

# Terrestrial vertebrate toxicology in Australia: An overview of wildlife research

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## Abstract

Terrestrial vertebrate wildlife toxicology in Australia makes up a small proportion of the national body of ecotoxicology research. It is resource intensive to study larger, long-lived, free-ranging animals, and research funding is highly competitive. Australia's landscapes and fauna are unique, which exacerbates the general lack of baseline data for chemical risk assessment. Although environmental protection regulation has reduced the incidence of acute poisoning of wildlife, there is still much to be learned about the effects of anthropogenic chemicals in Australian wildlife. This review outlines several examples of long-term research collaborations that have investigated Australian terrestrial wildlife toxicology issues, including industrial fluoride toxicosis, cyanide toxicosis at gold mines and nontarget impacts of chemical locust control, and outlines some of the challenges in the field. Australia's economic reliance on resource extraction and processing and agriculture accounts for most wildlife toxicology scenarios outlined in this review.

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## Introduction

Australia is a vast island continent and one of the world's biologically 'megadiverse' countries. Many of Australia's species are endemic, including 87% of mammals and

45% of birds [87]. However, there have been major declines in many components of biodiversity since European settlement in 1788, and available information indicates continuing losses at the genetic, species, ecosystem and landscape levels owing to a number of different threats linked to human activities [15]. The main pressures facing the Australian environment are climate change, land-use change, habitat fragmentation and degradation and invasive species, with interactions between these and other pressures resulting in cumulative impacts [87].

Terrestrial vertebrate wildlife toxicology in Australia, focussing on free-living populations, makes up a small proportion of the national body of ecotoxicology research. Increasing focus on population, community and ecosystem responses is needed to develop biologically meaningful regulatory guidelines that will protect natural resources [75]. We are challenged with the task of causally linking knowledge about the molecular actions of chemicals to their possible interference with biological processes and population dynamics to develop reliable predictions about the consequences of chemical use and misuse [53]. To add to this complexity, chemicals are rarely applied in isolation, which may result in multiple stressor effects that are additive, synergistic, antagonistic or delayed, and difficult to tease apart [36,64]. Unless studies involve large numbers of animals or the effect of a chemical is very pronounced, there is often an inability to detect changes at the population level.

Although environmental protection regulation in developed countries, including Australia, has reduced the incidence of acute poisoning of wildlife due to chemicals, the risk of deleterious effects due to chronic exposure is still present and often unquantified [53]. It is difficult to obtain funding to investigate impacts that lack obvious and immediate 'cause-and-effect' mechanisms. Of all environmental compartments, the risk to terrestrial vertebrates (birds and mammals) most often fails to be fully addressed in chemical risk assessments [93]. It is resource intensive to study these larger, long-lived, free-ranging animals compared with small and readily reproducing laboratory species. In Australia, limited information is available for the vast majority of taxa, and few long-term monitoring programmes are in place [87], making chemical risk assessments for native

species problematic. Recent findings from environmental monitoring research in Australia highlight the existence of potential impacts and the need for ongoing studies (e.g. Richmond et al [76]). State government agencies have progressively reduced the human and financial resources allocated to monitoring, and in the absence of large-scale environmental disasters, further expenditure on environmental monitoring and regulation is highly unlikely [40]. Our federated political system in Australia presents additional challenges, such as inconsistencies with monitoring approaches and effort across state borders and different funding priorities and species conservation status by states [67]. Despite being a wealthy, environmentally and politically stable nation, native Australian fauna continue to decline [67].

In Australia, as in the United States of America, the changing business model for higher education and decreased discretionary funding at the federal and state level over the past 25–50 years has created a hyper-competitive environment between government agencies and for academics seeking funding, a result of which is less support for science as a public good [20]. Australian governments, both federal and state, have allocated substantial resources to support research commercialisation and university–business partnerships, with the aim of enhancing university links with industry and increasing nongovernment research funding [43].

Partnerships with industry can buffer government funding shortages and the short-term nature of postgraduate university research projects. This review provides several examples of long-term research collaborations between university researchers, consultants and industry and government technical specialists, which have informed environmental management and regulation. One thing these studies all incorporate is the industry desire for corporate social responsibility outcomes in the face of increasing community and government expectations around environmental management. The environmental performance of large companies receives close attention from the government; therefore, the interaction between these companies and their sociopolitical environment is a key area of contemporary corporate management [79]. The aim of this review is to provide some examples of Australian terrestrial vertebrate wildlife toxicology research, most involving public–private partnerships, and outline the historic and future challenges in the field.

## Case studies

### Fluoride toxicosis in marsupials

Gaseous and particulate emissions of fluoride are deposited on, and absorbed by, vegetation surrounding fluoride-emitting industries, potentially impacting local herbivorous wildlife [8]. Although dental and skeletal

fluorosis has been described in livestock (e.g. Shupe et al [84] and Suttie [94]) and various free-living eutherian mammals internationally (e.g. Garrott et al [28], Kierdorf et al [50] and Vikøren and Stuve [97]), research into the impact on Australian marsupials has been more recent. The initial investigation into fluoride-related impacts on eastern grey kangaroos (*Macropus giganteus*) [5] was initiated after incidental observations of lame kangaroos and abnormal skeletal remains by ecologists [7] surveying wildlife around an aluminium smelter in south-eastern Australia. This collaboration between the University of Melbourne, state government agencies and Portland Aluminium Ltd. (Alcoa) was facilitated by pre-existing personal relationships and motivated by animal welfare concerns. The availability of baseline life history and health data for eastern grey kangaroos, and the relatively specific suite of symptoms caused by excess fluoride outlined in other species, enabled the conclusion that the dental and skeletal lesions were consistent with fluoride toxicosis [5].

This initial study was expanded by the work of Hufschmid et al [46,47] and Death et al [9–12], working within the same group but extending the investigation to multiple marsupial species and developing an international collaboration that resulted in further detailed pathological analysis by Kierdorf et al [51,52]. While the amount of available baseline health and life history data varied by species, the elevated bone fluoride concentrations and the consistency of the pathological lesions seen in the exposed/high-fluoride population compared with the nonexposed/low-fluoride populations supported the diagnosis of fluoride toxicosis to varying extents in all the marsupial species assessed (red-necked wallaby, *Notamacropus rufogriseus*; swamp wallaby, *Wallabia bicolor*; koala, *Phascolarctos cinereus*; common brushtail possum, *Trichosurus vulpecula* and common ringtail possum, *Pseudocheirus peregrinus*) [9–11]. These studies were not long enough or large enough to detect more subtle population-level changes. Fecundity did not appear to be affected, however, and the most likely impact was hypothesised to be a general lowering of the population age structure owing to potential reduction in longevity.

The success of this work was based in the willingness of a multinational industry partner to support a transparent and detailed investigation, culminating in co-authorship of the findings in the peer-reviewed literature. There was recognition that harm had been inadvertently caused to the wildlife living in the vicinity of the smelter, secondary to the attempt to manage the site as the ‘Smelter in the Park’ [45]. In this case, the reporting of negative welfare impacts in the local and national media drew negative attention from the community, so the resulting investigation was management focused, seeking to find solutions to minimise harm on the

resident wildlife. Bone fluoride levels of exposed mammals should be kept below 2000  $\mu\text{g F}^-/\text{g}$  to reduce the incidence of skeletal fluorosis, and the modelling performed by Death *et al.* [12] supported restricting kangaroo access to vegetation <1500 m from the central emission point to achieve this aim. Studies such as these are required to corroborate model estimates with field measures, and the findings have led to changes in land management at the smelter, as well as positive corporate sustainability outcomes and enhanced awareness within jurisdictional government regulators.

### Wildlife cyanide toxicosis at gold mines

Cyanide ( $\text{CN}^-$ ) is used extensively in the metallurgical process of extracting inert precious metals from ores. Consequently, cyanide is the most significant contaminant influencing wildlife mortality at gold and silver mining operations worldwide [18]. Cyanide extraction can result in large waste tailings ponds of sediment and contaminated water and heap leach facilities, which are hazardous to wildlife if not properly managed [16,21]. In response to historical environmental incidents involving cyanide, the International Cyanide Management Code (the Code) was developed to promote the industry-wide protection of human health and the reduction of environmental impacts [49]. Since its inception, leading international gold mining companies, including Barrick Gold Corporation, Goldcorp Inc., Newmont Mining Corporation, AngloGold Ashanti and Newcrest Mining Ltd., have embraced the Code. Industry-funded research conducted in Australia, New Zealand and Africa has led to signatory mining operations successfully implementing systematic, auditable cyanide chemistry and wildlife monitoring protocols that assess the risk posed to wildlife as part of preventative, rather than reactive, management programmes [17]. This proactive approach has effectively reduced the rate at which diurnal wildlife (predominantly birds and terrestrial mammals) interacts with cyanide-bearing solutions stored in open impoundments [16]. Although frogs, lizards and small mammals may be affected, birds are by far the most at-risk wildlife group in this context [18]. However, a significant knowledge gap remains in managing risks of nocturnal wildlife, such as insectivorous bats, being exposed to cyanide-bearing waste solutions [35].

To address the risk to bats, Griffiths *et al.* [33,34] used passive electronic monitoring of echolocation calls to quantify activity and behaviour of bats in the airspace above water bodies at several Australian gold mines. Echolocation call sequences containing terminal buzzes, indicative of foraging and drinking [32], were recorded at all water bodies monitored. These findings were consistent with those of previous investigations into wildlife interactions with water bodies at gold mines

[18,35,86] and underscore the need for paired monitoring of nocturnal wildlife visitations and cyanide chemistry at gold mining wastewater bodies [33]. This need is highlighted by the evidence that when cyanide concentrations exceed a critical toxicity threshold, significant cyanide-related mortality events can occur in bat populations. For example, in North America, between 1980 and 1989, microbats and rodents were the most commonly reported mammal mortalities at cyanide-extraction gold mines located in California, Nevada and Arizona [4].

There are currently more than 90 active and 200 historic gold mines located across all Australian states and the Northern Territory (Figure 1; Geoscience Australia [29]). The available evidence suggests that bats are likely to be using open wastewater impoundments at these sites for drinking and foraging [18,33–35,86]. However, despite the evident risk of cyanide toxicosis, monitoring of microbats at most gold mines in Australia is either inadequate or nonexistent (Donato *et al.* [18] and National Industrial Chemicals Notification and Assessment Scheme [70]). Consequently, determining the impacts on bat populations from exposure to cyanide used in the Australian gold industry is problematic [33]. Given that the availability of drinking water strongly influences the diversity, distribution and activity patterns of bats on a continental scale, pollution of water bodies is likely to have negative effects on local bat populations across all Australian ecoregions [2]. This is particularly true in the xeric and desert habitats of Australia, where permanent anthropogenic sources of polluted water may constitute a form of ecological trap [81] for bats and other wildlife.

The risks associated with heap leach facilities are less well documented, monitored and audited, compared with tailings storage facilities [16]. Although a number of heap leach operations are certified as compliant with the Cyanide Code, systematic monitoring regime data have not been published. Without such monitoring and further knowledge, wildlife deaths on heap leach facilities are likely to remain largely unrecorded [16].

### Ecotoxicological risk to Australian endemic terrestrial birds and mammals associated with chemical pesticide use

Locusts, most importantly, the Australian plague locust *Chortoicetes terminifera*, pose a threat to agriculture when their populations increase dramatically [3]. Control programmes rely on the aerial application of chemical insecticides, and although the economic argument for locust control is significant [1,63], delineating the environmental impacts associated with chemical control is more problematic [88,92].

Locusts are capable of migrating hundreds of kilometres overnight, allowing them to move easily between pest control jurisdictions [48]. Consequently, locust control is viewed by federal and state governments as being for the public good because it is not always possible to identify the direct beneficiary of the control. Within environmental legislation, locust control organisations as the ‘proponents of a threatening action’ must be able to quantify the environmental effects of their activities [92]. In Australia, this has been an ongoing process bringing together agribusiness, commercial laboratories, locust control bodies and universities using industry-linked government funding, resulting in many scientific publications.

In the ‘boom and bust’ environment of the Australian arid and semiarid zone, the seasonal rainfall conditions that give rise to increases in locust populations are also responsible for increases in populations of vertebrate predators [26,95,96], and these resource pulses are critical to the continued population viability of both pests and predators [58–60]. The overlap between locust and bird populations has been quantitatively modelled, and field validation of these models has confirmed pesticide exposure in birds [96] and mammals (Story, unpublished data). Two pesticides used frequently for this purpose are fenitrothion (CAS: 122-14-5), an organophosphate (OP), and fipronil (CAS: 120068-37-3), a phenylpyrazole.

As outlined in the studies by Story et al [90,92], the use of fenitrothion for locust control in Australia gained approval based on international environmental research. Most risk assessments base the hazard posed by OPs on native Australian fauna on estimated toxicities in

nonendemic test species [90]. Although the impact of OP exposure within Australian metatherian mammals would be expected to be similar mechanistically to eutherian species, the Australian native dasyurids, *Sminthopsis crassicaudata* and *Sminthopsis macroura*, have been shown to be 10–14 times more sensitive to fenitrothion than a similar-sized eutherian, *Mus musculus domesticus* L. 1758 [90]. Dasyurids suffer transient reductions in locomotory performance after exposure to fenitrothion [3,89], at levels of acetylcholinesterase (AChE) suppression equivalent to those measured during locust spraying events (Story, unpublished data). Studies on movement patterns of small mammals in the arid zone indicate dasyurids can cover significant distances quite rapidly [13] and that this high mobility may be an adaptive response to the low productivity and variable rainfall at Australian deserts [57]. Reductions in locomotory performance could therefore impact dasyurids at the population level. In some international studies, impacts on avian thermoregulation have been seen owing to AChE pesticides [37], and under Australian conditions, fenitrothion exposure caused dose-dependent reductions in flight metabolism [25]. Reductions in plasma AChE activity during locust spray events have been confirmed in four Australian endemic bird species [26].

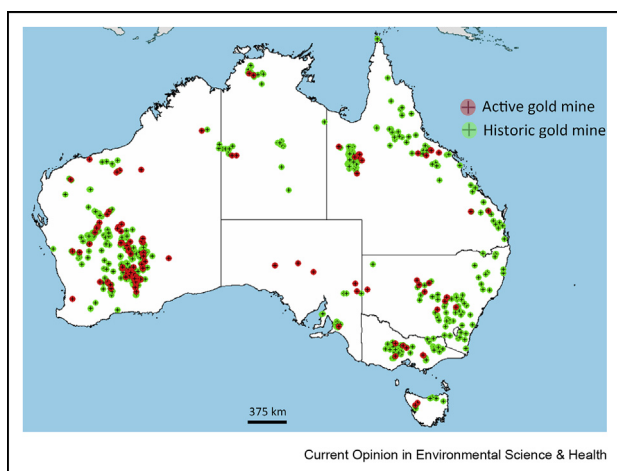
Despite high interspecies variability in the acute oral toxicity of fipronil to birds, there appear to be groupings of sensitivity at the ordinal level, with Galliformes showing high sensitivity and Passeriformes showing moderate sensitivity [54]. In addition, the sulphone metabolite of fipronil acts synergistically with the parent compound [41,55], causing reduced food intake in Galliformes [56]. Such reductions in feeding behaviour may persist beyond the standard acute oral toxicity timeframe and exacerbate the toxic effects of pesticides, with these effects not currently considered within pesticide risk assessments. Australian avian research has also shown that the maternal transfer of both fipronil and its sulphone metabolite is associated with a significant reduction in egg hatching success, after exposure to sublethal but ecologically realistic doses [55].

Although Australian mammals demonstrated higher than expected sensitivity to fenitrothion, *S. macroura* has demonstrated a lack of sensitivity to fipronil, with unexpectedly high median lethal dose estimates compared with similar eutherian mammals (Story, unpublished data).

#### Implications for pesticide risk assessments in Australia

The application of agricultural pesticides has been identified as a ‘threatening process’ for various species in New South Wales, Australia, and ‘active management’ has been recommended to prevent further attenuation and loss of the remaining species [14,91]. However, the paucity of data on the effects of pesticides on native Australian vertebrates constrains the development of

Figure 1



Map of Australia showing active (green target) and historic (red target) gold mines (source: Geoscience Australia [29]). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



biologically relevant risk assessments in Australia [90]. Very little research has been undertaken to quantify whether these evolutionarily unique Australian faunas display similar sensitivities to pesticide exposure when compared with nonendemic test species, and furthermore, there is little understanding of the impact on free-living populations.

Within standardised pesticide risk assessments, conventional toxicity testing tends to fix exposure time (e.g. for the determination of median lethal dose values) to quantify mortality limits [71]. However, in reality, exposure duration and intensity interact in determining the lethal effects of toxicants, and focussing on short-term toxicological fate in acute oral toxicity studies, while statistically convenient, limits the ecotoxicological relevance of such results [98,99]. Quantitative extrapolation of such data is often inadequate because either interspecies sensitivity to pesticides varies or the effects of toxicity and differences in exposure patterns between laboratory and wild animals are largely unquantified [83]. Based on the limited evidence available, errors in the direct extrapolation of dose–response data from laboratory to field situations may be as large as three orders of magnitude [73]. Moreover, some of the aforementioned outlined effects of pesticide exposure (e.g. performance measures such as locomotory impairment in mammals and reductions in avian flight metabolism) indicate that responses of Australian native species to pesticide exposure will likely fall outside scenarios encompassed by the current risk assessment framework used for pesticide registrations. When attempting to assess the impact of atrazine levels in Queensland waterways that were regularly above available Australian and New Zealand ecosystem protection guidelines, it was observed that informed and meaningful data interpretation was difficult owing to issues such as lack of basic guideline levels for several commonly detected pesticides, complex and potentially interacting mixtures of contaminants in receiving environments and minimal knowledge as to the effects of chronic, long-term exposure of relevant biota to low pollutant concentrations. This sentiment is supported by Sánchez-Bayo and Tennekes [78] who assert that chronic toxicity tests designed to detect time-cumulative effects should be a requirement for assessing delayed mortality, as well as population end points such as fecundity.

With the increasing identification of agricultural activities, including agrochemical use, as threatening processes [69] coupled with legislated environmental due diligence in Australia, there is increasing pressure placed on proponents to quantify their environmental impacts [90]. Consequently, there is an urgent need to (1) further evaluate the effects of pesticides on Australian endemic species, which differ phylogenetically from the standard range of species represented in environmental

risk assessments, and (2) ensure that such studies fully evaluate ecologically relevant end points.

## Other chemical impacts on nontarget terrestrial vertebrates

### i. Anticoagulant rodenticides in wild birds

Vertebrate pest management in Australia relies on a variety of pesticides, and their use has come under increasing scrutiny, with a growing attention to ethics, efficacy, environmental safety and best practices [68]. Although work has been completed on the effects of private and agricultural use of anticoagulant rodenticides (ARs) on wildlife in Australia (collated by Lohr and Davis [62]), these require further assessment. In one recent study, ARs were detected in almost three-quarters of Southern Boobook (*Ninox boobook*) owls found dead or moribund in Western Australia, and exposure was correlated with proximity to urbanised habitat [61]. Regulatory action has been urged [62] and is underway to harmonise and update Australian management of ARs, perhaps including increased focus on alternatives to chemical pest control, such as immunocontraception (e.g. McCallum [66]).

The management of Australia's vertebrate pests such as rabbits, foxes and wild dogs has historically relied heavily on the use of a variety of pesticides [68], despite potential risks to human health, impacts on nontarget native species, secondary poisoning, environmental uptake and suffering to the target species [30]. Although some Australian studies have shown impact on native species (e.g. Dundas *et al.* [19]), others have demonstrated no effect on nontarget animals (e.g. Fenner *et al.* [23]). A large number of toxicity studies have been carried out in New Zealand to develop new alternatives to persistent anticoagulants and sodium fluoroacetate (1080) for field control of pest animal species relevant to Australia. These alternatives include cholecalciferol and para-aminopropiophenone, both of which show relatively reduced toxicity to (nontarget) birds [100]. Delivery systems that facilitate contact with target species and minimise nontarget species exposure are critical.

### ii. Lead poisoning of wildlife

Exposure to lead carbonate from inappropriately transported lead dust resulted in approximately 9500 bird deaths in 2006/2007 in Esperance, Western Australia [38,101]. Species affected included white-tailed black cockatoos (*Calyptorhynchus baudinii*) and purple-crowned lorikeets (*Glossopsitta porphyrocephala*), with dust ingested from flowers and via preening. A parliamentary inquiry found that the 'native bird deaths

acted as a sentinel event; otherwise, the exposure of the community could have been tragic' [101]. The unusual isotopic signature of the lead concentrate allowed unequivocal identification of the source and contribution of the lead concentrate in the birds, local people and the environment, an important aspect of the associated legal proceedings and remediation activity [39].

Recreational duck hunting is only legal in four of the eight states/territories of Australia. The use of lead-based shot in wetlands by recreational waterfowl shooters was banned between 1994 and 2004 after international research (e.g. Mateo et al [65], Pain [72] and Scheuhammer and Norris [80]), but lead shot remains in waterways [22]. However, lead concentrations in Victorian wetland sediment samples in 2017 were considerably lower than the sediment quality guideline values, and although water levels of lead at four of the sampled water bodies slightly exceeded the 95% species protection guideline value, urban sources of lead may be more likely sources than legacy recreational hunting as levels of other metals such as arsenic, boron, chromium, copper, manganese, nickel, zinc and antimony were also elevated [22]. Lead bullets are still the primary ammunition for quail and game (e.g. deer, kangaroos, wild pigs, foxes, rabbits) hunting, culling or harvesting in Australia. This practice may pose a public health risk and lead to wildlife exposure [42]. Although Australia is already involved in several multidisciplinary, international lead management forums, increased collaboration among researchers with expertise in different taxa is needed to advance our knowledge of the impacts of lead on wildlife in the Australian environment [74].

### iii. Pharmaceuticals and heavy metal contaminants in waterways

Richmond et al [76] demonstrated that aquatic insects are a biological vector transporting pharmaceuticals to riparian predators. They suggested that representative vertebrate predators feeding almost exclusively on aquatic invertebrates (such as platypuses and brown trout) could consume some drug classes such as antidepressants at as much as half of the recommended therapeutic dose for humans, based on their estimated prey consumption rates [76].

In 2015, Scott et al. [82] reported that although trace organic contaminants were found in 92% of river water samples from 73 sites across Australia, most pharmaceuticals were at concentrations posing negligible risk. However, three of the 42 compounds monitored were at levels that may be causing adverse effects at the most polluted sites. Subsequent to these studies, the demonstration of any adverse effects at the animal or population level in terrestrial vertebrate wildlife requires further exploration.

Finger et al [27] sampled blood and moulted feathers of the little penguin (*Eudyptula minor*) from southern Australian colonies subject to varying levels of anthropogenic impact. Nonessential trace metal and metalloids concentrations in the penguins were associated with the level of industrialisation. This trend was more distinct in blood than in moulted feathers, although they found a clear correlation between blood and feathers for mercury, lead and iron, which could be useful for noninvasive biomonitoring [27]. Another Australian study conducted by Ficken and Byrne [24] was the first to provide evidence for a negative association between metal contamination and anuran species richness and distribution in the southern hemisphere.

### Future directions

Negative impacts of anthropogenic chemicals on wildlife are not commonly investigated in Australia unless they have caused acute or obvious health or welfare impacts on wildlife populations or there is an associated threat to public health. Evidence of wildlife mortality or welfare impacts in the media can inflame public outrage and may constitute a breach of operating conditions for industry, so there is a significant incentive to manage impacts. It is difficult, however, to obtain funding for the investigation of more subtle impacts of environmental contaminants, when motivated solely by wildlife health and conservation outcomes. It is very difficult to address the reality of multiple stressors in small, short-term studies despite many new statistical methods; often, baseline data are lacking, and sample sizes are not large enough to tease out effects. There is a strong desire to use modelling to predict impacts and make management decisions, but models that are built on scant empirical data may not provide useful output [31].

Industry co-funding of research activities has been a successful model in some Australian scenarios, with multinational companies and government contributing funding and in-kind support for research into wildlife contaminant impacts. The Minerals Council of Australia states that 'the Australian minerals industry strongly supports the role of a "social licence to operate" as a complement to a regulatory licence issued by government' [15]. However, small polluting enterprises with no public reputation to protect have less incentive than large, reputation-sensitive corporations to pursue collaborative research ventures [40]. An opportunity lies in the cooperative approach that underpins environmental regulation in Australia [40]; however, increased collaboration with agrochemical industries may be required. Moreover, within the context of Australian Commonwealth and State environmental legislation, proponents of threatening actions are obligated to provide adequate due diligence or environmental duty of care in addressing the potential environmental impacts

of their activities [92]. However, what remains unclear is the level of due diligence considered by regulatory authorities to be sufficient to satisfy this legislation.

Because university–industry collaborations involve nonacademic parties, performance must encompass the sharing and transfer of knowledge, skills and techniques and the translation of research into economically profitable output [85] and public policy benefits. However, care must be taken to avoid perverse incentives [20] due to goal misalignment [85]. Methodology, data analysis and reporting need to be robust and transparent as large amounts of unpublished monitoring data in the grey literature are unlikely to improve environmental management on a national level.

One important challenge is to complete wildlife studies that are long enough and large enough to describe subtle effects on populations of long-lived free-living vertebrates. This necessitates careful consideration of the contaminant mode of action, and potential individual and community responses, when designing studies to investigate the impacts [6,10,77]. Monitoring the most appropriate, and ecologically significant, response variable is essential. Australia requires programmes and processes for collecting relevant and adequate data to provide early warning of threats [87]. Moving forward, accounting for uncertainty will be even more essential as we attempt to monitor the impacts of climate change as an additional stressor [44,65] in Australian wildlife populations affected by anthropogenic chemicals.

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## Conflict of interest statement

Nothing declared.

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Papers of particular interest, published within the period of review, have been highlighted as:

- \* of special interest
- \*\* of outstanding interest

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