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ANTIPARASITICS AND THEIR IMPACT ON SOIL AND DUNG FAUNA

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- Environmental contamination of rural and suburban areas by medicinal residues constitutes a problem that has yet to be adequately regulated

Among the sources of medication discharge, **farming activities hold a special place**, due in particular to the diffuse nature of discharges which occur without any specific preliminary treatment.

Over the past decade, concerns have been increasingly expressed by the scientific community regarding the

possible unintended side effects of chemicals used in veterinary and agricultural practices and, more particularly, **in the widespread use of anthelmintics to control gastrointestinal parasites of grazing livestock and companion animals**.

This situation has raised concerns, not only for the possible impact on dung degradation, but also for the consequences on grassland insect communities, ecosystem stability and on the sustainability of pasture fertility

Development of anthelmintics

- The development of anthelmintics, and latterly endectocides with a broad range of target pathogens, **has provided more efficient and economic options** for the treatment and control of parasitic disease both in ruminant and monogastric animals.

In pastures, most antiparasitics are excreted in the faeces of animals, creating a concern for their effect on the organisms that feed and/or breed in animal dejections.

As the spectrum of activity of antiparasitics has enlarged, **the potential for affecting non-target organisms has increased equally.**

The processes of dung dispersal

Many of the non-target organisms play a vital role in the processes of dung dispersal.

They are crucial for maintaining pasture hygiene, nutrient cycling, soil aeration, humus content, water percolation and pasture productivity.

The organisms of the dung community

These non-target organisms ensure that the livestock grazing area is not drastically reduced by an accumulation of dung.

Dung feeder flies, coprophagous beetles and annelid worms are the most important organisms of the dung community.

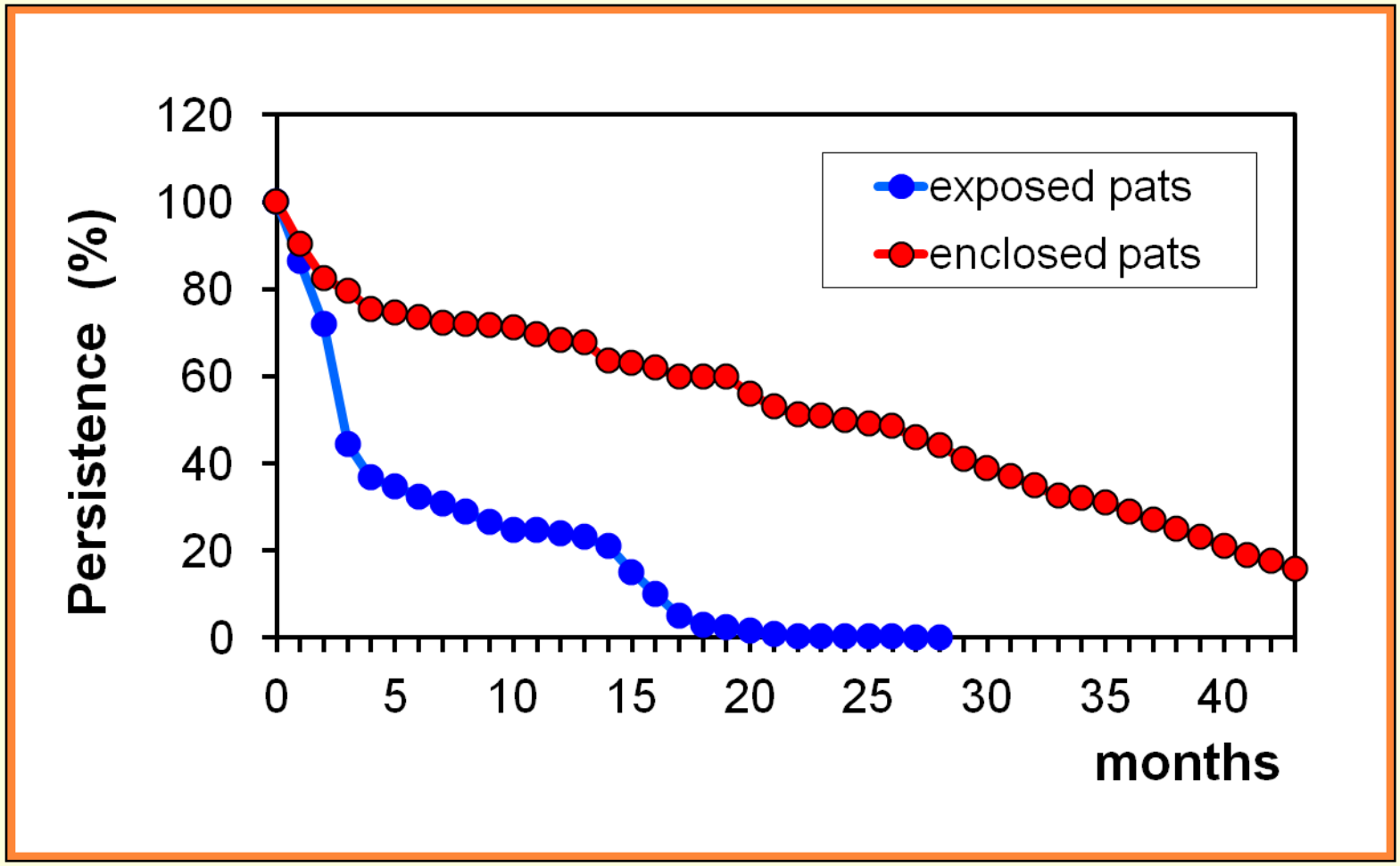
When beetles colonize dung pats, they dig tunnels which weaken the pats and, **at the same time, beetles inoculate the heart of pats with microorganisms as they carry spores of telluric fungi and microorganisms on their integument.**

Under such conditions, pats become progressively an annex of soil, with a network of tunnels making easier the colonization of pats by edaphic mesofauna.

Dung pat several weeks after insect colonization

Mechanical exclusion of insects for one month after the deposit of cowpats in the field

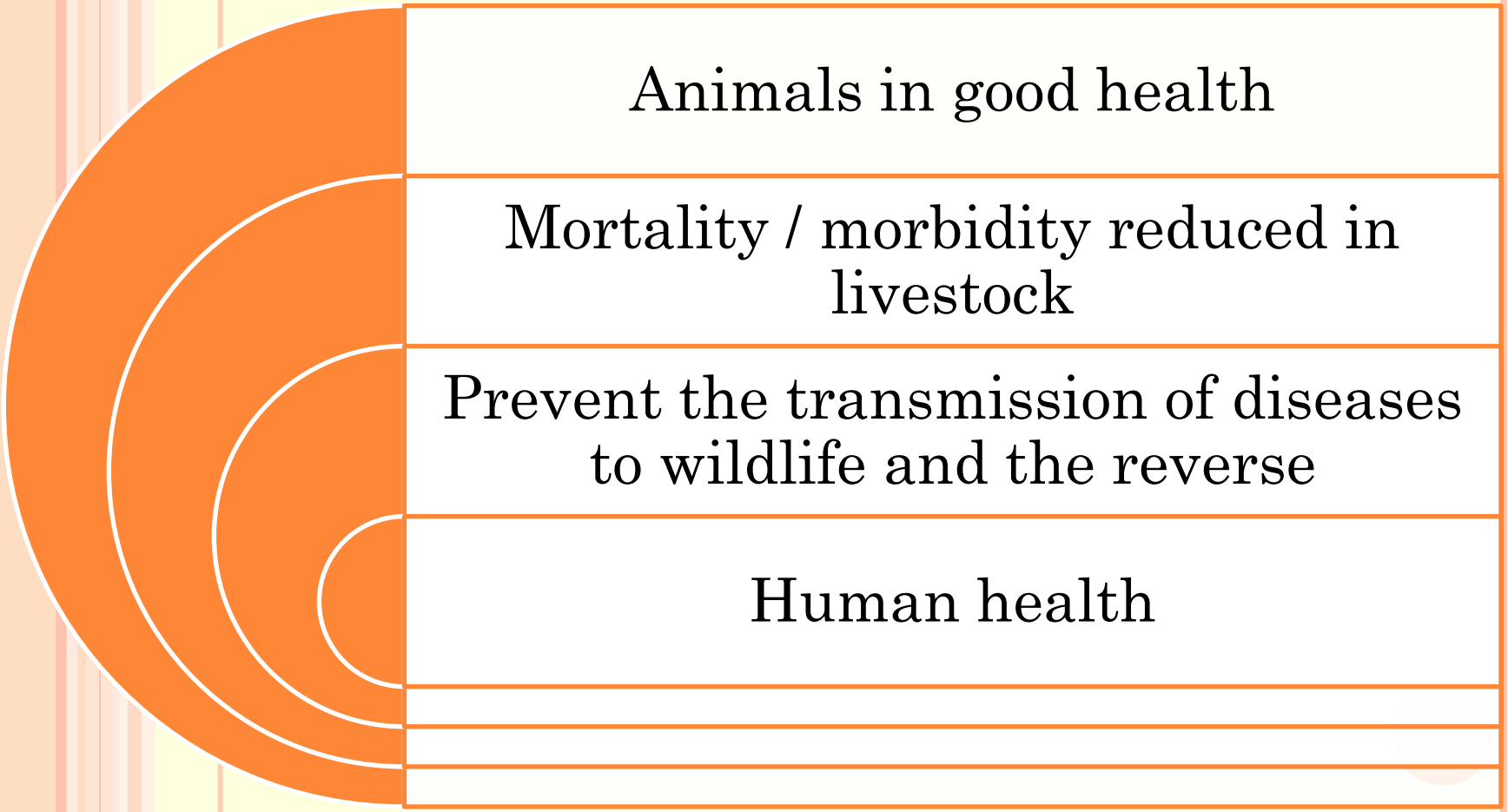
Mechanical exclusion of insects for one month: impact on the degradation



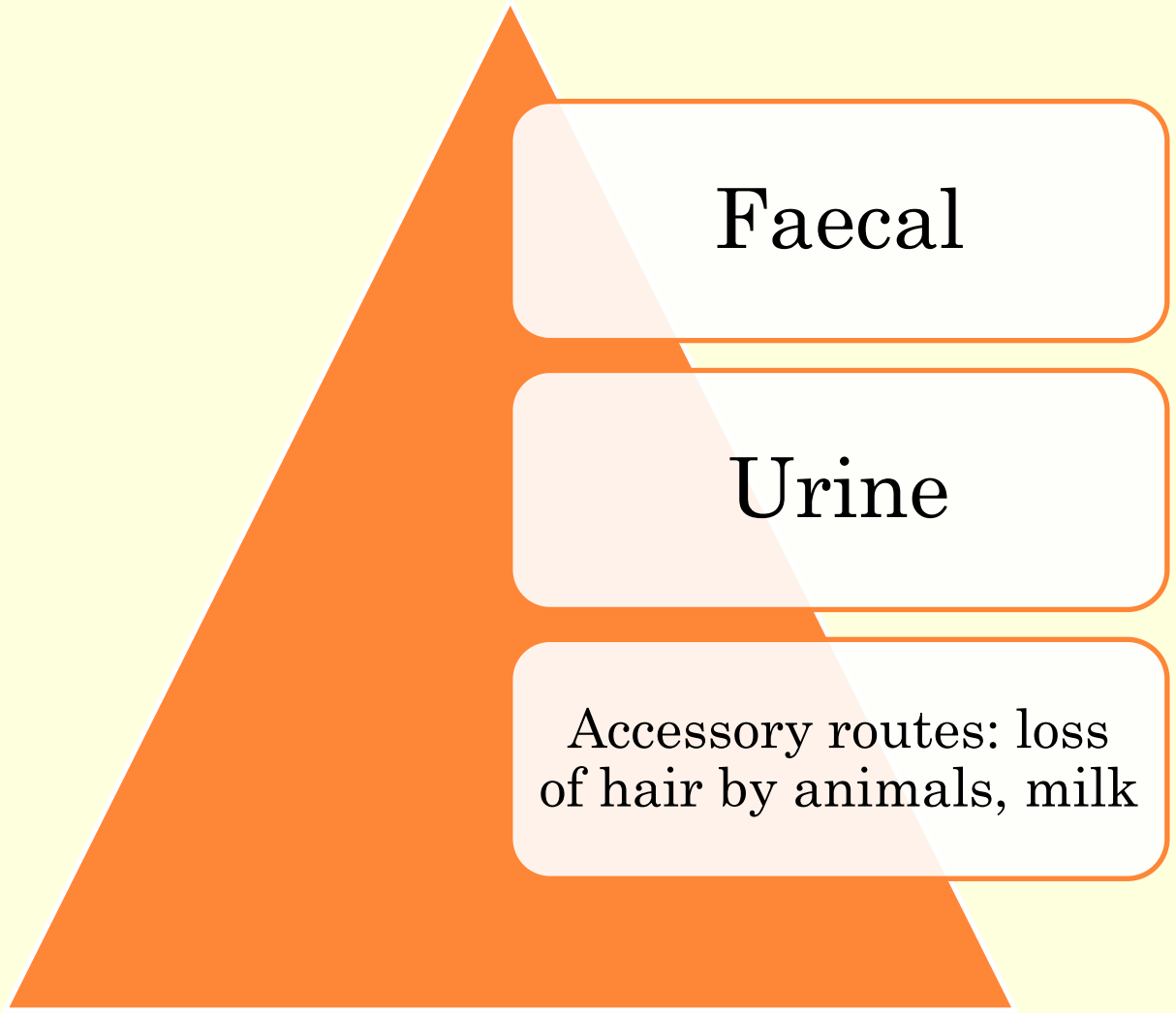
Mediterranean conditions (South of France)

Lumaret & Kadiri *Pedobiologia* 39 (1995): 506-517

Treatment of animals



Two main routes of elimination of compounds and their metabolites



Two therapeutic classes dominate the field of veterinary medicine: **antiparasitics and anti-infectious drugs**.

Four families (Tetracyclines, Sulfonamides, Penicillins and Macrolides) of veterinary medicinal products (VMPs) **account for over 80% of all veterinary sales in Europe**.

Urine route

This route is direct, with a short latency between treatment and excretion : a few hours or days.

Dung beetles and flies are not affected

Main anthelmintics excreted in urine

Imidazothiazoles (Levamisole)

Benzimidazoles (Albendazole)

Phenol derivatives, including salicylanilides (Nitroxinil)

No information about their action on earthworms and soil mesofauna, but probably no lethal effect.

Organophosphates (Diazinon, Fenthion): earthworms and soil mesofauna **may be concerned**, but we have no information about them.

Faecal route

Compounds and residues which are rapidly eliminated in faeces and are relatively harmless to coprophagous organisms

Benzimidazoles and related substances (cambendazole, fenbendazole, mebendazole, oxfendazole)

Imidazothiazoles (levamisole)

Salicylanilides (closantel)

Tetrahydropyrimidines (pyrantel, morantel)

In a field study, using a pulse release formulation (750 mg **oxfendazole**)

- **No observable effects of oxfendazole** on
  - - the rate of degradation of dung
  - - the number or weight of earthworms in pasture

• Wratten et al., *Vet. Res.* 133 (1993): 365-371

24 hours after oral administration of **morantel** at 10 mg • kg^{-1} bodyweight:

Morantel did not affect the development of the yellow dung fly in the faeces.

• McKellar et al., *J. Vet. Pharmacol.Ther.* 16 (1993): 87-92

Compounds which are rapidly eliminated in faeces and affect coprophagous fauna

Organophosphorous compounds	• Dichlorvos • Coumaphos • Crufomate (ruelene)
Piperazine and derivatives	• Piperazine (inhibition of GABA receptor; selectivity for helminths)

Other compounds are rapidly eliminated in faeces and affect coprophagous fauna (../..)

Benzene sulphonamides

- clorsulon (control of adult liver flukes (*Fasciola hepatica*) in cattle)

Benzoylureas (act as insect growth regulators by inhibiting synthesis of chitin)

- Diflubenzuron (stomach and contact poison)

Diflubenzuron: after **oral administration to cattle and pig**: about 70% to 85% of the administered dose is excreted unchanged in the faeces, and about 5% in urine.

In sheep, excretion through urine and faeces is equally distributed.

Classified as a Restricted Use Pesticide (RUP) in the United States.

Currently: only used against insects in livestock housing

DICHLORVOS (EQUIGARD)

In the years 1980-2000, dichlorvos (Equigard) was used in routine in horse treatment against roundworms.

All droppings of the first 5 days after treatment were toxic to insects

In summer, droppings of a single horse could potentially kill more than 20,000 dung beetles

Lumaret, *Acta Oecol., Oecol. Appl*. 7 (1986): 313-324

The droppings of horses treated with dichlorvos disappeared much more slowly than those of untreated animals.

Lumaret, *Acta Oecol., Oecol. Appl.* 7 (1986): 313-324

	% disappearance of horse droppings (dry matter)	
	After 1 month	**After 8 months**
Treated animals	**0%**	**43%**
Control	**22%**	**100%**

In France, almost complete disappearance of dung beetles (mostly rollers) in the sand dunes of the Mediterranean coast during the period 1990-2000.

This coincided with the treatment in routine of most horses with dichlorvos (development of equestrian tourism)

Veterinary preparations with progressive release

Pyrethroids

Macrocyclic lactones

Pyrethroids: stability in the environment

Some of the more recently developed pyrethroids can persist in the environment for a few months before they are degraded.

Deltamethrin, cypermethrin, permethrin, and their degradation products **not very mobile, especially in soils containing a high clay content or a large percentage of organic matter**

(Kaufman et al. *J Agric Food Chem* 29 (1981): 239-245)

Pyrethroids: stability in the environment

Stability during a few days and up to a few weeks when exposed to daylight

- half-life of about 6 days for Phenothrin
- 60% of Permethrin remained intact after 20 days

Long half-life in the absence of light (in soil, in dung and manure)

- Fenvalerate and Deltamethrin appear to be the most persistent compounds.

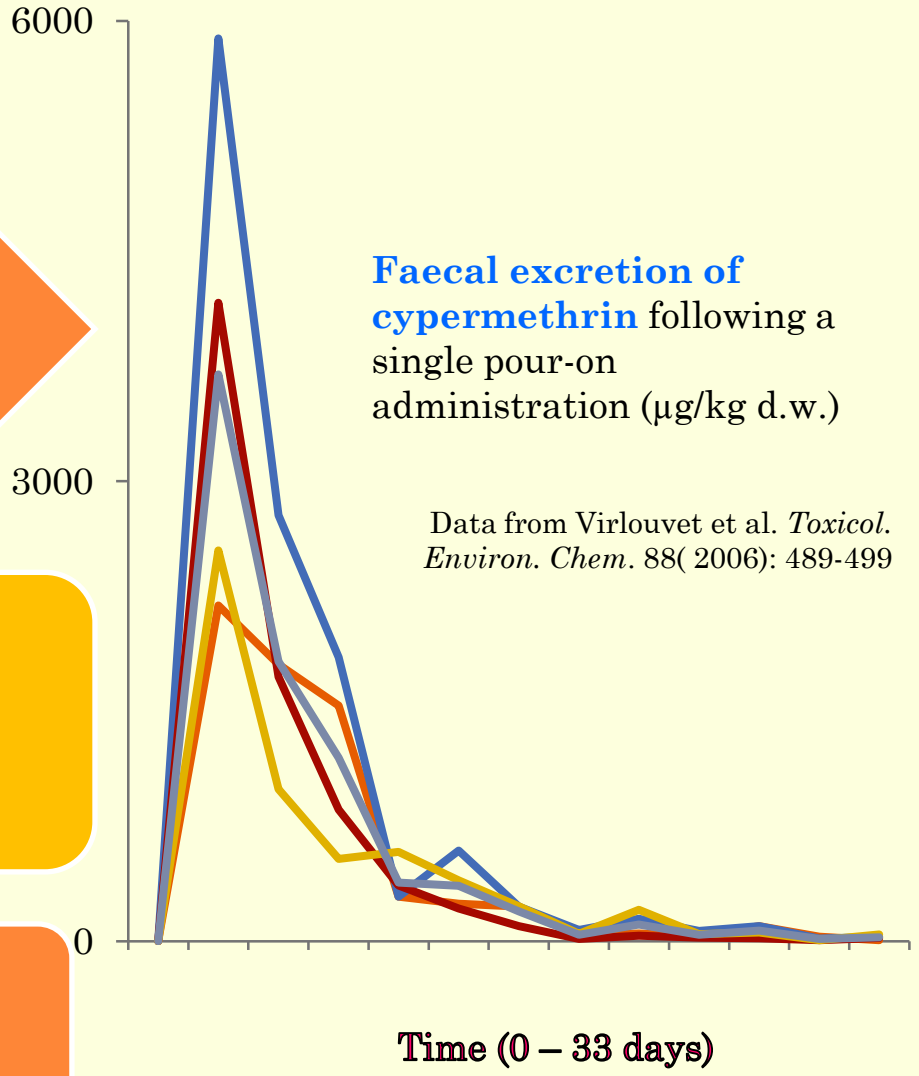
(WHO 1990. Environmental Health Criteria 94)

Pyrethroids: application methods and elimination

Ear tags with pyrethroids (flucythrinate, cypermethrin, permethrin). **Action against external parasites: 3 to 5 months.**

Pour-on application to control ectoparasites.

Faecal elimination



Faecal excretion of cypermethrin following a single pour-on administration (µg/kg d.w.)

Data from Virlouvet et al. *Toxicol. Environ. Chem*. 88(2006): 489-499

Pyrethroids: not as safe as you think !

- **Causal relationship between the pyrethroid treatments of livestock** and the mortality of dung beetles (Scarabaeidae).

- Pyrethroid residues (**alpha-cypermethrin, deltamethrin, flumethrin**) found in the faeces of cattle at concentration enough to be toxic to dung beetles. Significant residues were found in dead beetles found around dung pats of treated animals.

Wardhaugh, Longstaff, Lacey *Aust. Vet. J.* 76 (1998) 273-280

Krüger, Scholtz, Reinhardt *South Afr. J. Sci.* 94 (1998) 129-133

- **Under field conditions, deltamethrin is non-toxic to earthworms**

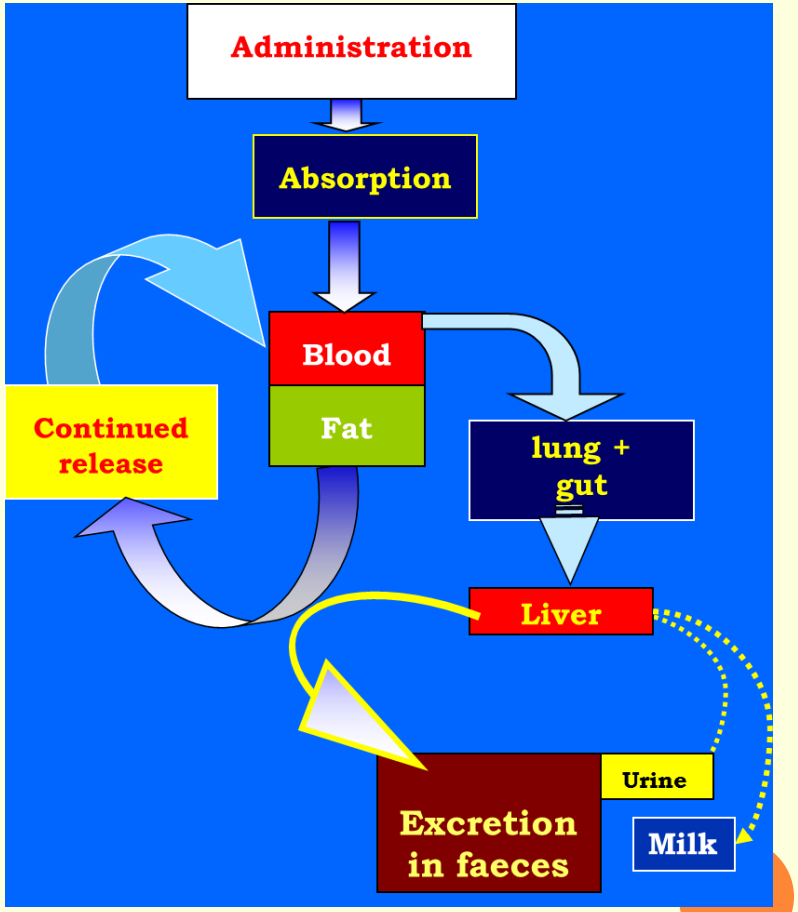
LC50 (14 days) >1290 mg/kg soil

Macrocyclic Lactones (MLs)

Extensively used as antiparasitic agents

These are systemic **endectocides** (drugs effective against both **endo**parasites and **ecto**parasites)

Absorbed after oral administration or injection or subcutaneously (pour-on), **then gradually released for several weeks or months**, depending on the mode of administration.



Macrocyclic Lactones (MLs)

- According to their chemical structure, two different groups: **Avermectins** and **Milbemycins**

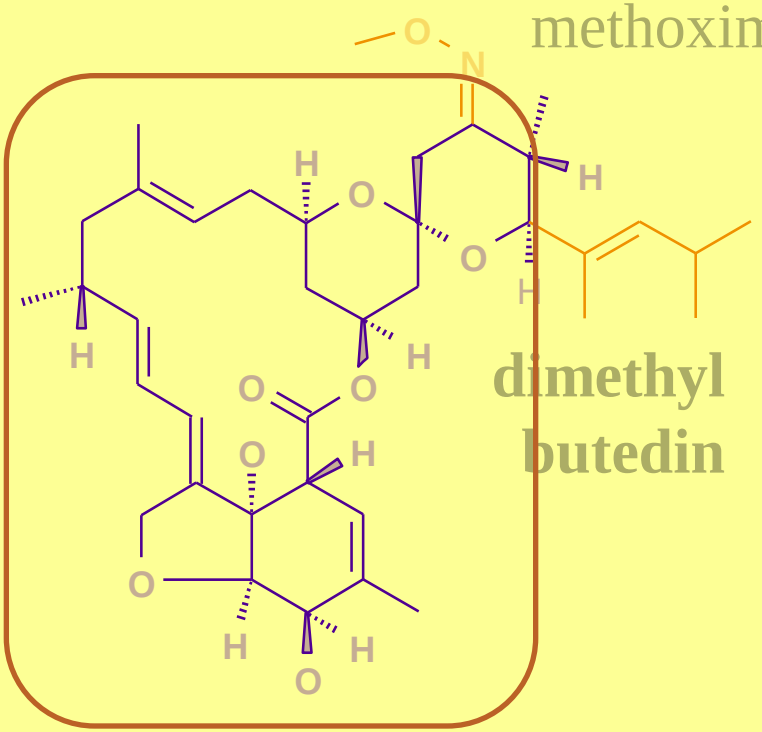
  - **Avermectins**: Abamectin, Doramectin, Eprinomectin, Ivermectin (used massively on livestock and pets), Selamectin.

  - **Milbemycins**: Milbemycin oxime, Moxidectin

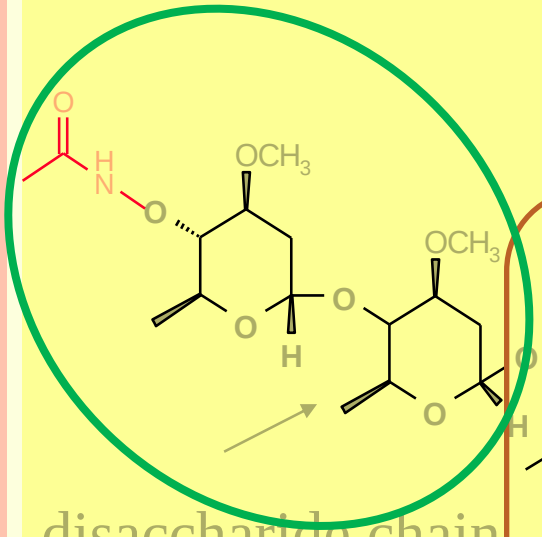
methoxim

MILBEMYCINS

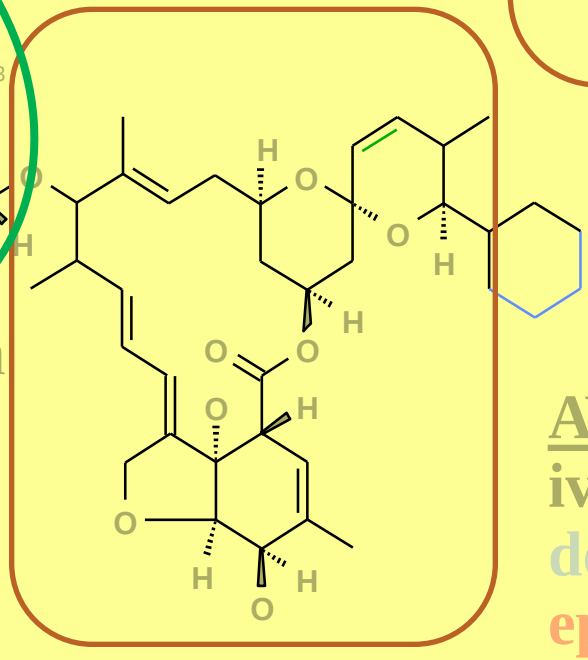
moxidectin



dimethyl butedin



disaccharide chain



AVERMECTINS

ivermectin

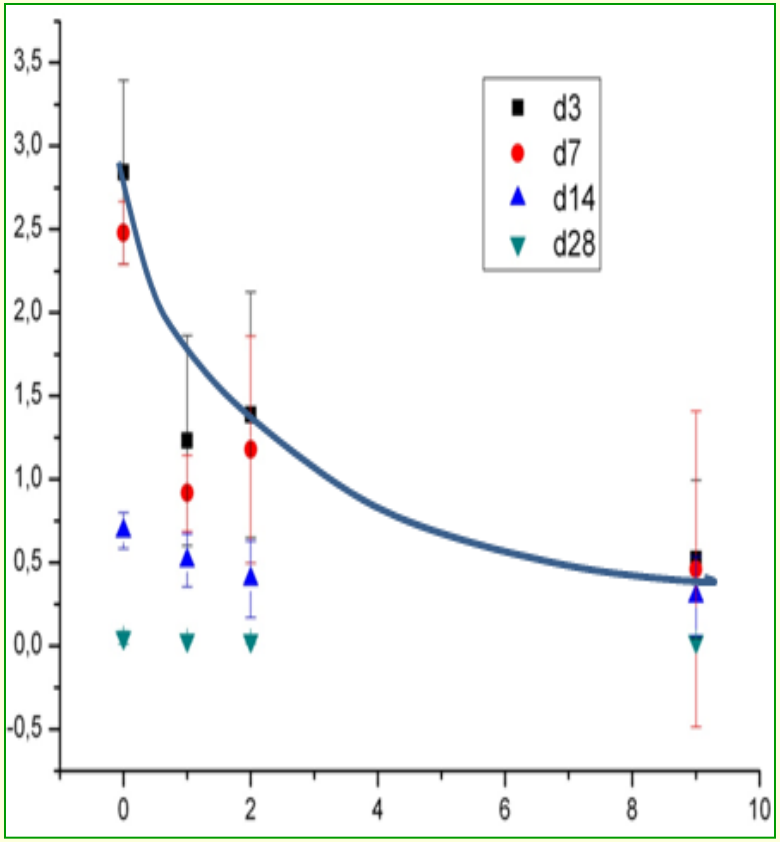
doramectin

eprinomectin

Low biodegradation of MLs in faeces and soil

- **Eprinomectin**: only 3% of the molecule converted to carbon dioxide after 64 days.
- **Ivermectin** in winter : **half-life 91–217 days.**
- Outdoors in summer (U.V. rays effect): **half-life: 7–14 days in soil.**
- **Much more longer in dung pats**

IVM concentration in cattle dung pats (mg/kg dung dry weight) according to time (months)



Tixier Thomas, PhD in progress, Univ. Montpellier
Manuel Wohde, PhD in progress, Univ. Giessen

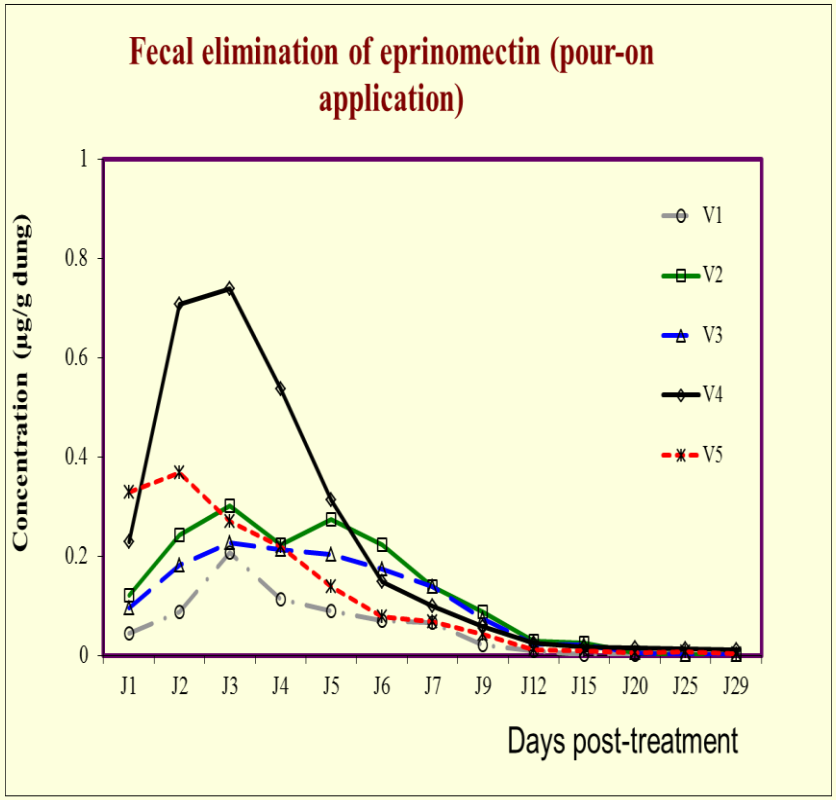
MLs are primarily excreted in the faeces

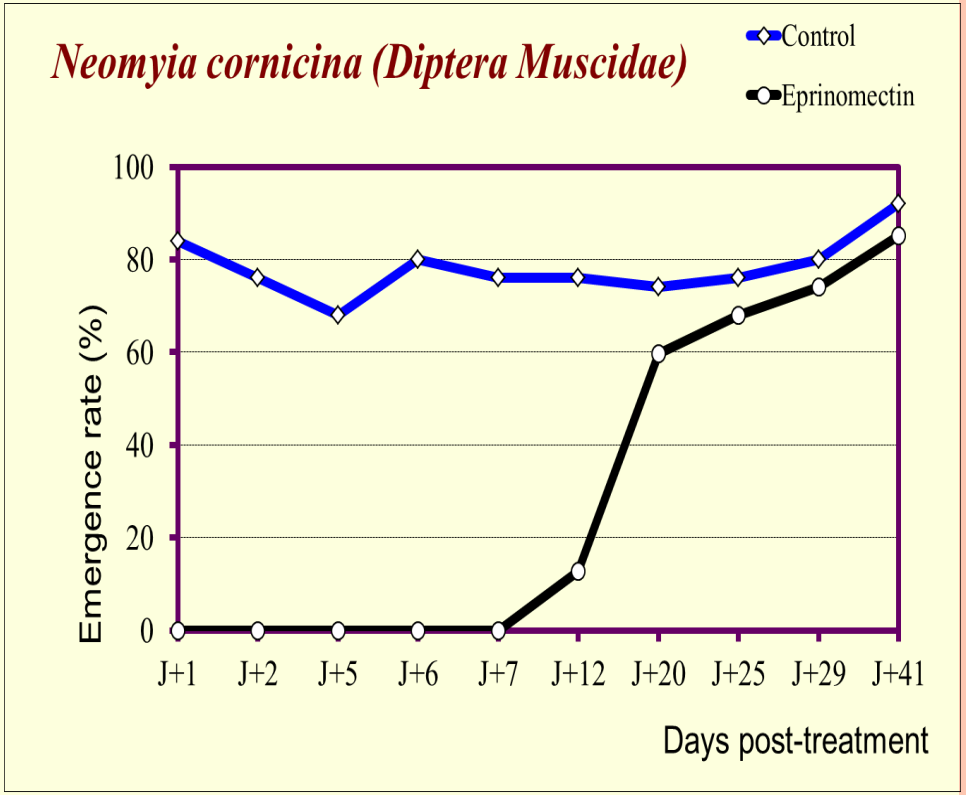
Residues affect arthropod development

- Very significant toxicity towards aquatic organisms (Daphnia).
- **Acute toxicity less pronounced towards terrestrial organisms (adults).**
- The larvae of Diptera are generally more sensitive to macrocyclic lactones than Coleopteran larvae.

Lumaret et al., *Current Pharmaceutical Biotechnology* 13 (2012): 1004-1060

Eprinomectin elimination and effects

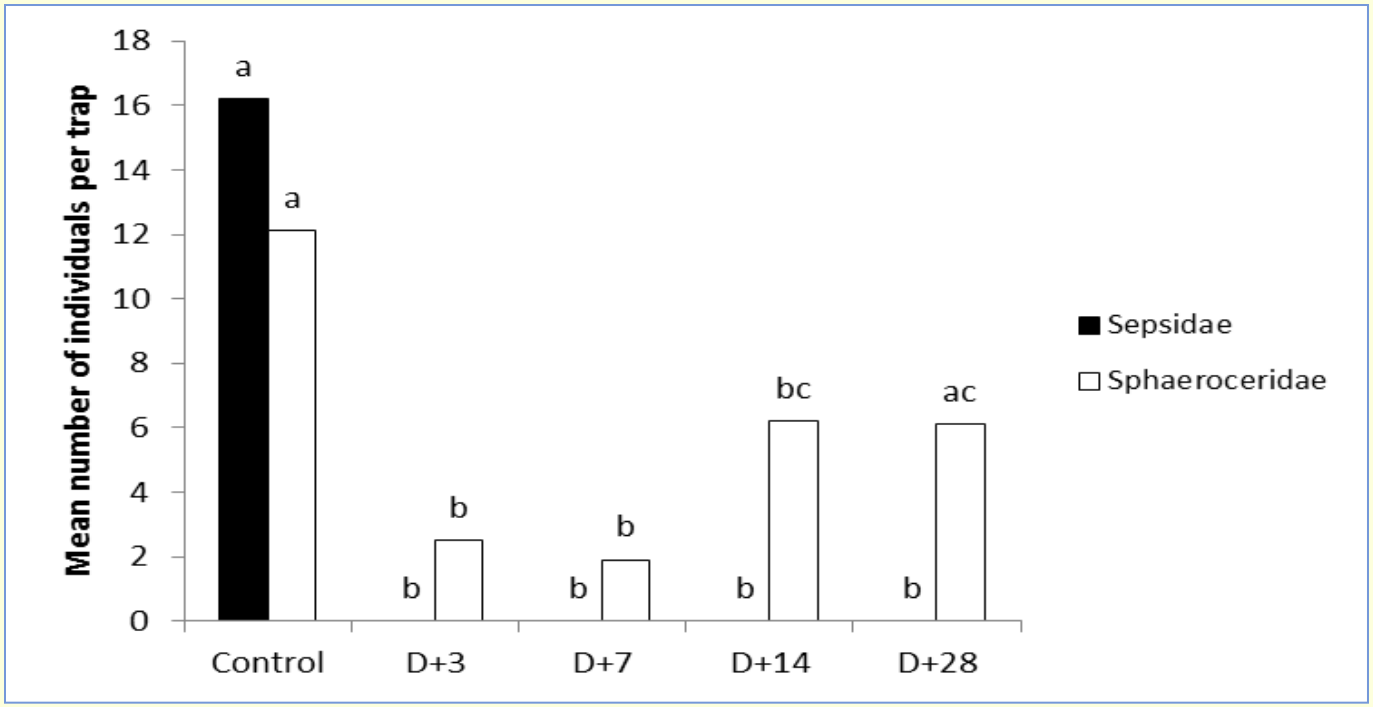




(Licking behaviour of animal V4:
higher concentration of EPR in dung)

Lumaret et al., *Environmental Toxicology and Chemistry* 24 (2005):797-801

Ivermectin (pour-on) Effects on Diptera



No emergence of Sepsidae flies during the first month following the treatment of animals

Tixier, PhD 2013

Sensitivity of flies to MLs

Decreasing toxicity :
Doramectin > Ivermectin ≈ Eprinomectin >> Moxidectin

Floate, Spooner & Colwell, *Med. Vet. Entomol* 15 (2001): 117-120

Mature adult dung beetles are usually unaffected by macrocyclic lactone residues found in dung

But high mortality of newly emerged adults fed with faeces containing ivermectin residues

Copris hispanus (L.)

Wardhaugh et al. *Vet. Parasitol.* 48 (1993): 139-157

Wardhaugh et al. *Aust. Vet. J.* 79 (2001): 125-132

Larval stages of dung beetles very sensitive to residues of MLs

High larval mortality reaching up to 100% during the first week after treatment

Aphodius constans larvae

Aphodius constans (dung beetle), a good model for ecotoxicological testing

- **<u>IVM pour-on</u>** (cattle): **larval mortality during the first 3 weeks post-treatment**

LC50 = 590 µg kg^{-1} dung (fresh weight)

Aphodius constans Duft.

Lumaret et al. *Vet. Res.* 38 (2007): 15-24

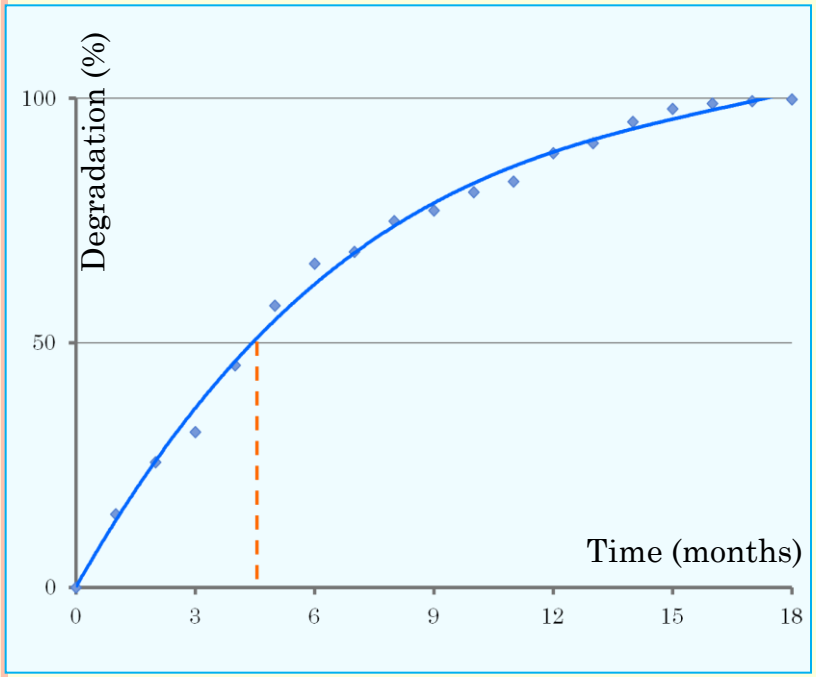
Degradation of cattle dung pats according to time

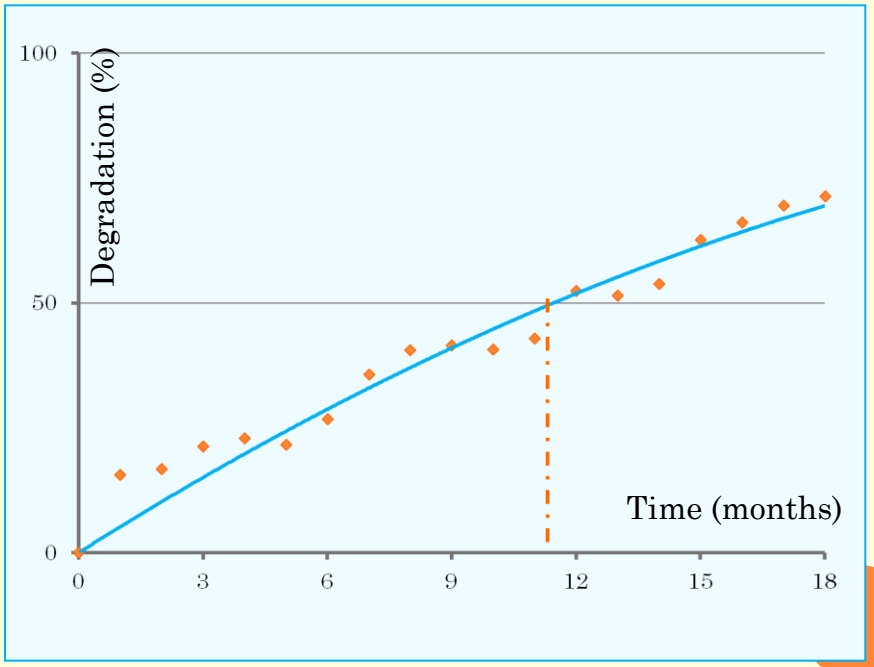
Control animals

Half-time degradation : 4.5 months

Treated animals (IVM bolus)

Half-time degradation : 11.5 months





Errouissi & Lumaret, submitted

These findings can be generalized

- **Canada**
  - Slowdown in the degradation rate of dung associated with the reduction of insect activity
  - Direct addition of ivermectin to dung (spiked dung) at concentration equivalent to the levels observed in dung of treated animals:
    - droppings little degraded after 340 days of exposure
    - control dung extensively degraded after 80 days

Floate, *Bull. Entomol. Res.* 88 (1998) 25-35

- **Australia**
  - A field study confirms these findings

Dadour, Cook, Neesam, *Bull. Entomol. Res.* 89 (1999) 119-123

Possible effect of antibiotics on dung beetles

- The gut of dung beetles contains many symbiotic microorganisms.
- **Hypothesis: microflora could be impacted by antibiotics**, causing mortality or at least delay in insect development.
- This hypothesis should be tested in the coming years.

JP Lumaret

Hump-backed larva of *Onthophagus vacca* (L.)

Indirect impacts of veterinary medicinal products on other organisms

- The use of certain chemicals may indirectly affect vertebrates by reducing their **food resources**.
- This applies to many **birds**, some **bats** (Greater Horseshoe Bat, Serotine, Noctules) that feed on dung beetles and Diptera (Bat News, 50, 1998) and various mammals like **hedgehogs**, **moles**, **shrews** and **badgers** whose diet includes many invertebrates.

THE FUTURE, A RATING SYSTEM FOR BETTER INFORMATION?

During the 1990`s the Scarab Research Group at Pretoria University (South Africa) started screening parasiticides for non-target effects.

The Dung Beetle Friendliness Trademark was registered in 2003

How does the Trademark work? – basically a 3-Star rating:

1 star – product is only fit for limited use in already disturbed setting (e.g. feedlots)

BUT NOT in pastures, severe negative effect on dung beetle fauna found in tests

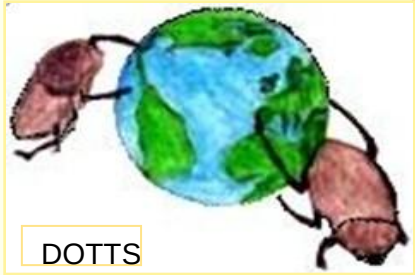
2-stars – product is suitable for occasional use in pastures

3-stars – product is suitable for regular use in pastures, since there were no negative effects on dung beetle fauna found in tests

No trademark on package = product has not been tested yet

Acknowledgements

- Nicole Adler, Federal Environment Agency, UBA, Germany, for supporting our group research.
- All the members of the Dung Organism Toxicity Testing Standardisation (DOTTS) Group



Thank you for your attention