EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public consultation regarding the request to the European Medicines Agency from the European Commission for a scientific opinion regarding the risks to vultures and other necrophagous bird populations in the Union in connection with the use of veterinary medicinal products containing the substance *diclofenac*

Template for comments[1]

Comments to be provided by 10 October 2014

Comments from:

Name of organisation or individual
BirdLife International *Wellbrook Court, CB3 0NA* *Cambridge, United Kingdom* This document has been elaborated by BirdLife International and benefited from expert opinion of several senior scientists and conservation officers based in Spain, Italy, Portugal, France, UK and India. The International Fund for Animal Welfare IFAW and the Wildlife Conservation Society WCS have read this document and support all views and final recommendations expressed in it. Please direct any correspondence to the document coordinator Iván Ramírez, Head of Conservation for Europe and Central Asia at BirdLife International: ivan.ramirez@birdlife.org

[1] For further information see the original request

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Comments on Topic 1

Procedure of feeding vultures and other necrophagous birds species with animal by-products in and outside feeding stations and measures put in place to mitigate risks related to the potential for the by-products to contain residues of veterinary medicines.

In replying to this request from the EC, the CVMP welcomes comments and information from concerned stakeholders.

Comment

Introduction

BirdLife International is the official IUCN Red List Authority for birds. It is also one of the most experienced organisations in the field of *diclofenac* contamination and its effects to wild fauna. We draw on our ten years of experience dealing with *diclofenac* contamination of domesticated ungulate carcasses in South Asia to comment on this and the following two topics. Our comments focus largely on how *diclofenac* can impact on Spanish vultures. We do this because we are familiar with *diclofenac* use, livestock disposal and vulture feeding in Spain. Spain also holds the vast majority of vultures in Europe (>95%), including the Eurasian Griffon (*Gyps fulvus*), which we know is intolerant to *diclofenac* (Swan et al., 2006a); and the Spanish Imperial Eagle (*Aquila adalberti*), which is Endangered and we suspect is intolerant to *diclofenac* (SHARMA et al., n.d.).

There are three types of site where European vultures can consume *diclofenac*-contaminated tissue from domesticated ungulate carcasses: 1) vulture feeding stations (i.e., vulture restaurants: sites designed for vulture benefit); 2) carcass disposal sites (i.e., Spanish *muladares*: sites designed for both vulture and human benefit); and 3) fallen livestock in the field.

EMA's Public Consultation outcomes will have an immediate and direct impact on all European vulture populations. We believe that, before addressing your 3 main Topics, a brief analysis of the vulture conservation status in Europe is needed:

- Out of the 16 species of old-world vultures, 4 occur regularly and breed in Europe: the globally Endangered Egyptian vulture (*Neophron percnopterus)*, the globally Near-Threatened Cinereous vulture (*Aegypius monachus)* and Bearded vulture (*Gypaetus barbatus*) and the globally Least Concern Griffon vulture (*Gyps fulvus*). We already know that *Gyps fulvus* is intolerant to *diclofenac*.
- Europe holds the healthiest vulture populations in the old world, as the vulture populations in South Asia have collapsed totally due to *diclofenac* use, while Africa is now facing an unprecedented and large-scale vulture decline due to widespread poisoning (Botha et al., 2012). In Europe, three of the four species (except Egyptian vulture) have been increasing steadily, partly due to the intensive conservation effort funded by European Union budget lines – since 1996, the European Union and national governments have invested significant financial resources for the conservation of vultures, and there have been at least 67 LIFE projects related to these species – only between 2008 and 2012, nine vulture conservation projects alone received 10.7 million Euro (see here).
- Beyond their historical breeding grounds, and because of the local extinctions that happened during the past century, the European Union has funded vulture reintroduction projects in many European areas. The reintroduction of the Bearded vulture in the Alps (with 30 pairs now breeding in the wild) and in Andalusia (Spain) and the various

reintroduction programmes of the Griffon vulture in France, Italy and Bulgaria, totalling hundreds of millions of Euros, give an idea about the size and importance of such biodiversity investment in Europe

- Spain, Portugal, France and Italy hold the bulk of the European Union vulture populations (BirdLife International, 2004)

Vulture populations in Spain and Italy:

Veterinary *diclofenac* has been made commercially available in two key vulture countries.

Spain: More than 70,000 Griffon vultures (90% of the European population), 5,000 Cinereous vultures (97% of the European population), 3,000 Egyptian vultures (85% of the European population) and 300 Bearded vultures (67% of the European population). Spain is the most important country on the continent for these species – and for some of them (e.g. Griffon and Cinereous vultures) the most important country in the world. It is also the key country to secure a sustainable recovery of vulture populations across Europe, which the healthy populations in Spain have been supporting, both through normal dispersion, and through human-induced reintroduction and restocking projects with Spanish-origin birds.

Italy: Italy has a small and decreasing population of Egyptian vultures in the south (8 pairs in 2012). The estimated breeding population of Griffon vultures is about 90 breeding pairs, but the total population in summer, when immature birds arrive from either France or Spain, boosts the population up to 300-400 individuals. There is also a small but stable Bearded vulture population (20 individuals). The most important areas for vultures in Italy are Sardinia and the Abruzzo region. Italy plays also a fundamental role in the migration routes followed by other vulture populations in Western Europe on their way to the Eastern/Balkan regions.

Vulture population feeding and legislative framework

The availability of food for scavengers in Western Europe during recent decades permitted the existence and growth of huge vulture populations. This is the result of both legal protection and high food availability. During the second half of the 20th century, food availability was well above that required to maintain the scavenger populations, leading to a spectacular increase in population size, especially that of the Griffon vulture. This situation was exacerbated by a failure to comply with sanitation laws introduced in the 1950s, which forbade the abandonment of carcasses in the field (Donázar et al., 2010)

In 1999, bovine spongiform encephalopathy (BSEs) brought about strict EU legislation (CE 1774/2002) aimed at the elimination of animal by-products. As a consequence, state and regional administrations enforced measures requiring farmers to remove or destroy the remains of dead livestock. In 2006 / 2007, these feeding stations were closed as part of BSE control measures (Donázar et al., 2010).

Food scarcity after the BSE crisis triggered a change in the foraging behaviour of vultures. Faced with a reduced supply of carcasses, many individuals moved to exploit garbage dumps, a lower-quality food source, not exploited previously. The closure of these feeding stations, in combination with other human-related threats, such as poisoning and wind-farms, caused a decline in the number of breeding pairs by c. 24%, adult survival by 30% and fecundity by 35% (data for *Gyps fulvus*), as well as an increase in the number of birds entering rehabilitation centres (Martínez-Abraín et al., 2011).

The relevance of vultures for safe, cheap and natural disposal of livestock carcasses has been recognized in the most recent EU Animal by-products regulation (CE 142/2011) [2], implementing Regulation (EC) No 1069/2009, which includes specific authorizations for managing "carrion-dumps" and leaving carcasses in nature, in areas frequented by vultures. This regulation, adopted in Spain since 2011 (Real Decreto 1632/2011, de 14 de noviembre) with a number of provisions, includes:

- The definition of Protection Areas for birds of prey and/or feeding scavenger species of Community interest. In these areas, where scavenger birds are already present, free-ranging animals don't need to be recovered when dead and therefore might be available for vultures (except if they die of infectious diseases). According to data provided by SEO/BirdLife,15 Spanish autonomous communities have approved such areas while 2 haven't. These areas cover most or all the surface in some regions
- The establishment of carrion-dump sites (*muladares*) for birds of prey and/or feeding scavengers where intensive indoor or free-ranging farmed animals can be disposed of, with certain conditions: if they die because of disease, specified risk materials (SRM) should be removed, and for certain death causes, the whole animal should be incinerated. The dump-sites are locked enclosures and the items disposed should also be controlled. SEO/BirdLife data confirms that 11 autonomous communities have established these *muladares*, totalling 199 "official" sites in Spain.

BirdLife International experience from Asia and comparison with the European scenario

In Nepal, we manage vulture feeding stations. Old, ailing and unwanted cattle are donated to the site by local communities and cared for until their natural death by our staff. Only cattle that die after 10 days in our care are provided to vultures. In this way we can ensure that any *diclofenac* that these cattle may have been treated with previously has been fully metabolised (see our response to Topic 2). vulture feeding stations in Spain, France and other European countries largely obtain abattoir by-products (mostly viscera). *Diclofenac* is more slowly depleted from viscera and withdrawal periods are only designed to protect human health (see our response to Topic 2). Any given quantity of by-product obtained by feeding stations is likely to come from multiple individual animals and often-different species. Therefore, European wildlife managers presently rely on livestock owners not using *diclofenac* 10 days prior to slaughter.

In Spain, withdrawal periods for cattle and pigs are both greater than 10 days, but no withdrawal period exists for horses because they are not slaughtered for human consumption. Yet, horses are often slaughtered and processed at the same abattoirs as cattle. Our data from South Asia shows a very high proportion of horses (33.3%), higher than for cattle, are treated with *diclofenac* before death (Taggart et al., 2007). This is possibly a welfare measure that is likely to be similar in Europe. Thus, the by-products of a horse treated with *diclofenac* prior to slaughter can be supplied to a vulture feeding station in an indistinguishable and contaminated mix.

In India, we survey carcass disposal sites to determine *diclofenac* prevalence in vulture food. Despite the ban on veterinary *diclofenac* in 2006, we still find *diclofenac*-contaminated carcasses. This is because Indian pharmaceutical companies are circumventing the ban by producing human *diclofenac* in the vial size adequate for treating cattle and distributing these to veterinary pharmacies. However, it is veterinarians and livestock owners that are purchasing and administering *diclofenac* in South Asia. We are currently advocating a ban on all *diclofenac* in vials

[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:054:0001:0254:EN:PDF

larger than 3ml (adequate for human treatment), which is expected to occur in India later this year. We do not think pharmaceutical companies, pharmacists and veterinarians will circumvent laws in Europe as they have in South Asia; but this scenario highlights the sometimes irresponsible attitude of veterinarians and livestock owners to environmental issues. This bears on the large network of managed carcass disposal sites in Spain, which were re-established to prevent vulture declines as a result of a lack of food.

These *muladares* also provide livestock owners, who are responsible for these sites, an easy and inexpensive means of carcass disposal. Our colleagues in Spain have received reports of poorly or badly managed *muladares*. In the worse cases, chemicals, including vials of veterinary medicine, are discarded among carcasses. While it is therefore likely that vultures can be exposed to *diclofenac* by consuming tissue doused in discarded *diclofenac*, we are more concerned that these same irresponsible livestock owners will dispose of carcasses contaminated with *diclofenac* at sites where vultures have access.

Patterns of vulture foraging and feeding in nature

Vultures have evolved to be nature's most efficient undertakers. Vultures can see for vast distances while soaring. In addition, they monitor their soaring neighbours' behaviour and, in this way, vultures work together to scan vast areas of countryside for fallen livestock. Further, vultures are adapted to quickly and effectively consume a carcass. We have seen firsthand, in South Asia, 20 vultures consume a cattle carcass in less than 1 hour. Given the tendency for animals to die at night and the many responsibilities of livestock owners, a wake of vultures could locate and consume a contaminated carcass before many livestock owners could organise its retrieval. Further, in mountainous areas of Spain, livestock owners are exempt from retrieving carcasses. In these cases, livestock could be treated with *diclofenac* during round-ups. It is generally considered that domestic livestock constitute more than half of the biomass eaten by vultures in Europe. Scientific data confirm that vultures, and Griffon vultures in particular, can identify a dead animal much quicker than any other necrophagous species. An average of 31 minutes has been established for Griffon vultures, reinforcing the idea that vultures will be ready to feed on recently dead animals (Cortés-Avizanda et al., 2012) (Duriez et al., 2012).

All livestock are rounded up once or more during their lives, and *diclofenac* may be used to treat ailments at these times. If these animals are released and then die within 10 days of treatment, they could in turn kill vultures. In fact, the stress and physical nature of a round-up itself may increase the likelihood that an animal might die.

As explained before, vultures feed mostly on: a) Carcasses and other animal products made available to them in registered and custom-built vulture feeding stations b) carcasses of dead animals found in the field in a more natural foraging and feeding pattern (with more unpredictability, both temporal and spatial).

Feeding patterns are extremely variable and cannot be characterised – in some regions with lots of feeding stations, some vultures feed almost exclusively at feeding stations, while in other places with no or few feeding stations they feed mostly on carcasses in the field. Further, some vultures feed at feeding stations in some parts of the year and may migrate to areas with no feeding stations in another season, making the overall situation rather fluid and variable.

In Spain alone, there are approximately 200 authorized feeding stations, and these vary greatly in size and management. Some of the "muladares" are managed by the local authority, city council, county council or even by conservation NGOs. There are also cases of legal muladares run by

birdwatching companies or individuals that will receive donations of dead animals or meat by-products and will leave them in a specific semi-controlled area. Only considering the 10 authonomous communities that provided data, these muladares receive about 2.700 tonnes of carrion per year.

As to which parts will be left out for vultures to feed, there is a great variability, from whole animals to bones, organs or muscle tissues.

In Spain, the Ministry of Agriculture and Environment (MAGRAMA) keeps a register of all carcasses (and in some cases parts of carcasses) transferred to vulture feeding stations. Data provided indicates that, approximately, 345 and 38,500 carcasses of indoor raised cattle and pig, respectively, could be left out in *muladares* per year. This constitues a very important food-resource for the wild vulture populations.

Further, there is solid scientific evidence suggesting that almost all of the carcasses that are left out in the fields and are not collected, following the new sanitary regulations, are consumed by vultures - Cortés-Avizanda et al. 2012 has suggested that 89% of observed carcasses attracted vultures to feed.

Beyond those carcasses left at specifically opened muladares, data from MAGRAMA suggest there will be another 27,000 carcasses left out yearly in the open fields and therefore accessible for vulture consumption in the scavengers' protection areas. Thus, summing all muladares and "open field" available carcasses, there would be, on average, 66,000 dead animals available for vultures per year.

There is no such data available for Italy, but LIPU (BirdLife Partner in Italy) informs that a few thousands of carcasses are also left out for vultures to feed in Sardinia and the Abruzzo region.

Potential measures to mitigate risks from veterinary *diclofenac*

Despite the measures put in place by regulation CE 142/2011, there are currently no measures in place to test for the presence of *diclofenac* in tissues of dead animals. Neither the Spanish drug-alert system (VIGIAVET) not its European equivalent (EUDRAVIGILANCE VETERINARIA) have ever registered an alert for necrophagous-birds intoxication by this drug. There is therefore no system in place to routinely detect veterinary *diclofenac* in tissues of animal by-products. Further, testing for *diclofenac* is very expensive, and can be done only in handful of laboratories – none of which is in Spain.

BirdLife International has been unable to get a solid estimate of the current usage of veterinary *diclofenac* in either Spain or Italy. This is of critical importance, given the large numbers of carcasses referred in the previous paragraphs. Local access to the drug, despite being limited to veterinarians, seems to be far easier and uncontrolled than it should (data from SEO/BirdLife), and neither the governments nor us can present accurate data for this report.

The Spanish Government recently released a risk-assessment report for veterinary *diclofenac* in Spain (MAGRAMA, 2014) where three scenarios are given. In this report they estimate that only 1-2% of all the carcasses available to vultures may have been treated with *diclofenac*. BirdLife International cannot agree with such a conservative estimate, because of the absolute lack of field-data and detailed information about *diclofenac* availability around vulture strongholds.

Day to day operations for animals left out in the field (either open field or *muladares*)

Data from our partners in Spain and Italy confirm that the control measures in place are weak and rarely followed for the vast majority of the animals left in the open. A better enforcement does occur in *muladares*, given their more regulated functioning and intrinsic value both as research

stations or bird watching spots. The chances that a *diclofenac*-treated carcass is left out in the open are high and could already be happening.

It should be taken into account that in most Spanish regions, budgetary cuts have been very serious on environmental issues, and that surveys and monitoring by environmental law enforcement officers, in particular forest and rural rangers, have been restricted, and available budgets for such testing have decreased dramatically over the past decade.

It is therefore impossible to assume that free ranging cattle are not treated with veterinary *diclofenac* in Spain – on the contrary, the precautionary principle would recommend we do consider it may be used. In this case, and unless treated animals are permanently confined, it is virtually impossible to guarantee that a treated animal may not be available to vultures if it dies in the fields. Griffon vultures usually eat 90% of dead carcasses, which they normally reach less than 1 hour after death, often well before the farmer.

Day to day operations of intensive farming

As for the case of penned animals, such as pig farms, veterinarians do not supervise directly the disposal of dead animals. On most occasions, veterinarians will only visit the farm when called by stockbreeder and will not be present if a *diclofenac*-treated animal dies. To believe those cattle-owners, on top of their daily responsibilities, will ensure adequate separation and disposal of these animals is, to say the least, a very risky judgement to be made.

Addressing the risks posed by the mere commercial availability of veterinary *diclofenac* in Spain and Italy would require a complex set of additional controls and practices that are not only extremely expensive, but complex and even counterproductive– given that there is an alternative readily available (meloxicam), equally cheap, and with the same therapeutic properties. Some of the steps that would need to be incorporated would include:

- Establish a system to routinely test tissues of animals for this drug, within the EUDRAVIGILANCE VETERINARIA programme framework
- Establish additional control mechanisms in all livestock explorations. This would need to secure that all extensive livestock treated with *diclofenac* should be isolated and kept indoors for at least 7 days (and not 2 as the MAGRAMA report suggests) after treatment: and that in the intensive operations cattle and pigs treated with veterinary *diclofenac* should also be separated from the rest, checked regularly by a veterinarian, and not sent to the vulture feeding stations in case of mortality
- In case any of the *diclofenac* treated animals die, the carcass should be collected by a specialized company and destroyed, so as not to enter the vulture food chain

These measures entail considerable costs, regulation and red tape. Given the proven effects on vultures, the status of the birds, the considerable investment made, our opinion is that the alternatives are too costly, complicated and unnecessary, when there is an alternative readily available.

Risk assessment carried out to date

In Spain veterinary *diclofenac* is marketed under two brand names, Diclovet and Dolofenac, (registered by FATRO Iberica SL). In Italy, Italy, veterinary *diclofenac* is commercialised under the name Reuflogi (registered by FATRO S.p.A.).

As per the three drugs risk assessment, general conclusion is that "the risk-benefit profile for the target species is favourable, and that the quality and biosecurity of the drug for humans and the environment is acceptable". No mention of their well-known impact on vultures is made.

On the contrary, on page 4 of the risk assessments for Diclovet, it is written "the drug is safe for the people administering it, for the consumers of animal products from treated animals, and for the environment, when recommendations are used".

In relation to Eco-toxicity, the manufacturer has only presented a phase I report, which dismissed the need for a phase II report, according to directive CVMP/VICH/592/98.

The authority responsible for its control in Spain (Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) has not carried any pharmacological, toxicological or residues studies for the drug's impact on necrophagous species. This is because, according to Spanish legislation (article 7 of the *Real Decreto* 1246/2008 of 18 July), this is not necessary when the drug is for a bioequivalent of a generic medicine with reference values established. There is, for the case of the Spanish products, a simple statement in its technical dossier stating, " Do not administer to animals susceptible to enter wild animals food chain". Having in mind that recommendations of medicines are not always respected, even for human consumption, we are convinced that a significant amount of corpses will be disposed of, disregarding this statement.

BirdLife International believes that given the known effects of *diclofenac* on vultures and the major depletion of their population caused by this drug in Asia, this and other NSAIDs should always be evaluated against secondary poisoning by scavenger birds. Yet, monitoring and tracing all the animals that could have been treated, or exposed to this drug, would require additional resources, both to public administrations responsible for the monitoring, and cattle-owners. This, according to data provided by BirdLife partners in Spain and Italy, would be prohibitively expensive. It would also be an illogical measure, considering that vulture-safe alternatives exist (Meloxicam).

Vultures are already being poisoned by NSAIDs in Europe

We know that Spanish vultures are exposed to NSAIDs, because we have found *flunixin* in the tissue of a dead Griffon vulture from southern Spain with severe visceral gout (paper in press to appear soon in Biological Conservation). We are confident that *flunixin* poisoning caused renal failure and death in this vulture. How this wild bird consumed *flunixin* is unknown but it had to be via one of ways described in this report. At least in Spain, *diclofenac* and *flunixin* are recommended for treatment of the same livestock species and for similar ailments (actually, *diclofenac* is recommended for more types of ailments than flunixin). Further, both drugs have similar withdrawal periods. Therefore, the *flunixin* case provides indisputable evidence that Spanish vultures are exposed to *diclofenac*.

It is very important to remember that only a small number of carcasses contaminated with *diclofenac* are needed to cause serious declines in vultures. Modelling our data from India and Pakistan indicate as few as 1 in 760 domesticated ungulate carcasses contaminated with lethal levels of *diclofenac* caused declines in the Oriental White-backed vulture (*Gyps bengalensis*) of about 50% per year (GREEN et al., 2004) . There is no reason to think that the closely related

European Griffon vulture would differ greatly in response, given it too is intolerant to low concentrations of *diclofenac* (Swan et al., 2006b). From our observations and calculations, we can say with high confidence that even if only 1 in every 2000 carcasses available to Europe's vultures were contaminated with lethal levels of *diclofenac*, their populations could be halved in six years (Margalida et al. 2014 submitted).

Comments on Topic 2

Depletion of diclofenac residues in food-producing species.

In replying to this request from the EC, the CVMP welcomes comments and information from concerned stakeholders.

Comment

BirdLife International has carried our detailed analysis on *diclofenac* depletion for Indian cattle (*Bos indicus*) and goat (*Capra hircus*) (Taggart et al., 2007). The EMA has data on *diclofenac* depletion for European cattle (*Bos taurus*) and pig (*Sus scrofa*) (EMAE 2004 *diclofenac* summary report). Both studies followed similar methods. A key difference, however, between the two is the dose of *diclofenac* given to the two species of cattle. Specifically, we used 1 mg/kg doses while the EMA used 2.5 mg/kg doses. The dose used by the EMA is the recommended dose per day for veterinary *diclofenac*.

In both studies, *diclofenac* depleted from the cattle species slower than from the smaller-bodied animals (e.g. *diclofenac* was undetectable in goats after 26 hours). Our results show that *diclofenac* was detectable after 167 hours (~7 days) in cattle viscera. The true concentration of *diclofenac* in this tissue was below our level of quantification at 10 µg/kg. The EMA results show that *diclofenac* was detectable after 144 (6 days) in cattle liver (27 µg/kg) and muscle (5 µg/kg). The experiment conducted by (Oaks et al., 2004) shows that a dose as low as 7 µg/kg can kill an Oriental White-backed vulture (*Gyps bengalensis*; there is no reason to think that Griffon vulture (*Gyps fulvus*) would differ greatly from this response given it too is intolerant to low concentrations of *diclofenac*). In addition, among the carcasses of cattle that we sample in India, we have found some that appear to have been treated with double the recommended dose (Taggart et al., 2007). Larger doses would increase the time needed for *diclofenac* depletion. It is possible that *diclofenac* will be misused in this way in Europe, just as it is in India.

Therefore, cattle tissue may be lethal to vultures for more than 1 week after *diclofenac* treatment. This is why we only use cattle that have lived longer than 10 days in our care at vulture Safe Feeding Sites in Nepal; to ensure that they have metabolised all *diclofenac* that they may have been treated with. In Europe, withdrawal periods of greater than 10 days for cattle should ensure *diclofenac* is sufficiently depleted for vulture consumption as well. But vultures can consume carcasses of animals not for human consumption, like horses (Spain). These animals can be slaughtered without prior withdrawal periods. Further, we do not know the time needed for *diclofenac* depletion in horses, but it is likely to be greater in these larger-bodied animals.

There are four obvious problems associated with withdrawal periods in general: 1) it is up to the livestock owner to adhere to withdrawal periods; 2) what happens to animal products that are found to be within the withdrawal period; 3) withdrawal periods are designed to protect humans not vultures; and 4) withdrawal periods are only relevant to slaughtered animals – not to fallen stock. Despite good regulation, European laws are not immune to human cheating; therefore, it is fair to assume that on occasion withdrawal periods are not adhered to. A livestock owner can be

found to be breaching the withdrawal period, through either inspection of veterinary treatment logbooks, which can be incorrectly filled, or tissue sampling, which leads to tissues requiring disposal. Where do scraps, like intestines, from carcasses with *diclofenac* levels above the maximum residue level, and tissues that fail maximum residue level tests, end up? Some may be supplied unknowingly to feeding stations and irresponsibly dumped in *muladares*. Even if tissues considered unsafe for humans are not provided to vultures, the maximum residue level for *diclofenac* in beef muscle in Spain is 5 µg/kg, which is associated with a 27 µg/kg level of *diclofenac* in the liver of the same animal (EMA results above) and a similar concentration of *diclofenac* in intestines (Taggart et al., 2007). There is no maximum residue level for intestines in Spain, suggesting this tissue is not tested, and therefore, intestines containing lethal levels of *diclofenac* can be provided to vultures from cattle considered "safe" with maximum residue levels lower than 5 µg/kg. Finally, where do fallen, sick or diseased carcasses (i.e., those considered unfit for human consumption) end up? Quite often in *muladares* and it is highly likely that many of these would have been treated with drugs in the days prior to death, precisely because they were ailing.

We reiterate, only a very small proportion of carcasses contaminated with *diclofenac* can cause massive declines in vulture populations. In this way, a more precautionary approach is needed to protect Europe's vulture than simple relying on measures designed to protect humans.

Comments on Topic 3

Use of veterinary medicinal products containing diclofenac in the field – which species are treated and how often? What measures are taken to ensure that necrophagous birds are not exposed to residues of diclofenac in treated animals either through feeding stations or inadvertent exposure (e.g. death of treated animals in regions where necrophagous birds are present)?

In replying to this request from the EC, the CVMP welcomes comments and information from concerned stakeholders.

Comment

Which species are treated and how often

In Spain veterinary *diclofenac* is marketed under two brand names, Diclovet and Dolofenac, (registered by FATRO Iberica SL). In Italy, Italy, veterinary *diclofenac* is commercialised under the name Reuflogi (registered by FATRO S.p.A.).

According to data compiled by BirdLife International, this drug will be particularly used to treat MMA (mastitis-metritis-agalactia syndrome) on lactating females, especially sows, or respiratory diseases, and limps in cattle. Although the drug is probably more used in penned animals, we are aware that unofficial/illegal dumping of corpses is not rare. Official veterinarians interviewed informed that they are not aware by the authorities of any specific measure to deal with corpses treated with *diclofenac*.

Diclofenac could also be used on extensive livestock, in particular cattle. BirdLife International partners inform that in most cases, dead animals will be discovered first by vultures and later (and not always) by farmers. This has to do with the very particular characteristics of such farms, occupying very large areas with medium to low cattle density. If any of the *diclofenac*-treated animals dies in the open, it will be virtually impossible for the farmer to collect it before vultures gain access to it. According to scientific evidence, a small number of carcasses with *diclofenac* can have a significant impact on vulture populations and not only locally, but in a wide area, as vultures travel and forage far and wide. A *diclofenac*-laced carcass can impact on vultures from a neighbouring region, or even country, hundreds km away.

In Spain, cattle, pigs and horses are the only target species. There is extensive horse farming in many regions, especially, but not only, in northern Spain. Free-range cattle farming is common in most regions. Extensive pig farming is common in southwest Spain. Intensive pig farming is extremely regular in Avila and Segovia provinces as well as in Catalonia, but also in other areas. vultures are abundant in all mentioned areas.

We we not given access to official data on the use of *diclofenac* on cattle and pigs in Spain. The product has only been available for a short time, and potentially the amount available is relatively low (although even small amounts can have dramatic effects on vultures). Although in some places they still use the same treatments as before, the spread of the use of any product of this kind depends on the experience of neighbouring farmers. Once a new product starts to be used, it spreads very fast.

The only measure taken in the *diclofenac* drug package is the inclusion of a technical note in its technical dossier stating "do not administer to animals susceptible to enter wild animals food chain". This is clearly not enough, having in mind the little attention paid to this kind of

recommendation by many users. *Diclofenac* is supposed to be administrated under the supervision of veterinary staff, but in practice this means only that the veterinary will prescribe the drug, but is the farmer who treats the animal.

Expansion to other world regions

Legalising the use of veterinary *diclofenac* would send the signal that its use is acceptable – also probably creating an export market from Europe to other regions. We all know that control systems and procedures elsewhere are substantially weaker than in Europe, so even if billions were spent in setting up the new mechanisms described above in the EU, these would not certainly be followed through in other places, where veterinary *diclofenac* could continue or start to kill vultures. Availability of *diclofenac* in Europe would effectively mean worldwide availability, with significant impacts on vultures worldwide. Vultures are already suffering a steep decline in parts of Africa (Botha et al., 2012), and the mere presence of *diclofenac* in the Mediterranean basin threatens even more of these wild vulture populations.

General conclusions

From our work in South Asia, coupled with our work in Southern Africa, we have direct evidence that *diclofenac* kills vultures (Oaks et al., 2004) (Swan et al., 2006a)and indirect evidence that it kills eagles as well (SHARMA et al., n.d.). In fact, we now think that *diclofenac* may threaten more than 30 species of scavenging raptor worldwide ((unpublished data, but see Sharma et al. 2012 Bird Conservation International).

Various other commonly used NSAIDs are also problematical. We also have direct evidence that *ketoprofen* kills vultures (Naidoo et al., 2010) Further, we have indirect evidence that *aceclofenac* (Sharma, 2012) *flunixin (*Zorilla et al. in press) and *nimesulide* (Cuthbert et al. in preparation) kill vultures. Note that evidence for *flunixin* comes from Europe *(*Zorilla et al. in press). We are also currently safety-testing *carprofen* and preliminary results suggest that the level of residue of this NSAID (and maybe others) at the injection site is lethal, even if levels in other tissues are not ((RSPB/UP/UHI, unpublished data). The toxicity for some untested NSAIDs, and very small levels of known vulture-toxic NSAIDs, may not be acute, but cumulative – gradual killing individual vultures over a period.)

The only NSAID shown to be vulture safe (to date) is *meloxicam* (Swan et al., 2006a)

Many other NSAIDs are available globally; the toxicity of which is unknown. We hope that one or more of these may prove to be vulture-safe to give veterinarians and farmers more choice. There is no impetus in South Asia or Europe to test these drugs and all the above knowledge has been gained through the efforts of non-profit organisations and the donations of the global community concerned with vulture conservation. What is more disturbing is that injectable NSAIDs are effectively exempt from Phase II risk assessment in Europe (due to the way the legislation is currently constructed).

Therefore, until this present assessment, the portfolio of peer-reviewed evidence complied over the last decade showing, without a doubt, that veterinary *diclofenac* caused unprecedented declines in vulture populations in South Asia, seems not to have been read before FATRO's *diclofenac* products were approved. Most veterinary NSAIDs in Europe are *meloxicam*-based, which is considered to have fewer side effects for both animals and humans.

There is no current market need for *diclofenac*-based products in Europe and, had our work been acknowledged, a precautionary decision might have been made. That decision would have ensured the safety of Europe's vultures; not jeopardised Europe's financial investment in the conservation of vultures; and avoided this current assessment. Therefore, we see a greater problem with how pharmaceutical drugs are approved in Europe, particularly NSAIDs, and call for an immediate ban on veterinary *diclofenac* in Europe and a strengthening of the current environmental risk assessment system

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