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PRACTICE INSIGHTS

Current policies in Europe and South Asia do not prevent veterinary use of drugs toxic to vultures

Sophie E. Cook[1] | Rhys E. Green[2,3] | Eva Lieberherr[1] | Christopher G. R. Bowden[3] | Muhammed Jamshed Iqbal Chaudhry[4] | A. B. M. Sarowar Alam[5] | S. Bharathidasan[6] | Vibhu Prakash[7] | Abhishek Ghoshal[7] | Antoni Margalida[8,9] | Mohammed Shobrak[10] | Ishana Thapa[11]

[1]Natural Resource Policy Group, ETH Zürich, Zürich, Switzerland

[2]Department of Zoology, University of Cambridge, Cambridge, UK

[3]Royal Society for the Protection of Birds, Sandy, UK

[4]WWF-Pakistan, Lahore, Pakistan

[5]IUCN Bangladesh Country Office, Dhaka, Bangladesh

[6]Arulagam, Coimbatore, Tamil Nadu, India

[7]Bombay Natural History Society, Mumbai, Maharashtra, India

[8]Institute for Game and Wildlife Research IREC (CSIC-UCLM-JCCM), Ciudad Real, Spain

[9]Pyrenean Institute of Ecology (CSIC), Jaca, Spain

[10]National Center for Wildlife, Prince Saud Al Faisal National Research Center, Taif, Saudi Arabia

[11]Bird Conservation Nepal, Kathmandu, Nepal

Correspondence
Rhys E. Green
Email: reg29@cam.ac.uk

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Abstract

1. Population declines of vultures of the genus *Gyps* in the Indian Subcontinent in the 1990s and 2000s were among the most rapid global population declines recorded for any bird species.
2. Multiple lines of evidence identified veterinary treatment of cattle with the non-steroidal anti-inflammatory drug (NSAID) diclofenac as the principal cause of the vulture population crash. Diclofenac causes kidney failure and death within a few days of a vulture scavenging the carcass of a recently treated cow.
3. Despite coordinated regulatory action by governments to ban veterinary diclofenac in South Asia, enforcement has been incomplete in many areas. Progress in preventing the veterinary use of other NSAIDs now also known to be vulture-toxic has been slow. A mosaic of inconsistent licensing processes currently exists across South Asian vulture range states, leading to issues with successful policy implementation, legitimacy and effectiveness.
4. At present, mandatory safety testing to ensure NSAIDs already in use or proposed for use are vulture-safe is not part of drug licensing procedures in any vulture range state.
5. In 2021, Bangladesh became the first country to ban a vulture-toxic NSAID, in addition to diclofenac, by banning veterinary use of ketoprofen. In 2023, India became the second country to take this step when the government announced a ban on veterinary aceclofenac and ketoprofen. This government action in India may have been triggered by a recent legal challenge.
6. Despite its veterinary use now being banned in South Asian and the Middle Eastern countries, diclofenac has been authorised for sale since 2013 as a veterinary drug in Spain, even though Spain holds 90% of the vulture population of Europe. The European Commission's decision to leave the authorisation of this drug to Member States is at odds with a central pillar of environmental law in the

European Union (EU): the precautionary principle. Furthermore, this approach is not consistent with the stringent standards and burden of proof applied to the licensing of EU plant protection products.

7. *Solution*. A solution to this lack of protection of *Gyps* vulture populations is for regulatory regimes for veterinary NSAIDs to be augmented.

KEYWORDS
aceclofenac, diclofenac, drug licensing, flunixin, ketoprofen, meloxicam, nimesulide, NSAIDs, regulation, safety testing, tolfenamic acid, veterinary drugs

1 | INTRODUCTION

Effective action to minimise ecotoxic effects of chemicals emitted to the environment as a result of human activities requires a robust scientific and regulatory framework. This was lacking when veterinary use of the non-steroidal anti-inflammatory drug (NSAID) diclofenac was approved in South Asia in the 1990s. Within a decade of diclofenac's regulatory approval in India in 1993, its widespread veterinary use in cattle (*Bos taurus*, *B. indicus*) and water buffaloes (*Bubalus bubalis*) caused the collapse of global populations of three vulture species endemic to South Asia (Green et al., 2004; Oaks et al., 2004; Prakash et al., 2012). Affected vultures died from kidney failure within days of ingesting drug residues after scavenging on carcasses of recently treated cattle. By 2010, the white-rumped vulture (*Gyps bengalensis*), Indian vulture (*G. indicus*) and slender-billed vulture (*G. tenuirostris*) were listed as Critically Endangered on the International Union for the Conservation of Nature's (IUCN) Red List, having previously been in the category of Least Concern (BirdLife International, 2024). The future persistence of these species is threatened directly by exposure to veterinary NSAIDs, which might also be contributing to the precarious conservation status of several other vulture species (Table 1). Before 2004, the effects of NSAIDs on vultures were completely unknown. Vultures contribute to a range of ecosystem services beneficial to humans, including control of disease (Markandya et al., 2008). In parts of India where vultures were formerly numerous, the human mortality rate from all causes combined increased by more than 4% after vultures declined, relative to rates in other areas where vultures had always been scarce. This might be attributable to the rapid loss of vultures disposing of carrion and subsequent effects on pest and disease prevalence (Frank & Sudarshan, 2023).

In this Practice Insight, we use our experience as vulture conservation practitioners to assess the fitness for the purpose of regulatory efforts developed during the past 20 years to manage this problem and to prevent its recurrence. Our study focusses on *Gyps* vultures, because all seven species in the genus for which evidence is available are susceptible to poisoning by residues of nephrotoxic NSAIDs likely to be ingested in their food by wild vultures (see references cited in Table 2). Although *Gyps* vultures are also threatened in Africa, we focus on the regulatory situation in South Asia and Europe

TABLE 1 Vulture species found in Asia and Europe confirmed or suspected to be susceptible to diclofenac poisoning. Data from: Botha et al., 2017. Evidence for each species about the toxicity of diclofenac is coded as: D, population declines coincident with the introduction of diclofenac; E, experimental treatment with a dose simulating ingestion of tissue from a contaminated carcass causes death of captive birds from kidney failure; W, carcasses of wild vultures found with visceral gout and diclofenac residues. IUCN Red List categories are colour-coded green to red.

Species	Range	Global population	Evidence type	Global IUCN extinction risk
White-rumped vulture, *Gyps bengalensis*	South and SE Asia	4000–6000	E&W	Critically Endangered
Long-billed vulture, *Gyps indicus*	South Asia	5000–15,000	W	
Slender-billed vulture, *Gyps tenuirostris*	South and SE Asia	730–870	D	
Red-headed vulture, *Sarcogyps calvus*	South and SE Asia	2500–9999	D	
Egyptian vulture, *Neophron percnopterus*	Africa, Asia, Europe	12,400–36,000	D	Endangered
Himalayan griffon vulture, *Gyps himalayensis*	Asia	66,000–334,000	E	Near Threatened
Bearded vulture, *Gypaetus barbatus*	Africa, Asia, Europe	1675–6700	None	
Cinereous vulture, *Aegypius monachus*	Europe, Asia	16,800–22,800	W	
Eurasian griffon vulture, *Gyps fulvus*	Africa, Asia, Europe	80,000–900,000	E&W	Least Concern

because circumstances there make exposure of vultures to NSAIDs in carcasses of recently dosed farm animals especially likely.

2 | EFFECTIVENESS OF CURRENT REGULATION OF VETERINARY USE OF DICLOFENAC IN SOUTH ASIA

Gyps vultures are obligate scavengers on carcasses of large mammals. In South Asia, there are large numbers of domesticated cattle and water buffaloes and religious and cultural constraints on consumption of the meat of these animals by humans. As a result, carcasses of dead animals are often disposed of by leaving them in open sites for scavengers to eat, which potentially exposes vultures and other scavengers to any toxic residues of veterinary pharmaceuticals. In addition to this, in South Asian countries with many adherents to the Hindu religion, there is considerable attention to the welfare of cattle. In most of India, cattle are regarded as sacred and have been revered for thousands of years (Kennedy et al., 2018). For this reason, large quantities of pain-killing drugs are administered annually to alleviate the suffering of cattle when they are close to death, including by staff employed by cattle charities, some of which accommodate thousands of unwanted animals in dedicated shelters (Kennedy et al., 2018).

TABLE 2 Toxicity and safety to *Gyps* vultures of different non-steroidal anti-inflammatory drugs (NSAIDs). Evidence for each NSAID about its toxicity to *Gyps* vultures is coded as: E, experimental treatment with a dose simulating ingestion of tissue from a contaminated carcass causes or does not cause death of captive birds from kidney failure; W, carcasses of wild vultures found with visceral gout and NSAID residues (toxic) or with residues and no evidence of kidney failure (safe). References to toxicity/safety studies: 1. Oaks et al. (2004); 2. Shultz et al. (2004); 3. Swan, Cuthbert, et al. (2006); 4. Green et al. (2007); 5. Naidoo et al. (2010); 6. Galligan et al. (2016); 7. Chandramohan, Mathesh, et al. (2022); 8. Cuthbert et al. (2016); 9. Nambirajan et al. (2021); 10. Mathesh et al. (2023); 11. Galligan et al. (2022); 12. Zorrilla et al. (2015); 13. Herrero-Villar et al. (2020); 14. Fourie et al. (2015); 15. Naidoo et al. (2018); 16. Swan, Naidoo, et al. (2006); 17. Swarup et al. (2007); 18. Chandramohan, Mallord, et al. (2022). Toxicity to vultures is colour-coded from green (safe) to red (toxic).

NSAID	Evidence type (and references)	Toxicity
Diclofenac	E&W[1,2,3,4]	Toxic
Ketoprofen	E[5]	
Aceclofenac	E[6,7]	
Nimesulide	E&W[8,9,10,11]	
Flunixin	W[12,13,14]	
Carprofen	E[15]	Toxic at high doses
Meloxicam	E&W[8,16,17]	Safe
Tolfenamic acid	E[18]	

Convincing experimental evidence of diclofenac's toxicity to captive white-rumped vultures was first published in 2004, together with results from post-mortems showing that its residues and effects were widespread in wild white-rumped and Indian vultures found dead in India, Pakistan and Nepal (Oaks et al., 2004; Shultz et al., 2004). The drug was found in dead cattle at levels sufficient to indicate that it was the principal or sole cause of the rapid population declines observed during the 1990s and early 2000s (Green et al., 2004, 2007). National governments in South Asia responded by banning the veterinary use of diclofenac in 2006 in India, Pakistan and Nepal and in 2010 in Bangladesh. It was later decided that these actions and their implementation would be coordinated through an inter-governmental Regional Declaration, which was agreed in 2012 between India, Pakistan, Nepal and Bangladesh (Governments of Bangladesh, India, Nepal, & Pakistan, 2012). However, the statutory bans on diclofenac were often ignored in practice, with this evasion assisted by clandestine marketing of large 30 mL vials of human formulations of diclofenac as veterinary drugs (Galligan et al., 2021). The manufacture of human formulations of diclofenac in vials larger than 3 mL was therefore banned by the Government of India in 2015, with all veterinary diclofenac, regardless of vial size, having been banned since 2006. The ban on large vials was maintained, despite legal challenges from two Indian pharmaceutical companies (Madras High Court, 2017).

The death rate per meal from diclofenac poisoning of white-rumped vultures in India, estimated from surveys of drug concentrations in dead cattle, declined by 65% within 3 years of the ban in 2006 (Cuthbert et al., 2014). However, exposure to diclofenac was still sufficiently high in 2009 that carcasses of 72% of white-rumped vultures found dead in the wild in India were contaminated with diclofenac (Cuthbert et al., 2016). This occurred despite some replacement of diclofenac by the vulture-safe alternative meloxicam, which was substantial in some Indian states though minimal in others (Cuthbert et al., 2014). The degree to which the rate of vulture population decline slowed after the ban was consistent with modelled effects on vulture mortality of the observed changes in the prevalence and concentration of diclofenac in cattle carcasses (Prakash et al., 2012). Undercover surveys in India showed that the proportion of veterinary pharmacies illegally offering diclofenac for sale declined after the ban but remained at a high level in most states, with substantial differences among states: percentages of pharmacies selling diclofenac in the five states surveyed in 2017 ranged from 10% to 47% (Galligan et al., 2021). Vulture populations in India are no longer declining rapidly, but neither do they show signs of recovery (Figure 1; Prakash et al., 2024). In contrast to India, an effective public awareness campaign after the ban in Nepal led to a decline in the availability of diclofenac in pharmacies to a very low level within about 6 years (Galligan et al., 2021) together with a consistent and coincident vulture population recovery (Figure 1; Galligan et al., 2020). Only in the Indian state of Tamil Nadu are we aware of any efforts by any South Asian country or region to enforce the regulation on veterinary use of diclofenac by prosecution and punishment of offenders (Davies, 2022).

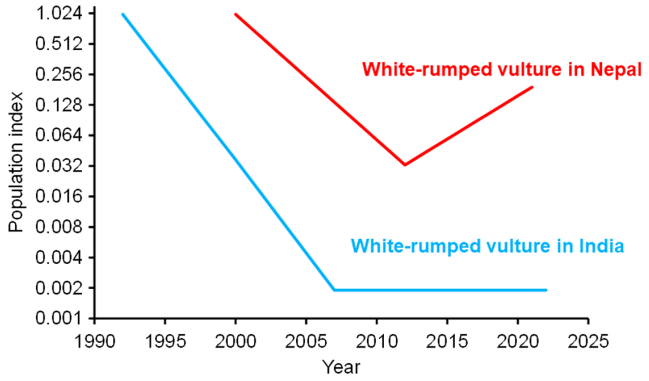

FIGURE 1 Summary of population trends of white-rumped Vultures in Nepal (red line) and India (blue line). Lines are based on regression models of road transect survey data reported by Galligan et al. (2020) and Prakash et al. (2024). Annual values upon which this graph is based are shown in the references cited. The vertical scale is logarithmic, and each tick mark represents doubling or halving of the population.

3 | REGULATION OF VULTURE-TOXIC NSAIDS BEYOND DICLOFENAC

Since the discovery of diclofenac as the sole or principal cause of South Asian vulture population declines, other NSAIDs have also been shown to cause kidney failure in *Gyps* vultures (Table 2). The continued, and even increasing, veterinary use of these legally approved toxic drugs has probably delayed vulture population recovery in several regions of South Asia. Undercover pharmacy surveys in India, Nepal and Bangladesh between 2012 and 2017 found that the NSAIDs nimesulide, ketoprofen and flunixin were offered for sale (Galligan et al., 2021). Veterinary use of these drugs was legally approved during this period. Proportions of pharmacies offering these drugs showed variable trends over this short period, but there were increases for nimesulide in some countries and Indian states (Galligan et al., 2021). Up to 2007, necropsy evidence of all deaths of wild vultures associated with exposure to NSAIDs only involved diclofenac (Cuthbert et al., 2016), but there have been eight recorded cases since 2008 of wild white-rumped vultures being found dead in India with visceral gout and substantial tissue residues of the toxic NSAID nimesulide (Cuthbert et al., 2016; Nambirajan et al., 2021). Only two NSAIDs have been confirmed as safe to vultures at concentrations likely to be encountered in the wild: meloxicam and tolfenamic acid. Others, including aceclofenac, ketoprofen, nimesulide and flunixin, have been established as causing kidney failure and visceral gout on ingestion of dose levels found in the wild (see evidence summaries for all drugs in Table 2). However, some of the NSAIDs known to be nephrotoxic to vultures remain approved for veterinary use in vulture range states (Table 3).

In 2021, Bangladesh became the first vulture range state to ban a second veterinary NSAID besides diclofenac, which was ketoprofen. India followed in July 2023 by banning veterinary ketoprofen and aceclofenac. This decision may have been hastened by a Public Interest Litigation at the Delhi High Court to challenge the lack of action taken by the Indian Government to ban drugs known to be toxic to vultures and to push for the banning of veterinary aceclofenac, ketoprofen and nimesulide (Supreme Court of India, 2022). The decision to ban veterinary aceclofenac and ketoprofen was rapidly gazetted into law within weeks of the Drugs Technical Advisory Board recommending the two drugs be banned (CDSCO, 2023). The Bombay Natural History Society first requested the banning of ketoprofen in 2009, and of aceclofenac in 2019 (Cook, 2023). Our experience is that these long delays are typical of the decision-making processes for restrictions on veterinary pharmaceuticals, but the rapid gazettement of ketoprofen and aceclofenac after announcement of the ban was unprecedented. However, nimesulide remained legally approved after the 2023 court case, despite published evidence of toxicity dating from 2016 (Table 2). However, there are recent indications that the Drugs Technical Advisory Board of India may soon also recommend a ban on veterinary nimesulide (Davies, 2024). In neighbouring Nepal, the banning of ketoprofen, aceclofenac and nimesulide has recently been proposed by the Ministry of Forest and Environment on the recommendation of the Nepal Vulture Recovery Committee and the decision is pending (Government of Nepal, 2023).

4 | FAILURE TO REGULATE VETERINARY USE OF TOXIC NSAIDS IN EUROPE

The European Commission has left the licensing of veterinary use of the vulture-toxic drug diclofenac in the hands of individual EU Member States (CVMP, 2014). The only species of *Gyps* vulture with a substantial breeding population in Europe is the Eurasian griffon vulture (*Gyps fulvus*) which breeds in Spain, Portugal, France, Italy, Croatia, Greece, Bulgaria, Serbia and North Macedonia (Terraube et al., 2022). Diclofenac is currently licensed for veterinary use in five EU Member States, but only two of these are within the vulture breeding range (Spain and Italy). Diclofenac's approval in Spain has caused the most concern (Green et al., 2016) because Spain has >30,000 breeding pairs of griffon vultures, compared with <300 pairs in Italy (Terraube et al., 2022) and because a substantial proportion of their food there is from the carcasses of farm animals, some of which are known to have residues of several veterinary NSAIDs in their tissues (Herrero-Villar et al., 2020). Spain also holds breeding populations of Egyptian (*Neophron percnopterus*) and cinereous (*Aegypius monachus*) vultures, for which there is also evidence of nephrotoxicity of NSAIDs (Table 1). Since its marketing authorisation in Spain in 2013 (Margalida et al., 2014), sales volumes of diclofenac in the EU have tripled and its annual use in Spanish livestock continues to increase (Moreno-Opo et al., 2021). Although no reliable information is available on the proportion of the drug sold which is administered to animals upon which vultures might feed, annual sales of diclofenac for use on bovine animals and pigs in Spain increased from doses sufficient for 40,000 animals to nearly 200,000 animals between 2013 and 2019 (Moreno-Opo et al., 2021). The case made by the authorities that licensing diclofenac would be safe was based

TABLE 3 Vulture-toxic veterinary non-steroidal anti-inflammatory drugs (NSAIDs) currently banned, restricted or licensed for veterinary use in South Asian vulture range states (Cook, 2023). 'Banned' refers to NSAIDs whose licences have been rescinded and their manufacture, sale and/or use disallowed. 'Not in use' refers to drugs which are not domestically manufactured, imported or registered. Some drugs are nationally licensed, but their use is 'restricted' in certain areas, for example, flunixin in Tamil Nadu, India. The status of each NSAID in each country is colour-coded green or red (yellow for 'not in use') to indicate potential hazard to vultures.

NSAID	India	Pakistan	Nepal	Bangladesh
Diclofenac	Banned (2006)	Banned (2006)	Banned (2006)	Banned (2010)
Multi-dose vials of diclofenac	Banned (2015)	Not in use	Not in use	Not in use
Ketoprofen	Banned (2023)	Licensed Restricted in Sindh (2018)	Licensed	Banned (2021)
Aceclofenac	Banned (2023)	Licensed Restricted in Sindh (2018)	Not in use	Not in use
Nimesulide	Licensed	Not in use	Licensed	Banned (for unrelated reason)
Flunixin	Licensed Restricted in Tamil Nadu (2019)	Licensed	Not in use	Not in use

upon the existence of sanitary regulations intended to prevent carcasses from recently treated animals from being available to scavenging vultures. However, residues of diclofenac and other veterinary NSAIDs have been recorded in carcasses provided at vulture feeding sites in Spain (Herrero-Villar et al., 2020) and a case of diclofenac poisoning of a cinereous vulture has been reported (Herrero-Villar et al., 2021). Four cases of death from poisoning of wild Eurasian griffon vultures in Spain by the NSAID flunixin have also been documented (Herrero-Villar et al., 2020; Zorrilla et al., 2015). The decision to licence veterinary diclofenac in Spain was made without consultation of all relevant government departments and several aspects of the assumptions and data used in the risk assessment supporting the decision were problematic (Green et al., 2016). In monitoring the prevalence and effects of veterinary NSAIDs in Spain since the approval of diclofenac use, sample sizes have been small and surveys subject to potential biases, such as managers of feeding sites being forewarned of carcass sampling visits (Margalida & Oliva-Vidal, 2017). So far, residues of four veterinary NSAIDs (diclofenac, ketoprofen, meloxicam and flunixin) have been detected in farm animal carcasses provided as food for vultures in Spain (Herrero-Villar et al., 2020). This would not have been the case if the supposedly protective sanitary regulations were effective, but there has been no published assessment yet of the potential pathways by which this unexpected contamination has occurred. Furthermore, although the NSAID flunixin is known to have caused deaths of vultures in Spain, no risk assessment has yet been conducted for veterinary use of this drug in Spain or the wider EU.

We restricted the geographical scope of our assessment of regulation of veterinary NSAIDs toxic to *Gyps* vultures to South Asia and Europe, even though the three species (*G. rueppelli*, *G. coprotheres* and *G. africanus*), found almost entirely in Africa, are all listed as globally threatened in the IUCN Red List (BirdLife International, 2024). This restriction is because there is little or no use in Africa of veterinary NSAIDs on cattle whose carcasses are disposed of after death by leaving them to be eaten by scavengers. African *Gyps* vultures are threatened for several other reasons, including the deliberate setting of poison baits either to kill vultures or to kill carnivorous mammals which have killed domestic livestock (Botha et al., 2017).

5 | FEATURES OF RETROSPECTIVE REGULATORY MECHANISMS FOR VETERINARY NSAIDS

Our extensive experience of decision-making in South Asian countries about withdrawing existing NSAID licences on environmental safety grounds is that decisions were made slowly and without the authorities defining clear requirements for the types of scientific evidence they needed. There are still no well-established existing policy instruments for retrospectively assessing the safety of previously approved NSAIDs to scavenging wildlife. Further details are given by Cook (2023).

Government agencies attempting to balance multiple conflicting interests often appear to be strongly influenced by advice from the profitable and influential pharmaceutical industry. Differences between range states in regulatory policies and their implementation are evident in countries with decentralised government systems or in border regions, such as in Bangladesh and Cambodia, where pharmaceuticals are largely imported from neighbouring states, principally from India or Vietnam respectively.

6 | RANGE STATES LACK PRE-EMPTIVE PROCEDURES TO REGULATE VULTURE-TOXIC NSAIDS

Lessons have been learnt from experience with diclofenac in the Indian Subcontinent. Precautionary bans on veterinary diclofenac were enacted in Cambodia, Iran and Oman before the drug was marketed there on a large scale because of what had happened on the Indian Subcontinent. This contrasts with the EU, where diclofenac was licensed in Spain a decade after the discovery of diclofenac as the cause of vulture population declines in India and Pakistan. Furthermore, in discussions in Saudi Arabia about the regulation of diclofenac, the policy of the EU and its Member States in approving its veterinary use was seen as running counter to arguments in favour of the introduction of restrictions there. Beyond these cases concerning drugs with already known evidence of toxicity, no vulture range state requires any evidence of safety of veterinary NSAIDs to vultures to be provided by companies in advance of obtaining approval for use of new-to-market veterinary compounds.

7 | PLAYING CATCH-UP IS INEFFECTIVE

Efforts to ban a licensed drug found to be toxic to vultures through retrospective assessment have been shown to be inefficient. The process required to detect the effects of each toxic drug through surveillance of wild vultures has taken several years (e.g., 10 years for diclofenac), and the studies required have usually not been conducted or funded by government agencies. Although veterinary use of diclofenac was banned in South Asia within 2–6 years of discovery of its effects, the equivalent delay was about a decade for aceclofenac, ketoprofen and nimesulide. As the continuing illegal use of diclofenac demonstrates, a ban can be followed by 6 years of incomplete compliance in the case of Nepal (Galligan et al., 2020) and more than a decade in the case of India (Galligan et al., 2021). Hence, the total time between the approval of veterinary use of a toxic NSAID and its disappearance from the food supply of vultures is likely to be at least 20 years.

The life history characteristics of vultures render their populations especially sensitive to the long periods of additional poisoning mortality that result from these delays in effective regulation. Vultures unaffected by poisoning have long lifespans, slow maturation and low maximum annual fecundity, meaning maximum population growth rates are low, even when conditions are optimal (Galligan et al., 2020). Hence, vulture populations are particularly sensitive to sudden increases in non-natural adult mortality: it typically takes a depleted vulture population about 10 years to double in size under optimum conditions (Neil & Lebreton, 2005), but the nephrotoxic effects of veterinary diclofenac successively halved populations of white-rumped vultures in India in each of the years between 1994 and 2005 (Prakash et al., 2024). This asymmetry in the potential rate of impact and the maximum rate of recovery means each year that passes without effective diclofenac regulation can delay full population recovery by at least a decade, even under optimal conditions. Furthermore, many vulture populations are recovering from the effects of diclofenac in far from optimal conditions; recovery is supressed by a range of other threats including collision with energy infrastructure, deliberate setting of poison baits to kill carnivores and the ongoing use of vulture-toxic NSAIDs (Botha et al., 2017).

8 | LACK OF CONSISTENCY IN THE APPLICATION OF THE PRECAUTIONARY PRINCIPLE TO ECOTOXIC CHEMICALS

Evidence for the ecotoxic effects of organochlorine and organophosphorus pesticides, including DDT and dieldrin, became widely accepted in the second half of the twentieth century, despite efforts by vested interests to undermine public trust in the science (Oreskes & Conway, 2010). These discoveries heightened global concern about the potential impact of other biocides on non-target species. An overhaul of EU regulations on the licensing of chemical plant protection products was undertaken to prevent future licensing occurring in ignorance of products' impacts. All new pesticide active substances in the EU must now be shown not to cause 'unacceptable effects on the environment, particularly with regards to non-target species and biodiversity' before they can be authorised for use (EFSA, 2024, p. 4). The burden of proof lies with the manufacturer to provide specified types of evidence that their product is safe to use, and such testing must be funded and commissioned by the licence applicant.

However, the same standards and obligations are yet to be extended to veterinary medicines and other pharmaceutical products. Surveillance of wild vultures and safety testing of veterinary NSAIDs on captive vultures has received no known funding from the pharmaceutical industry to date. Funding of work done so far has come from non-governmental conservation organisations and, more recently, there has been support from the Government of India for safety-testing studies led by the Indian Veterinary Research Institute and the Bombay Natural History Society. There has been no safety testing of veterinary drugs on vultures yet in Europe, except for a study in Spain demonstrating that administration of diclofenac was lethal to Eurasian griffon vultures (Swan, Cuthbert, et al., 2006).

The EU's guidelines for the application of the precautionary principle include that measures taken are based on the principles of proportionality, non-discrimination and consistency, as well as the examination of costs, benefits and scientific developments (Treaty on the Functioning of the European Union, 2016). The European Medicines Agency (EMA) concluded that there was a risk to European vultures from veterinary diclofenac (CVMP, 2014), but the use of this drug in the EU should have warranted a precautionary approach, as should veterinary use of all untested NSAIDs in vulture range states. The precautionary principle was directly cited in reasoning to uphold the restriction on the multi-dose vial sizes of human diclofenac in India (Madras High Court, 2017), but

safety testing data were not required in advance of licensing for any of the 11 NSAIDs currently authorised for veterinary use in Spain. Two of them, diclofenac and flunixin, have been identified as causing vulture mortality in Spain (Herrero-Villar et al., 2020, 2021; Zorrilla et al., 2015).

Adhering to the principle of consistency means that measures taken 'should be comparable in nature and scope with measures already taken in equivalent areas in which all the scientific data are available' (European Commission, 2000, p. 4). On examination of the EU's regulatory approach to other diffuse ecotoxic chemicals, it appears that such consistency is lacking. For example, the European Food Safety Authority's (EFSA) report on the risk posed by neonicotinoid pesticides to non-target species prompted an EU-wide ban on their use in bee-attractive crops in 2013, followed by a more stringent ban in 2018 on all outdoor use (EFSA, 2013). This contrasts with the EMA's conclusion that, although there was a risk to vultures from veterinary diclofenac, further regulatory action was not needed (CVMP, 2014; Margalida & Oliva-Vidal, 2017). Although the regulation of pesticides and pharmaceuticals falls under the jurisdiction of different EU agencies (EFSA and EMA), the cases of neonicotinoids and NSAIDs are similar: They are both diffuse ecotoxic chemicals whose use has been shown to cause adverse effects on a group of non-target species. However, the EU has afforded a more precautionary and centralised approach to the regulation of these insecticides than for veterinary NSAIDs and other pharmaceuticals with established environmental effects, such as the effects on wild fish of effluents contaminated with hormonal contraceptives (Tyler & Jobling, 2008).

9 | CONCLUSIONS AND RECOMMENDATIONS

The collapse in vulture populations in South Asia during the last 30 years indicates that a precautionary approach to the regulatory approval of veterinary NSAIDs should be considered as a high conservation and environmental health priority in vulture range states. The intrinsic life history characteristics of vultures mean they are disproportionately susceptible to population-level impacts of anthropogenic additional mortality from poisoning and other agents. Their vulnerability is recognised in the high level of legal protection from other threats afforded to them in most range states and internationally (Botha et al., 2017). There is currently no obligation or incentive for pharmaceutical companies to test the safety of veterinary NSAIDs on vultures as a necessary part of drug licensing procedures in either South Asia or Europe, despite this being called for in a Resolution of the Conference of the Parties to the Convention on the Conservation of Migratory Species of Wild Animals (Convention on Migratory Species, 2020). Such a process was eventually implemented for plant protection chemicals in the EU, but no equivalent exists for NSAIDs or other pharmaceuticals which have effects on non-target species. This is a serious gap in environmental protection in all vulture range states. It conflicts with the precautionary principle and the requirement for 'consistency' which should apply in the EU (Margalida et al., 2021).

Vulture-toxic veterinary NSAIDs remain in use across South Asia and the EU. There is no mechanism to prevent a new-to-market drug as toxic to vultures as diclofenac being approved in the future in any of the vulture range states. Until mandatory, prospective safety testing becomes an embedded part of NSAID licensing procedures, the time lag created by retrospective diagnosis, delayed regulation and imperfect compliance, combined with vultures' life history characteristics, will keep this group of species at high risk of global extinction and delay sustained population recovery.

AUTHOR CONTRIBUTIONS

Sophie E. Cook, Rhys E. Green and Eva Lieberherr conceived the research idea and designed the methods. Eva Lieberherr and Rhys E. Green supervised data collection by Sophie E. Cook. Christopher G. R. Bowden, Muhammed Jamshed Iqbal Chaudhry, A. B. M. Sarowar Alam, S. Bharathidasan, Vibhu Prakash, Abhishek Ghoshal, Antoni Margalida, Mohammed Shobrak and Ishana Thapa contributed information and experiences based upon their efforts to provide a scientific evidence base to underpin decision-making about vulture conservation in South Asia and Spain. Sophie E. Cook and Rhys E. Green compiled and analysed the information and led the writing of the first draft of the manuscript. All authors critically contributed to this study and gave final approval for publication.

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CONFLICT OF INTEREST STATEMENT

We, the authors, declare no conflict of interest.

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DATA AVAILABILITY STATEMENT

The detailed information used in this study is available in Cook (2023) and in the references cited in this paper.

ORCID

Rhys E. Green https://orcid.org/0000-0001-8690-8914

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