


Safety Assessment:  
Scavengers


10 November 2010

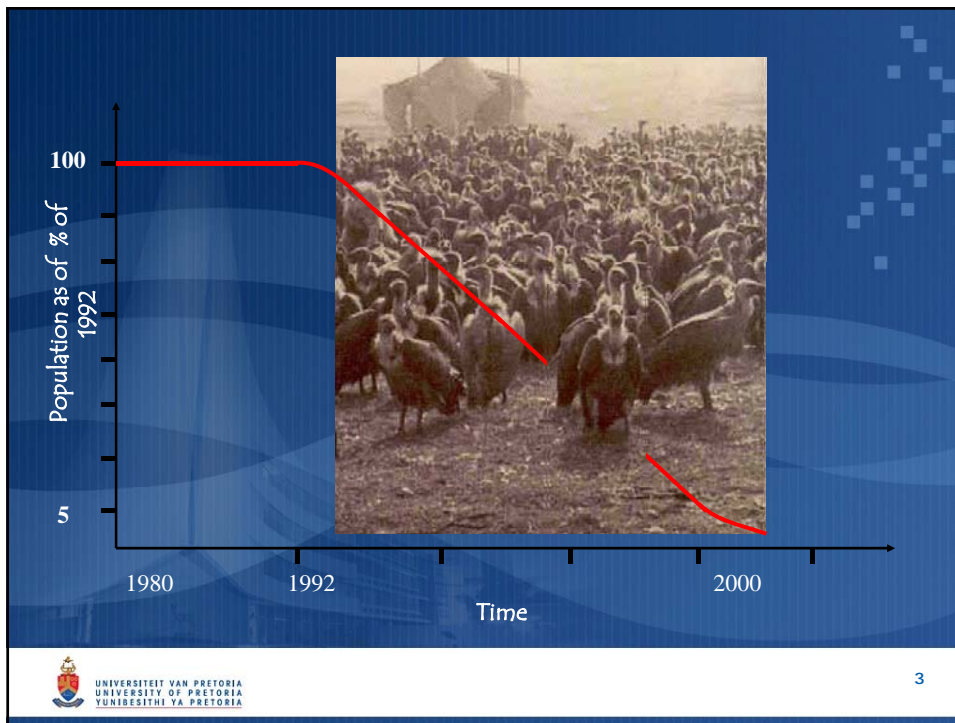
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## Introduction

- ◇ Drug residues are a potential hazard to animals feeding on animal carcasses or products
- ◇ Potential environmental hazard to predators and scavengers
- ◇ Different from environmental pollution and bio-accumulation of toxins (DDT)
- ◇ Acute toxicity (ARfD) e.g. pentobarbitone in lions
- ◇ Chronic toxic effects of diclofenac in vultures came as a surprise

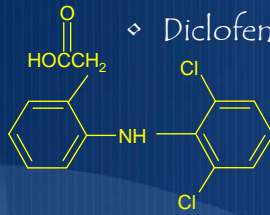
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- ◇ Only sign was severe visceral gout
- ◇ Of an unknown origin
  - Could it be an infectious agent?
  - Could it be an insecticide?
- ◇ Surprisingly it was diclofenac
  - A commonly used anti-inflammatory
  - Drug toxicity of an unprecedented scale




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◊ Diclofenac is an arylacetic acid NSAID



## Diclofenac exposure

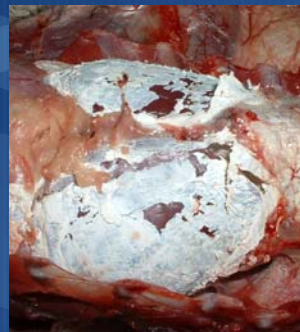


- ◊ Used extensively India and Pakistan for the treatment of inflammation, pain and fever in animals
- ◊ Exposure occurs through vultures consuming carcasses of livestock that were treated with diclofenac shortly before death



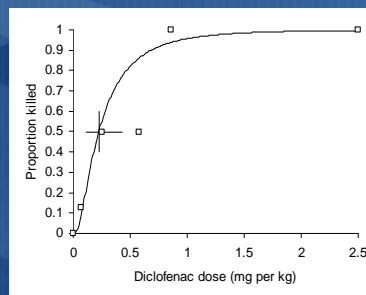
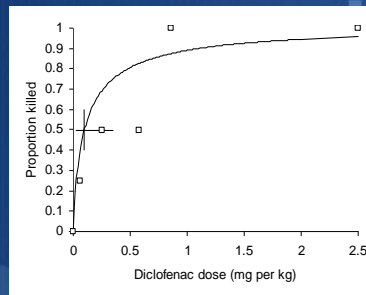
## Diclofenac toxicity in vultures

- Toxicity of diclofenac in OWBVs and Eurasian griffin vultures was first reported by Oaks *et al.* 2004;
- Acute toxicity with impaired renal function, extensive visceral gout and death through kidney failure was reported
- Mortality within 36 – 58 h after intake of a toxic dose



## Lethal dose

- ◇ Results of previous studies were used to estimate the median LD 50 on *G. bengalensis* by probit analysis
- ◇ Maximum-likelihood estimate of the mean LD50 was 0.098 mg/kg (95 % CI 0.027 – 0.351 mg/kg) and 0.225 mg/kg (95 % CI 0.117 – 0.1401) with outlier included and excluded, respectively



## Meloxicam Study

- ◇ Multi-phase study
  - Safety of drug only, at various doses
    - ◇ 0.5, 1, and 2 mg/kg orally
    - ◇ Monitored for toxicity
  - Safety of residues of the drug in meat
    - ◇ Meat from treated cattle fed to birds
    - ◇ Cattle double dosed as an additional precaution
  - Safety at multiple doses
    - ◇ Once daily im administration up to 2 weeks
  - Safety in multiple vulture species
    - ◇ Gyps coprotheres, Gyps africanus, Gyps Bengelensis, etc



## Dose selection of meloxicam in studies

- ◇ Tissue residues in 16 calves dosed with  $^{14}\text{C}$ -labelled meloxicam at 0.7 mg/kg for 5d
- ◇ Liver concentration of meloxicam residues 8.54 ppm (muscle 0.53 ppm)
- ◇ Represents a potential dose of 1,55 mg/kg in vultures (average weight 5.5 kg and meal size of 1 kg)



## Pharmacovigilance

- ◇ Wildlife species can not be simulated
  - Rely on information from the field
  - Requires reporting of toxicity by farmers, vets, etc
- ◇ Rely on other scientific studies
  - Publications
  - Results from similar species

## Conclusion

- ◇ Drug residues poses a risk to predators and scavengers as well as animal feeding on animal products
- ◇ Veterinary medicine residues that could potentially pose a hazard
  - Drugs that can cause acute toxicity or adverse reactions on single dose
  - Species susceptibility to drugs
  - Antimicrobial drugs