.1	194.9	Pyroxsulam	51	10	35	18
222.0	204.1	Quinmerac	24	10	23	2.8
307.9	162.0	Quinoxyfen	21	10	57	2.4
284.1	251.9	S-Metolachlor	14	10	19	3.3
732.4	142.1	Spinosyn A	81	10	39	10
298.3	144.2	Spiroxamine	41	10	27	2.3
346.0	139.0	Sulcotrione	41	10	31	2.3
308.1	70.0	Tebuconazole	86	10	51	10
230.2	174.0	Terbuthylazine	106	10	23	54

252.8	126.0	Thiacloprid	41	10	33	8
388.0	167.0	Thifensulfuron-methyl	29	10	21	10
402.1	167.1	Triasulfuron	44	10	25	2.5
409.1	186.1	Trifloxystrobin	19	10	23	10
446.0	195.0	Tritosulfuron	50	10	30	10
336.0	187.0	Zoxamide	36	10	31	16
253.0	172.0	Clothianidin D3 (Surr)	42	10	19	14
412.1	250.9	Difenoconazole D6 (Surr)	41	10	37	3.3
236.0	131.0	Dimethoate D6 (Surr)	14	10	29	10
235.0	179.0	Terbuthylazin D5 (Surr)	76	10	25	10
257.1	126.0	Thiacloprid D4 (Surr)	116	10	31	14
226.0	126.0	Acetamiprid D3 (IS)	56	10	31	10
221.1	179.1	Atrazin D5 (IS)	21	10	25	10
295.0	70.0	Cyproconazol D3 (IS)	16	10	35	10
260.0	213.0	Imidacloprid D4 (IS)	86	10	23	10
213.2	78.0	Isoproturon D6 (IS)	1	10	21	6
147.9	97.0	Methamidiohos D6 (IS)	56	10	23	10
229.2	168.9	Methiocarb D3 (IS)	15	10	15	25
Method C						
466.0	226.9	Amisulbrom	15	10	30	25
484.2	452.9	Chlorantraniliprole	91	10	23	10
325.1	107.9	Cyazofamid	15	10	20	15
327.2	205.1	Dimoxystrobin	49	10	15	10
304.0	240.8	Ethofumesate	15	10	20	20
364.0	194.1	Flufenacet	21	10	15	12
355.0	299.0	Flumioxazin	100	10	45	10
320.1	70.1	Metconazole	36	10	45	10
226.1	169.1	Methiocarb	15	10	15	20
409.1	209.1	Metrafenone	39	10	21	10
411.0	182.1	Nicosulfuron	41	10	25	10
214.1	109.0	Omethoate	31	11.5	35	10
282.1	212.0	Pendimethalin	1	10	15	10
368.1	145.0	Picoxystrobin	39	10	27	10
375.9	308.0	Prochloraz	25	10	20	15
189.2	102.0	Propamocarb	16	10	23	1.9
388.1	194.0	Pyraclostrobin	19	10	19	10
251.3	155.9	Sulfadiazin	106	10	21	10
279.3	186.0	Sulfamethazin	56	10	27	10
292.0	211.0	Thiamethoxam	34	10	17	10
296.1	69.9	Triadimenol	46	10	33	10
255.1	160.1	Sulfdiazin D4 (Surr)	71	10	23	10
221.1	179.1	Atrazin D5 (IS)	21	10	25	10
295.0	70.0	Cyproconazol D3 (IS)	16	10	35	10
147.9	97.0	Methamidiohos D6 (IS)	56	10	23	10
229.2	168.9	Methiocarb D3 (IS)	15	10	15	25
Method D						
332.0	314.0	Ciprofloxacin	1	10	29	16
360.0	342.1	Enrofloxacin	1	10	29	18
363.0	345.0	Marbofloxacin	76	10	29	18

339.9	322.1	Ciprofloxacin D8 (Surr)	121	10	29	18
221.1	179.1	Atrazine D5 (IS)	21	10	25	10
Method E						
218.9	160.9	2.4 D	-45	-10	-16	-13
239.0	132.0	Bentazone	-55	-10	-36	-9
275.7	81.0	Bromoxynil	-60	-10	-62	-7
232.9	160.8	Dichlorprop-P	-50	-10	-18	-15
293.9	250.0	Diclofenac	-55	-10	-10	-16
373.0	282.0	Famoxadone	-65	-10	-26	-25
434.9	329.9	Fipronil	-5	-10	-22	-19
247.0	180.0	Fludioxonil	-35	-10	-40	-9
205.0	161.0	Ibuprofen	-45	-10	-10	-9
199.0	140.9	MCPA	-60	-10	-20	-9
213.0	140.9	Mecoprop-P	-65	-10	-20	-17
338.0	291.0	Mesotrione	-20	-10	-20	-10
327.0	291.0	Sulcotrione	-20	-10	-10	-20
298.1	254.0	Diclofenac D4 (Surr)	-55	-10	-16	-19
312.1	161.0	Warfarin D5 (IS)	-95	-10	-28	-9

EPI (enhanced product ion spectra)				
Mass range		**DP**	**EP**	**CE**
50 – 450 m/z		-50/+50	-10/+10	-30/+30 (± 15)
EPI spectra in the sample agree > 80% with standards in the same sequence (response >500 cps)				

Software	Analyst 1.7.1
Quantification	Relative peak area

Matrix matched standard: 0.01 - 20 pg/µl

Table SI-6a: Validation - RECovery of analytes (10, 100, 1000 ng/ml pig blood; n =5 / in control samples all not detected; n = 2 / (RSD= relative standard deviation) and Reporting Limit (RL) (n. d. (not detected) = < RL) (HMP=human medicinal product; VMP= veterinary medicinal product).

Analyte	**Intended use**	**RL**	**REC**	**RSD**	**REC**	**RSD**	**REC**	**RSD**
		ng/ml	10 ng/ml		100 ng/ml		1000 ng/ml	
			%		%		%	
Brodifacoum	Biocide	5	**71**	15	**84**	5	**83**	8
Bromadiolone	Biocide	5	**79**	9	**101**	8	**94**	6
Chlorophacinone	Biocide	10	**84**	8	**90**	4	**88**	4
Coumatetralyl	Biocide	0.5	**95**	4	**87**	2	**86**	5
Difenacoum	Biocide	2.5	**86**	13	**94**	6	**89**	7
Difethialone	Biocide	2.5	**66**	16	**88**	10	**84**	11
Flocoumafen	Biocide	0.5	**74**	17	**93**	8	**87**	9
Warfarin	Biocide	0.5	**105**	6	**102**	4	**101**	4
2,4-D	Herbicide	5	**77**	8	**77**	5	**72**	10
Acetamiprid	Insecticide	5	**96**	9	**91**	4	**94**	4
Aclonifen	Herbicide	25	**n. d.**		**65**	5	**75**	9
Amisulbrom	Fungicide	5	**70**	24	**67**	10	**84**	9
Azoxystrobin	Fungicide	1	**99**	7	**93**	7	**99**	11
Bentazone	Herbicide	0.5	**88**	5	**90**	4	**90**	3
Bixafen	Fungicide	1	**89**	8	**89**	4	**94**	3
Boscalid	Fungicide	2.5	**92**	9	**82**	4	**91**	5
Bromoxynil	Herbicide	2.5	**79**	7	**79**	4	**90**	3
Chlorantraniliprole	Insecticide	1	**88**	6	**87**	4	**90**	3
Chloridazon	Herbicide	25	**n. d.**		**91**	5	**90**	5
Chlorotoluron	Herbicide	2.5	**92**	5	**85**	4	**85**	5
Chlorpyrifos	Insecticide	5	**57**	4	**44**	22	**33**	21
Clothianidin	Insecticide	5	**88**	18	**90**	13	**90**	9
Cyazofamid	Fungicide	0.5	**78**	9	**75**	8	**78**	3
Cyprodinil	Fungicide	25	**n. d.**		**62**	10	**62**	6
Dichlorprop-P	Herbicide	0.5	**72**	9	**77**	6	**75**	7
Difenoconazole	Fungicide	2.5	**86**	6	**79**	10	**81**	4
Diflufenican	Herbicide	5	**85**	12	**76**	9	**76**	10
Dimethachlor	Herbicide	2.5	**70**	11	**55**	33	**37**	21
Dimethenamid-P	Herbicide	5	**56**	15	**43**	37	**28**	33
Dimethoate	Insecticide	5	**86**	7	**82**	13	**70**	10
Dimethomorph	Fungicide	2.5	**96**	6	**93**	4	**96**	4
Dimoxystrobin	Fungicide	1	**89**	7	**83**	6	**84**	2
Epoxiconazole	Fungicide	2.5	**87**	5	**83**	7	**87**	4
Ethofumesate	Herbicide	10	**80**	14	**63**	12	**67**	15
Famoxadone	Fungicide	2.5	**69**	30	**69**	17	**57**	28
Fenpropidin	Fungicide	2.5	**63**	9	**50**	23	**20**	31
Fenpropimorph	Fungicide	1	**55**	6	**45**	25	**23**	24
Fipronil	Insecticide/Biocide	0.5	**91**	8	**88**	7	**95**	5
Florasulam	Herbicide	5	**96**	5	**91**	4	**88**	3
Fludioxonil	Fungicide	0.5	**87**	8	**84**	4	**94**	3

Flufenacet	Herbicide	0.5	**81**	6	**72**	11	**68**	6
Flumioxazin	Herbicide	5	**n.d.**		**41**	14	**71**	14
Fluopicolide	Fungicide	5	**91**	6	**87**	6	**94**	4
Flupyrsulfuron-methyl	Herbicide	5	**90**	12	**89**	8	**92**	7
Fluroxypyr	Herbicide	50	**n.d.**		**56**	11	**82**	8
Flurtamone	Herbicide	2.5	**98**	15	**94**	7	**91**	9
Fluxapyroxad	Fungicide	2.5	**94**	8	**91**	3	**97**	4
Foramsulfuron	Herbicide	5	**88**	13	**85**	8	**82**	4
Imazosulfuron	Herbicide	2.5	**98**	12	**108**	12	**124**	9
Imidacloprid	Insecticide	5	**74**	12	**84**	6	**86**	4
Iodosulfuron-methyl	Herbicide	5	**102**	5	**97**	5	**95**	1
Isoproturon	Herbicide	2.5	**88**	7	**82**	6	**80**	5
Isopyrazam	Fungicide	2.5	**97**	7	**93**	4	**95**	3
Lenacil	Herbicide	25	**n.d.**		**87**	10	**96**	10
MCPA	Herbicide	1	**69**	5	**74**	5	**72**	11
Mecoprop-P	Herbicide	0.5	**70**	2	**75**	5	**71**	13
Mesosulfuron-methyl	Herbicide	2.5	**101**	13	**93**	5	**94**	8
Mesotrione	Herbicide	50	**n.d.**		**76**	14	**106**	13
Metamitron	Herbicide	25	**n.d.**		**85**	13	**81**	6
Metazachlor	Herbicide	1	**90**	9	**81**	13	**70**	7
Metconazole	Fungicide	0.5	**94**	5	**90**	5	**92**	3
Methiocarb	Insecticide	0.5	**86**	7	**75**	12	**74**	7
Metosulam	Herbicide	5	**92**	3	**91**	6	**86**	3
Metrafenone	Fungicide	0.5	**90**	5	**80**	5	**86**	4
Metribuzin	Herbicide	5	**74**	9	**73**	18	**73**	9
Metsulfuron-methyl	Herbicide	5	**83**	13	**88**	6	**93**	6
Napropamide	Herbicide	5	**87**	5	**79**	10	**73**	7
Nicosulfuron	Herbicide	50	**n.d.**		**66**	19	**75**	6
Omethoate	Dimethoate metab.	2.5	**79**	15	**70**	14	**65**	16
Pendimethalin	Herbicide	5	**75**	9	**51**	26	**40**	7
Pethoxamid	Herbicide	1	**88**	11	**75**	12	**65**	9
Picolinafen	Herbicide	2.5	**86**	9	**75**	7	**82**	6
Picoxystrobin	Fungicide	10	**85**	17	**67**	19	**74**	17
Pirimicarb	Insecticide	2.5	**76**	7	**57**	28	**36**	19
Prochloraz	Fungicide	2.5	**83**	5	**78**	6	**84**	5
Propiconazole	Fungicide	5	**89**	9	**82**	8	**86**	5
Propyzamide	Herbicide	25	**n.d.**		**66**	12	**65**	11
Proquinazid	Fungicide	1	**80**	10	**64**	15	**61**	9
Prosulfuron	Herbicide	5	**96**	5	**94**	5	**101**	5
Pymetrozine	Insecticide	5	**95**	13	**88**	5	**85**	8
Pyraclostrobin	Fungicide	0.5	**87**	5	**80**	5	**87**	4
Pyroxsulam	Herbicide	2.5	**96**	10	**95**	5	**89**	6
Quinmerac	Herbicide	5	**58**	6	**62**	4	**72**	4
Quinoxyfen	Fungicide	5	**76**	14	**58**	10	**64**	7
S-Metolachlor	Herbicide	5	**77**	4	**60**	25	**45**	19

Spinosyn A	Insecticide	2.5	**95**	9	**90**	8	**88**	8
Spiroxamine	Fungicide	1	**58**	5	**44**	30	**20**	34
Sulcotrione	Fungicide	2.5	**84**	8	**85**	3	**84**	5
Tebuconazole	Fungicide	5	**89**	7	**84**	5	**90**	3
Terbuthylazine	Herbicide	5	**81**	5	**67**	15	**58**	12
Thiacloprid	Insecticide	2.5	**92**	7	**94**	13	**97**	3
Thiamethoxam	Insecticide	1	**97**	16	**88**	6	**89**	5
Thifensulfuron-methyl	Herbicide	5	**92**	10	**92**	5	**88**	8
Triadimenol	Fungicide	10	**59**	20	**87**	11	**100**	12
Triasulfuron	Herbicide	5	**96**	5	**96**	5	**89**	4
Trifloxystrobin	Fungicide	2.5	**103**	10	**89**	7	**90**	8
Tritosulfuron	Herbicide	5	**79**	19	**94**	8	**89**	7
Zoxamide	Fungicide	2.5	**92**	11	**85**	5	**85**	9
Ciprofloxacin	HMP	5	**62**	11	**76**	5	**96**	2
Diclofenac	HMP	1	**72**	10	**78**	5	**79**	4
Ibuprofen	HMP	5	**101**	35	**83**	8	**74**	7
Sulfadiazine	HMP	0.5	**85**	3	**85**	3	**88**	5
Enrofloxacin	VMP	2.5	**83**	5	**85**	4	**98**	4
Marbofloxacin	VMP	5	**65**	5	**81**	5	**96**	3
Sulfamethazine	VMP	0.5	**93**	5	**87**	5	**91**	2

Table SI-6b: Validation - RECovery of surrogates (100 ng/ml) added to samples of method development and in practice samples (RSD= relative standard deviation).

	Method		Practice	
Surrogate	**REC**	**RSD**	**REC**	**RSD**
	%			
Method A				
Acenocoumarol	**99**	7	**88**	3
Bromadiolone D5	**94**	8	**94**	6
Coumachlor	**86**	9	**91**	4
Diphacinone D4	**81**	23	**81**	4
Phenprocoumon	**92**	6	**85**	3
Method B				
Clothianidin D3	**99**	7	**94**	9
Difenoconazole D6	**96**	6	**85**	11
Dimethoate D6	**89**	12	**84**	17
Terbuthylazine D5	**90**	13	**68**	19
Thiacloprid D4	**98**	9	**92**	5
Method C				
Sulfdiazine D4	**79**	6	**84**	5
Method D				
Ciprofloxacin D8	**78**	29	**67**	5
Method E				
Diclofenac D4	**75**	7	**76**	4

Table SI-7: Median concentrations ($Q_{0.25}$-$Q_{0.75}$) in ng mL^{-1} for individuals with detectable residues and detection rate [%] of anticoagulant rodenticides (ARs), plant protection products (PPPs) and medicinal products (MPs) in blood of common buzzards (*Buteo buteo*, BUBT), red kites (*Milvus milvus*, MIML), Montagu's harrier (*Circus pygargus*, CIPY), white-tailed sea eagles (*Haliaeetus albicilla*, HAAL) and osprey (*Pandion haliaetus*, PAHA) from Germany. n. d. = not detected. n^+ = samples with detectable residues.

ng mL^{-1}		**BUBT** n=35	**MIML** n=53	**CIPY** n=29	**HAAL** n=64	**PAHA** n=23	**Overall** n=204
Anticoagulant rodenticides (ARs)	**Brodifacoum**	n.d.	13 (8-13)	n.d.	n.d.	n.d.	13 (8-13)
	Detection rate [%]	0	9.4	0	0	0	2.5
	Coumatetralyl	n.d.	1 (1-1.5)	n.d.	n.d.	n.d.	1 (1-1.5)
	Detection rate [%]	0	5.7	0	0	0	1.5
	Difenacoum	n.d.	6.5 (2.5-10.3)	n.d.	n.d.	n.d.	6.5 (2.5-10.3)
	Detection rate [%]	0	7.6	0	0	0	2.0
	Difethialone	27	n.d.	n.d.	n.d.	n.d.	27
	Detection rate [%]	2.9 (n^+=1)	0	0	0	0	0.5 (n^+=1)
	Warfarin	1 (1-1)	1	n.d.	n.d.	n.d.	1 (1-1)
	Detection rate [%]	5.7 (n^+=2)	1.9 (n^+=1)	0	0	0	1.5
	Bromoxynil	42 (29.5-154)	11.5 (9-25.8)	12 (12-16)	5	n.d.	15 (9-40)

Plant protection products (PPPs)	Detection rate [%]	20.0	22.6	31.0	1.6 (n^+=1)	0	14.2
	Fenpropidin	n.d.	n.d.	n.d.	6 (4.5-8.8)	n.d.	6 (4.5-8.75)
	Detection rate [%]	0	0	0	6.3	0	2.0
	Fenpropimorph	2 (2-2)	n.d.	n.d.	3	n.d.	2 (2-2.5)
	Detection rate [%]	5.7 (n^+=2)	0	0	1.6 (n^+=1)	0	1.5
	MCPA	n.d.	n.d.	1.5 (1.3-1.8)	n.d.	n.d.	1.5 (1.25-1.75)
	Detection rate [%]	0	0	6.9 (n^+=2)	0	0	1.0
	Spiroxamine	n.d.	n.d.	n.d.	3 (2.5-6)	n.d.	3 (2.5-6)
	Detection rate [%]	0	0	0	4.7	0	1.5
	Terbuthylazine	n.d.	n.d.	n.d.	4	n.d.	4
	Detection rate [%]	0	0	0	1.6 (n^+=1)	0	0.5 (n^+=1)
Medicinal products (MPs)	**Ciprofloxacin**	13 (12.5-13.5)	6 (6-6)	n.d.	n.d.	5.5 (5.3-5.8)	6 (6-12.5)
	Detection rate [%]	8.6	3.8 (n^+=2)	0	0	8.7 (n^+=2)	3.4

Figures SI-1-4

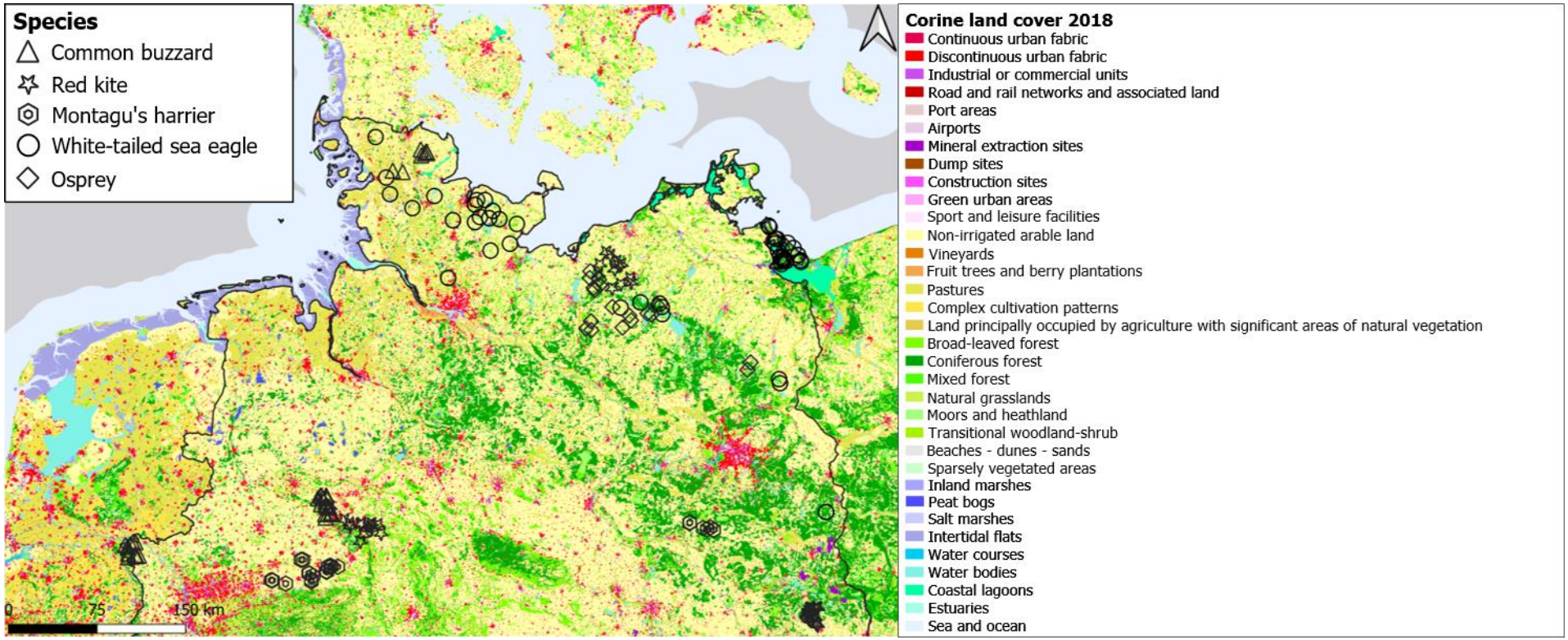

Figure SI-1: Land cover classes extracted from the Corine Land Cover 2018 (EEA, 2018) for the sampling area. Red coloured land cover classes approximate anthropogenic influences, yellow land cover classes approximate agricultural influences, green land cover classes approximate forest and semi-natural areas whereas blue land cover classes approximate aquatic areas. Sampling location of common buzzards (*Buteo buteo*, BUBT) are indicated by triangles, red kites (*Milvus milvus*, MIML) by stars, Montagu's harriers (*Circus pygargus*, CIPY) by doubled hexagons, white-tailed sea eagle (*Haliaeetus albicilla*, HAAL) by circles, and osprey (*Pandion haliaetus*, PAHA) by squares.

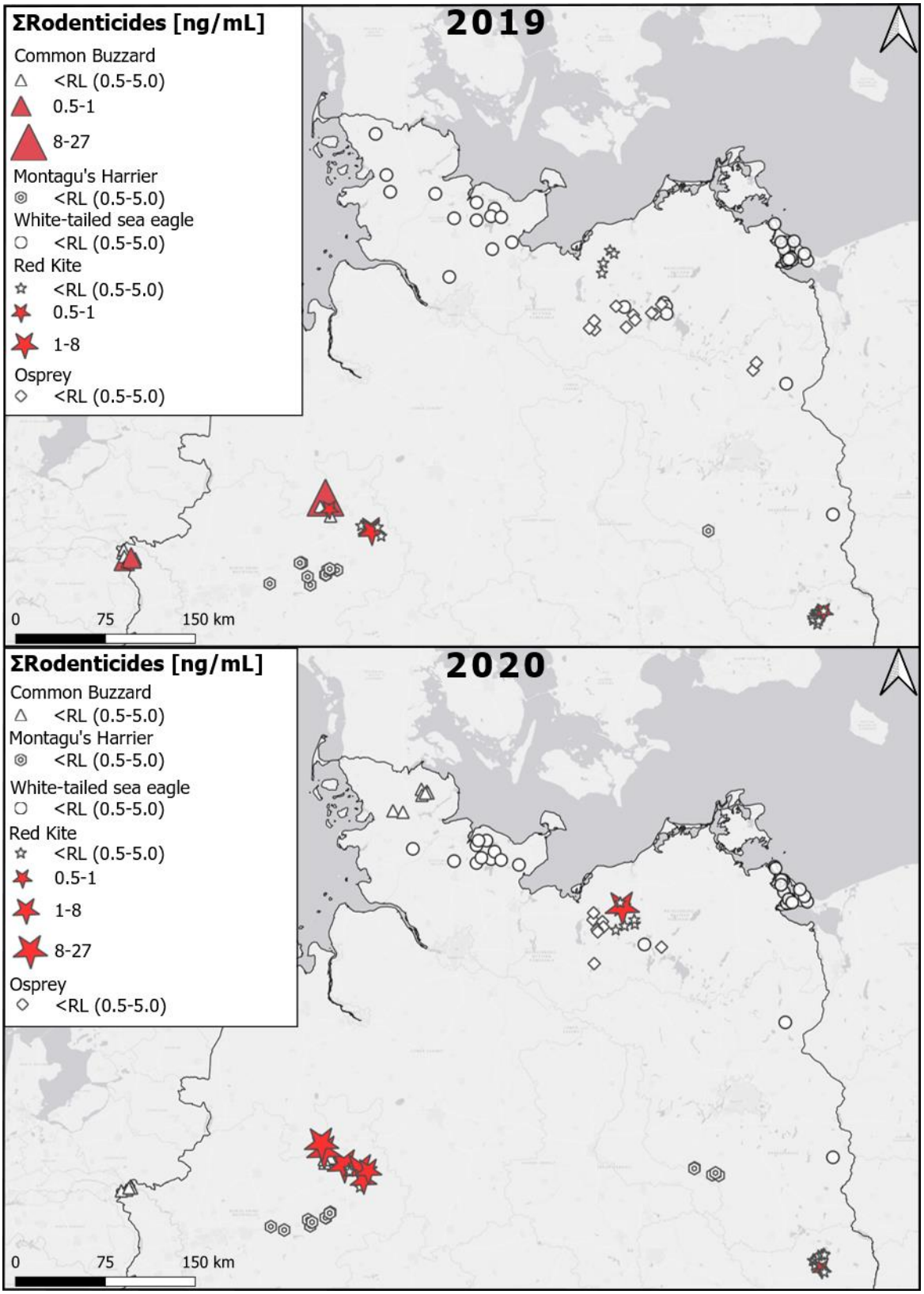

Figure SI-2: Spatial detection of ΣARs (rodenticides) (red) in blood of common buzzards (*Buteo buteo*, BUBT, triangles), Montagu's harriers (*Circus pygargus*, CIPY, doubled hexagons), white-tailed sea eagle (*Haliaeetus albicilla*, HAAL, circles), red kites (*Milvus milvus*, MIML, stars), and osprey (*Pandion haliaetus*, PAHA, squares) nestlings in 2019 and 2020 from Germany. White symbols indicate that the concentrations were below reporting limits (RL) in the respective species.

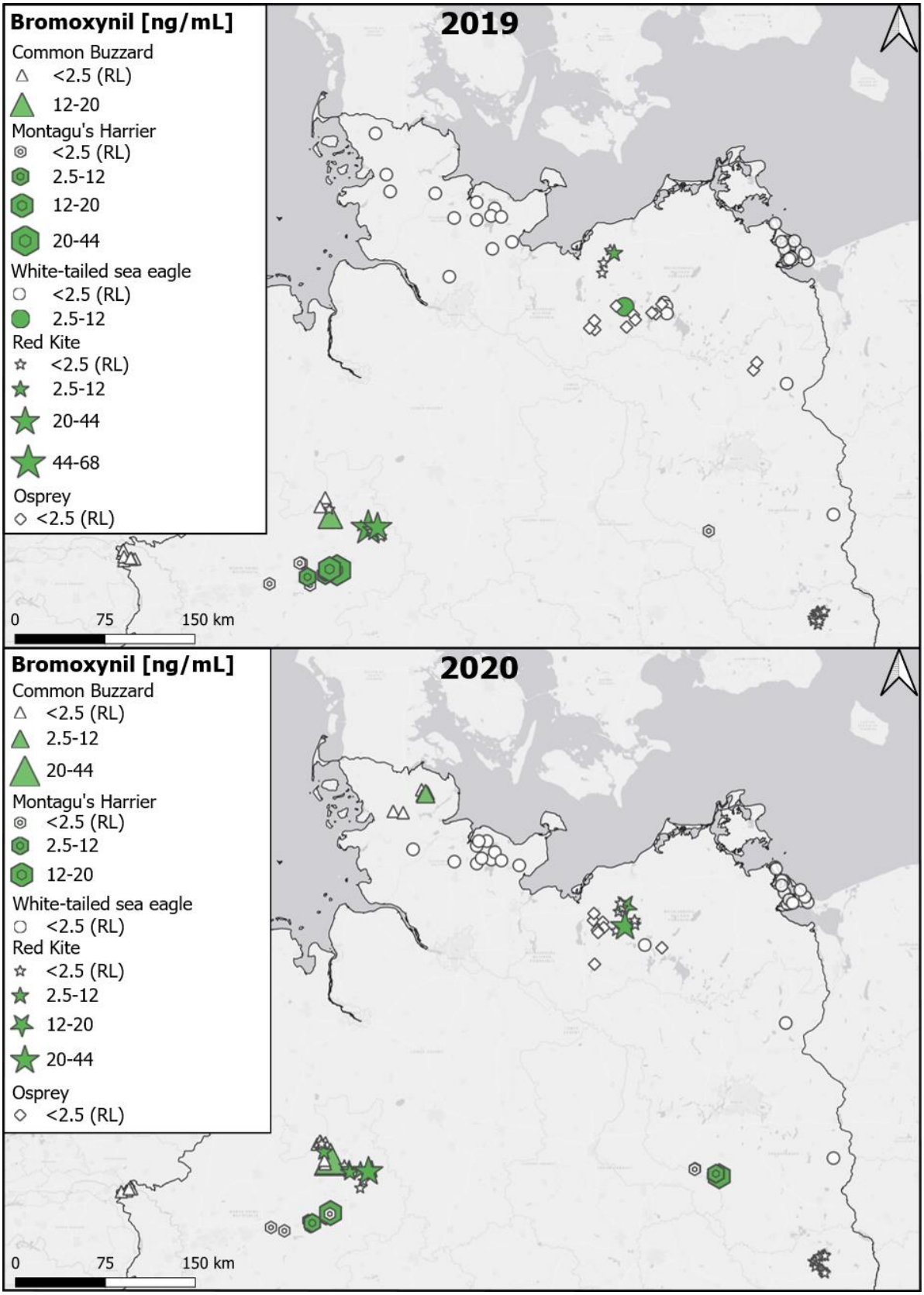

Figure SI-3: Spatial detection of bromoxynil (green) in blood of common (*Buteo buteo*, BUBT, triangles), Montagu's harriers (*Circus pygargus*, CIPY, doubled hexagons), white-tailed sea eagle (*Haliaeetus albicilla*, HAAL, circles), red kites (*Milvus milvus*, MIML, stars), and osprey (*Pandion haliaetus*, PAHA, squares) nestlings in 2019 and 2020 from Germany. White symbols indicate that the concentrations were below the reporting limit (RL) in the respective species.

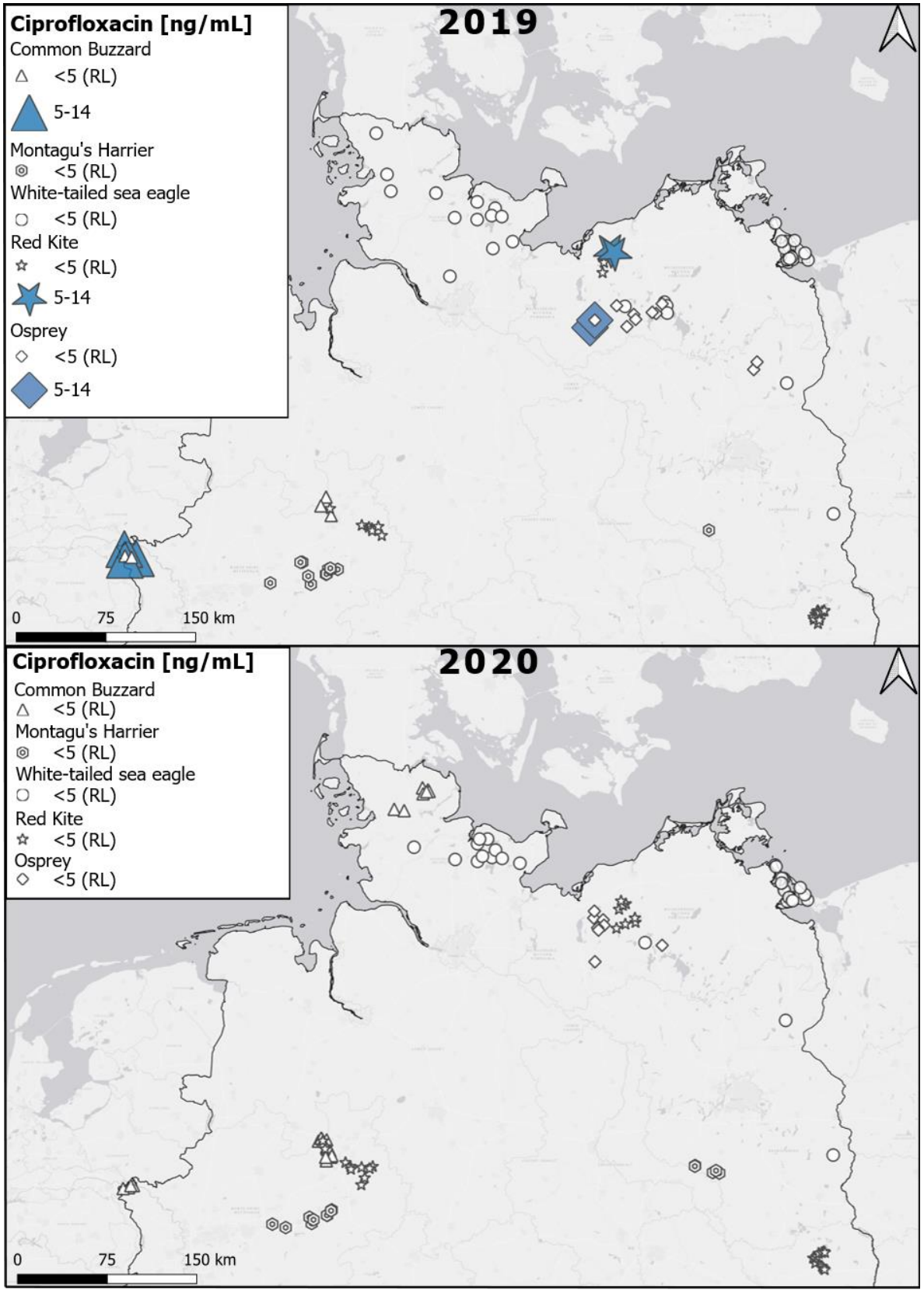

Figure SI-4: Spatial detection of and ciprofloxacin (blue)in blood common (*Buteo buteo*, BUBT, triangles), Montagu's harriers (*Circus pygargus*, CIPY, doubled hexagons), white-tailed sea eagle (*Haliaeetus albicilla*, HAAL, circles), red kites (*Milvus milvus*, MIML, stars), and osprey (*Pandion haliaetus*, PAHA, squares) nestlings in 2019 and 2020 from Germany. White symbols indicate that the concentrations were below the reporting limit (RL) in the respective species.