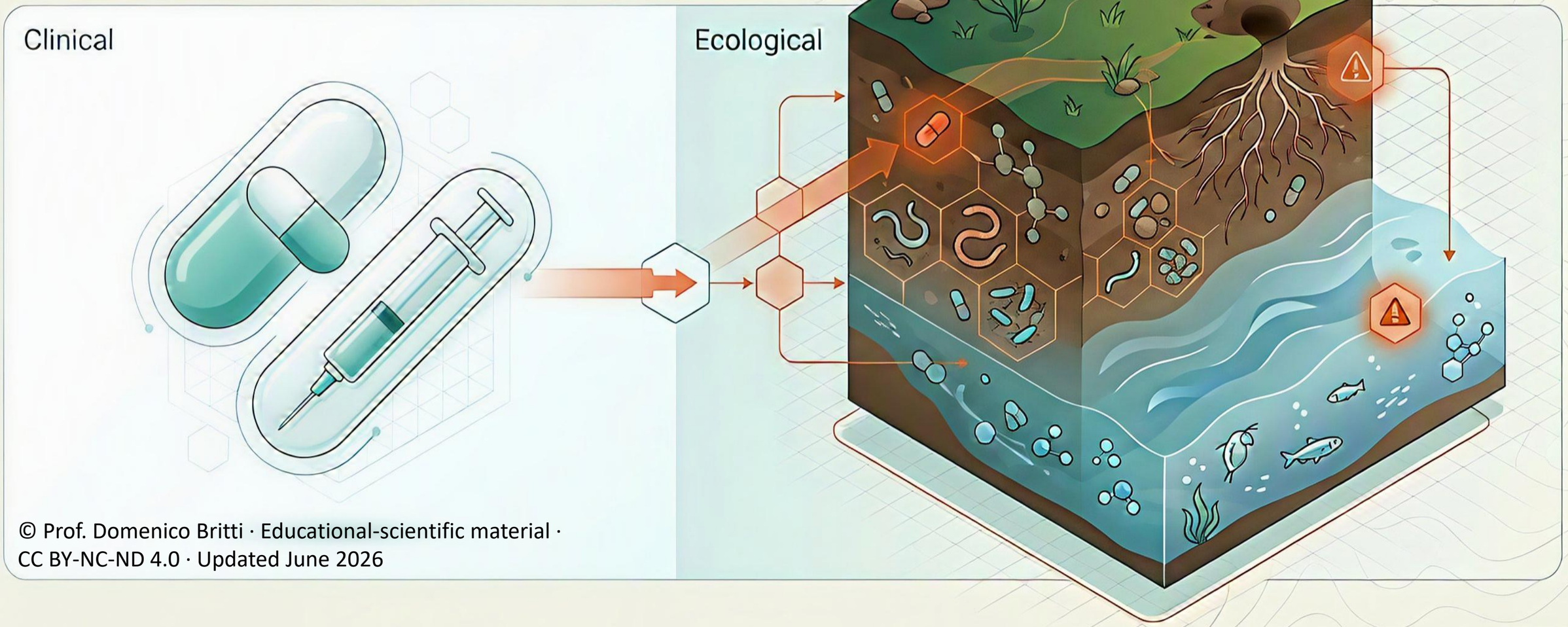
Environmental Risk Assessment (ERA) for Veterinary Pharmaceuticals

Focus on Antiparasitics: From VICH Guidelines to One Health Ecosystem Protection



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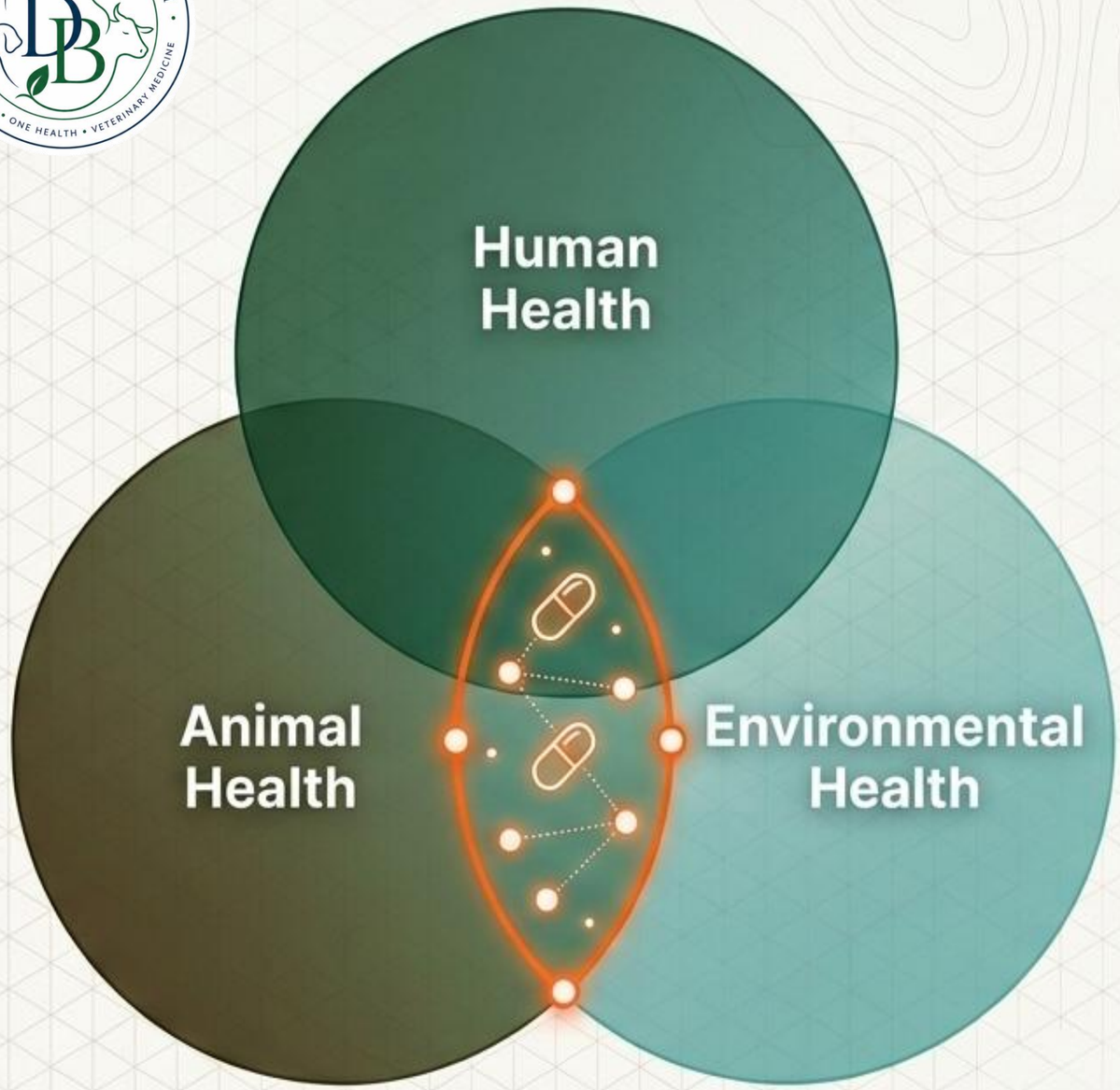


The One Health Imperative

Veterinary medicine has a direct impact on ecosystems.

Growing Risk Factors

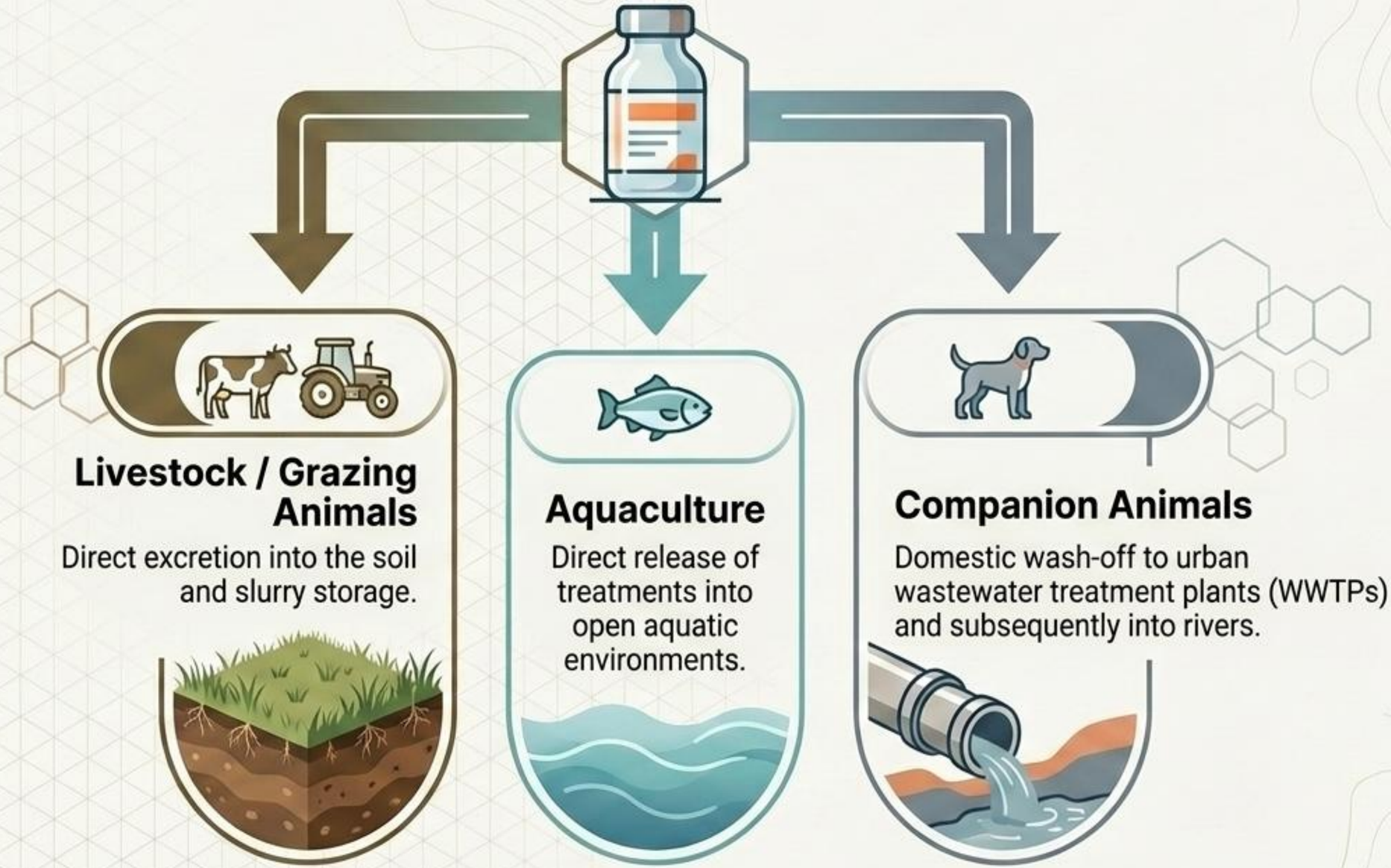
Climate change and population density reduce the natural dilution of contaminants.

The Key Fact

Up to 90%* of the active ingredient of some drugs is excreted (or washed) into the environment in its original form, keeping its chemical stability and toxicity intact.

*Source: OECD 2019, Environmental Risk Assessment of Veterinary Medicines

The Three Main Environmental Exposure Pathways



Livestock / Grazing Animals

Direct excretion into the soil and slurry storage.

Aquaculture

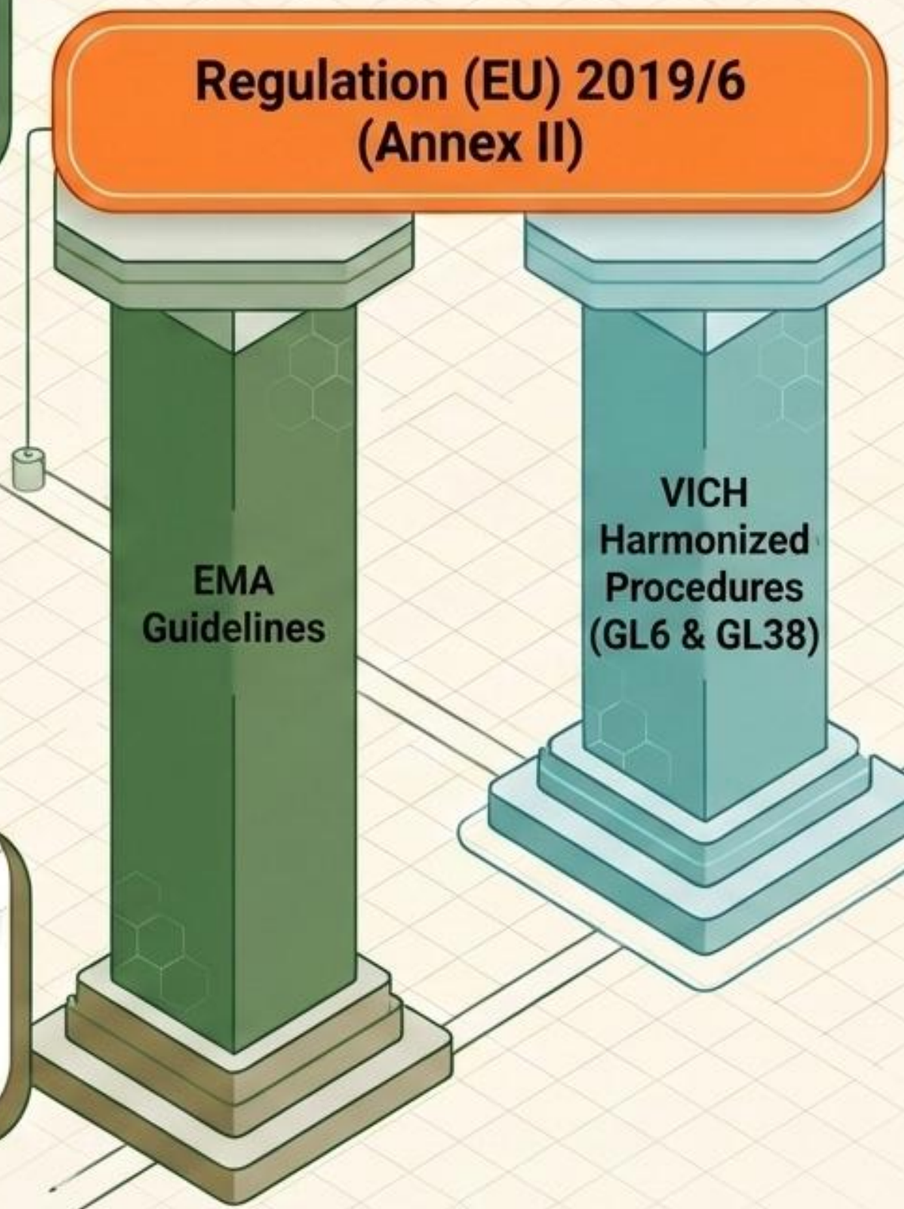
Direct release of treatments into open aquatic environments.

Companion Animals

Domestic wash-off to urban wastewater treatment plants (WWTPs) and subsequently into rivers.

The Regulatory Framework

The Marketing Authorization (MA) depends on an acceptable environmental risk.



The Scope of ERA

ERA assesses potential harmful effects from the use of the veterinary medicinal product, identifying necessary precautionary measures.

Scope Limitations

ERA only considers the clinical use and physicochemical properties of the substance, excluding risks related to industrial production or transport.

The ERA Architecture: Two-Phase Approach (VICH)

The Threshold Limits (Trigger)

The process stops in Phase I if:
- PEC_soil <= 100 µg/kg (Soil)
- EIC < 1 µg/L (Water)

Phase I (Exposure)

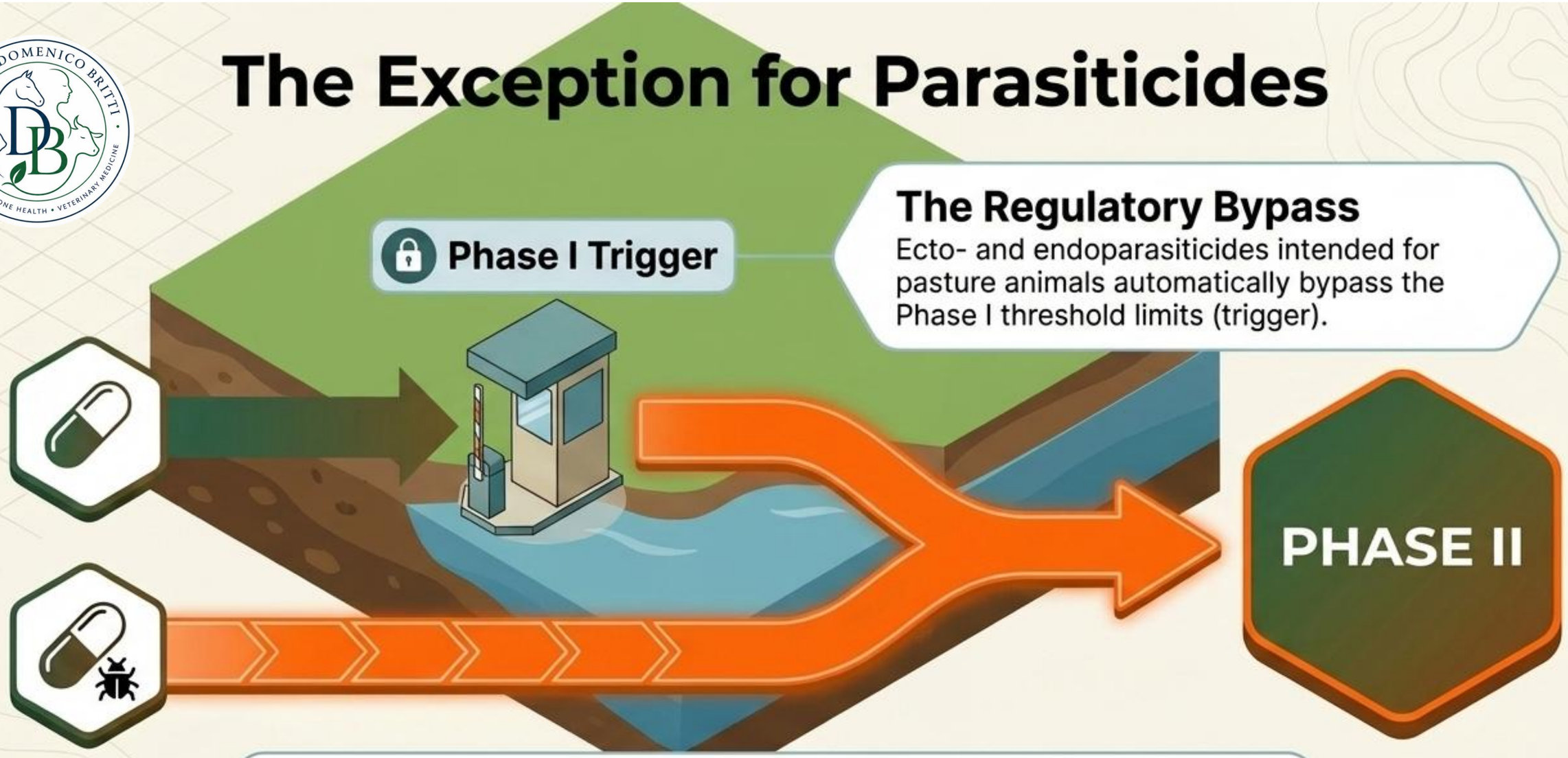
Calculation of the Predicted Environmental Concentration (PEC).

Basic assumption: if exposure is limited, there will be no ecological impact.

Phase II

Fate and Effects Assessment.

The Exception for Parasiticides



The Regulatory Bypass

Ecto- and endoparasiticides intended for pasture animals automatically bypass the Phase I threshold limits (trigger).

Why?

These drugs act intrinsically as biocides. They are designed to kill target organisms, making them by nature highly toxic also to non-target species in the ecosystem, regardless of concentration (PEC).

They must always proceed to Phase II.

Phase II: Fate and Effects Assessment

PNEC
(Toxicity Threshold)

PEC
(Real Exposure)

Unacceptable Risk:
PEC > PNEC

The Deterministic Model

Risk is assessed by comparing the real exposure (PEC) with the baseline toxicity threshold (PNEC) for the ecosystem.

Test Progression

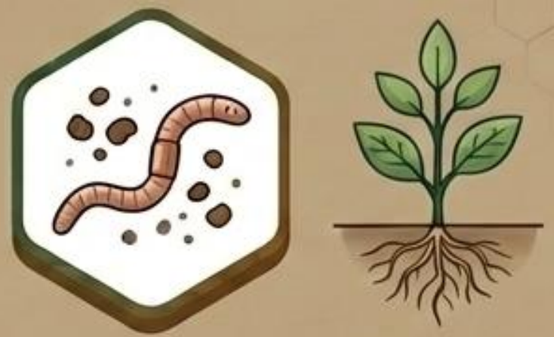
Tests progress from **Tier A** (standard single-species laboratory studies) to **Tier B** (complex terrestrial model ecosystems studies - TME).

Target Organisms and Test Parameters (Phase II)

Water

Benthic invertebrates, Daphnia, Fish, Algae.

Soil



Earthworms, Plants, Soil microorganisms.

Dung

Dung beetles, Flies.

Measured Endpoints

Not only acute mortality is assessed, but also chronic effects such as immobilization, reproduction, and growth inhibition.

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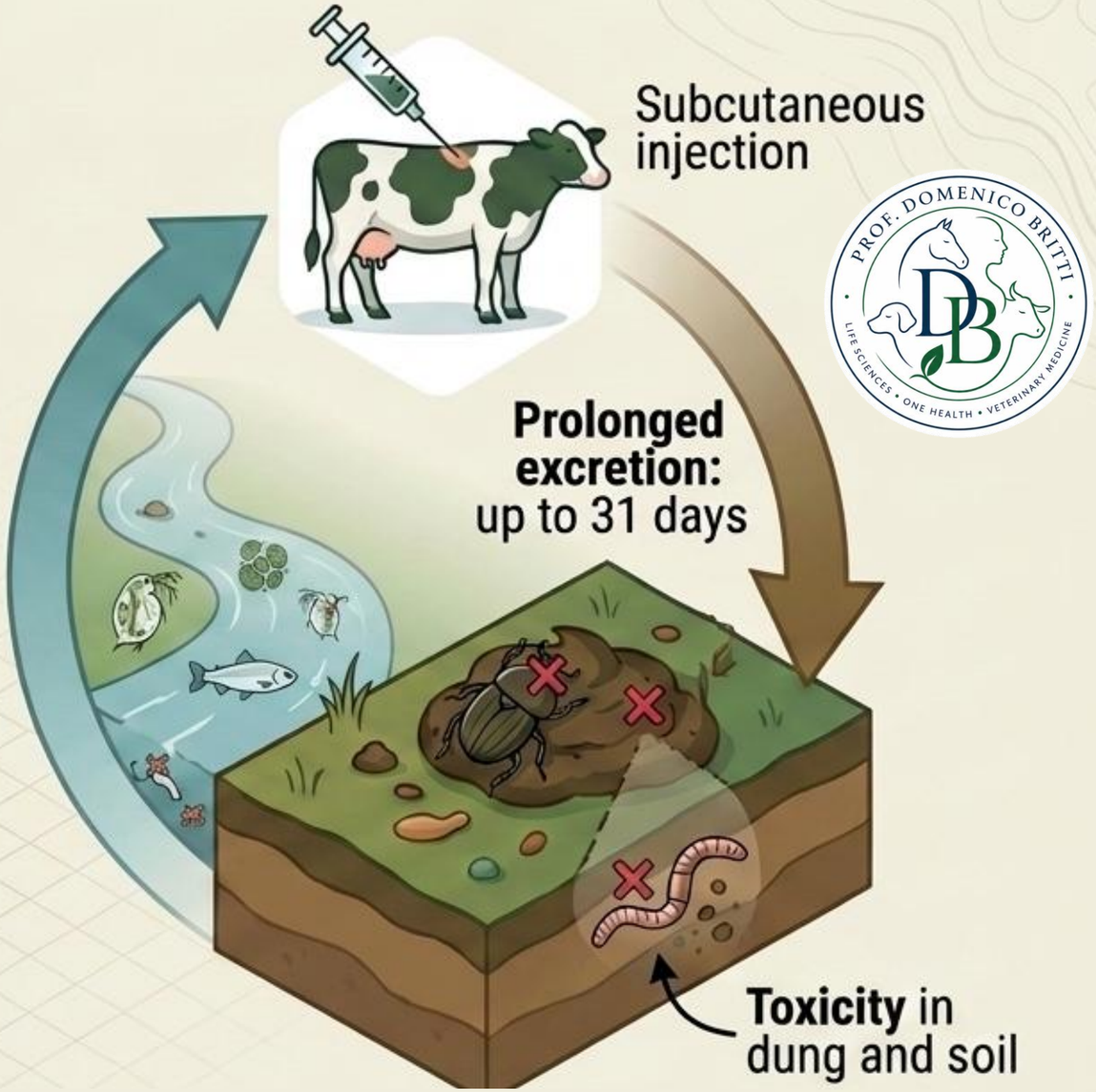
Case Study: The Failure of Ivermectin (Livestock)

ERAPharm Project Data:
Ivermectin is excreted in bovine dung for as long as 31 days[1] after subcutaneous application.

Assessment Error:
Historical assessments considered the effects on dung insect populations as transient.

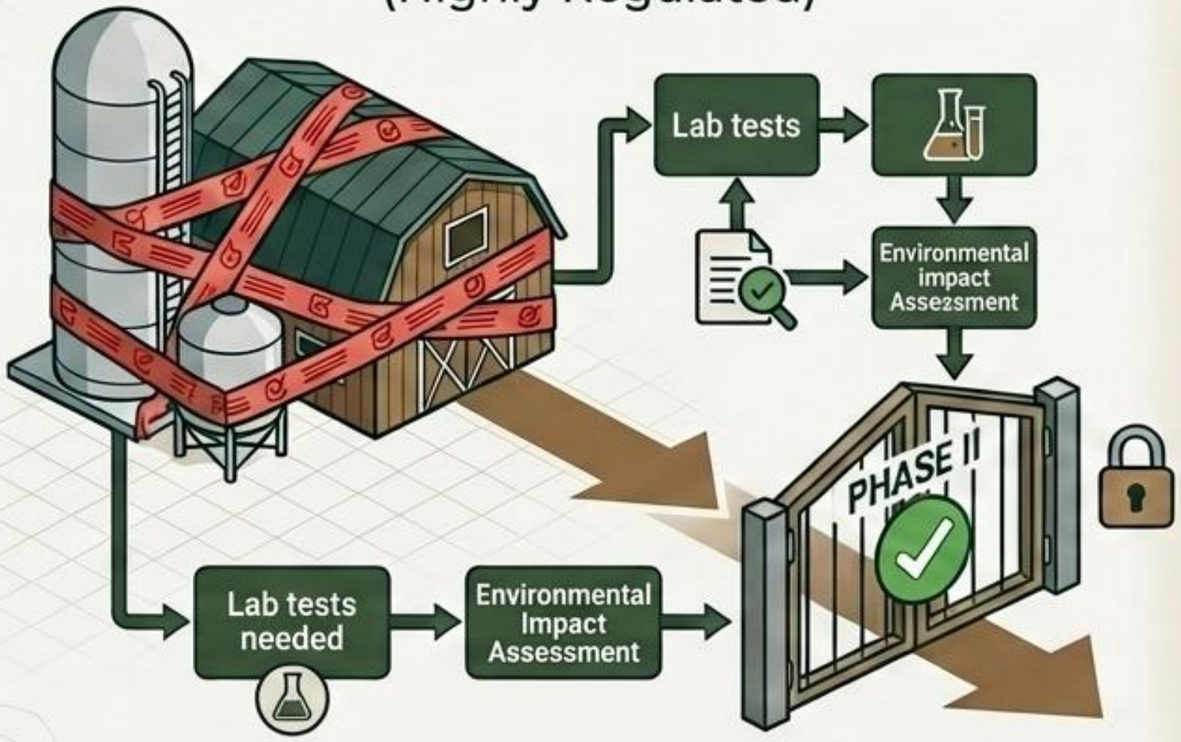
The Reality:
Long-term excretion of ivermectin in dung can sustain exposure of dung organisms beyond the immediate treatment period, supporting regulatory reassessment [2].



[1] Fernandez et al. (2009). Pharmacokinetic Profile of Ivermectin in Cattle Dung Excretion, and its Associated Environmental Hazard. Soil and Sediment Contamination, 18(5):564-575.
[2] ERAPharm Project Consortium (2010). Final Report on the Environmental Risk Assessment of Veterinary Medicines (EU FP6).

The Companion Animal Paradox

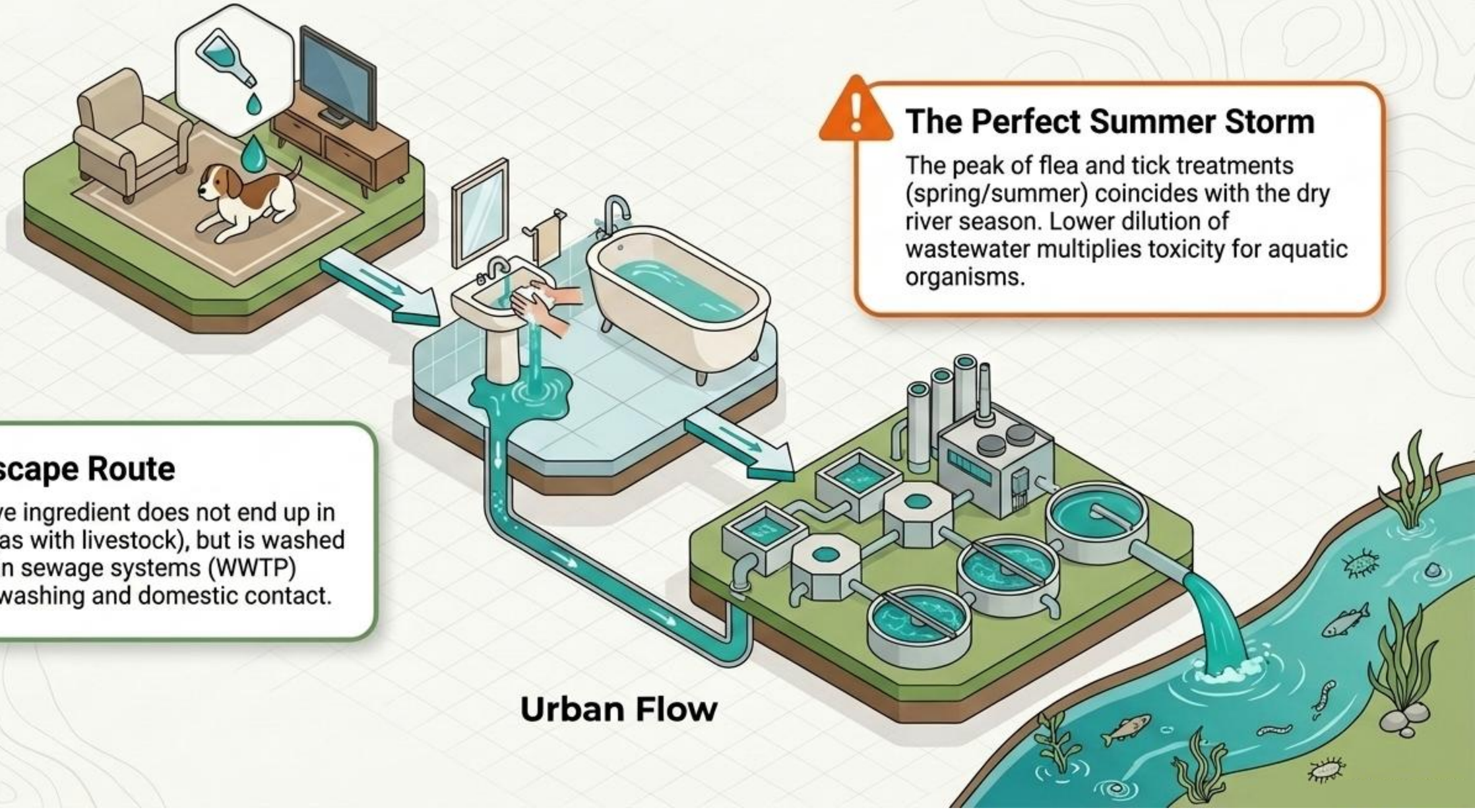
Livestock
(Highly Regulated)



Companion Animals
(Historically Exempt)

- **A Historic Exclusion:** Until recently, drugs for dogs and cats stopped at Phase I, assuming a negligible environmental footprint.
- **An Urban Pathway:** Companion-animal ectoparasiticides are widely used and may reach urban wastewater pathways through bathing, washing, and domestic contact.
- **The EMA Alert:** Topical products (spot-on, collars, shampoos) contain isoxazolines and highly toxic molecules now under regulatory review.

The New Urban Challenge: From Living Rooms to Rivers



The Perfect Summer Storm

The peak of flea and tick treatments (spring/summer) coincides with the dry river season. Lower dilution of wastewater multiplies toxicity for aquatic organisms.

The Escape Route

The active ingredient does not end up in the soil (as with livestock), but is washed into urban sewage systems (WWTP) through washing and domestic contact.

Urban Flow

Paradigm Shift: Comparison Matrix

	Livestock (Farming)	Companion Animals (Pets)
Main Exposure Pathway	Direct (Manure/Soil)	Indirect (Sewage/Water)
Dilution Factor	High dilution in open fields	Low (concentrated in dry season)
Phase II Activation (Trigger)	Immediate (Mandatory Bypass)	Historically exempt (currently under EMA review)
Primary Ecotoxicological Target	Dung beetles and earthworms	Aquatic ecosystems (WWTP)

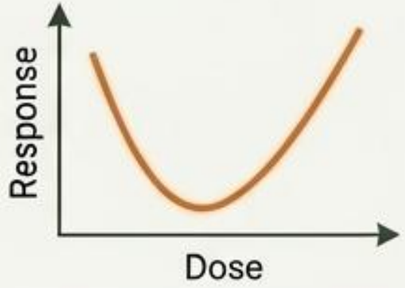
Beyond Acute Toxicity: Emerging Risks

ERA is evolving to measure chronic and invisible effects

Antimicrobial Resistance (AMR)

Sub-lethal doses in the environment act as a reservoir for bacterial resistance, may contribute to the selection and dissemination of antimicrobial resistance.

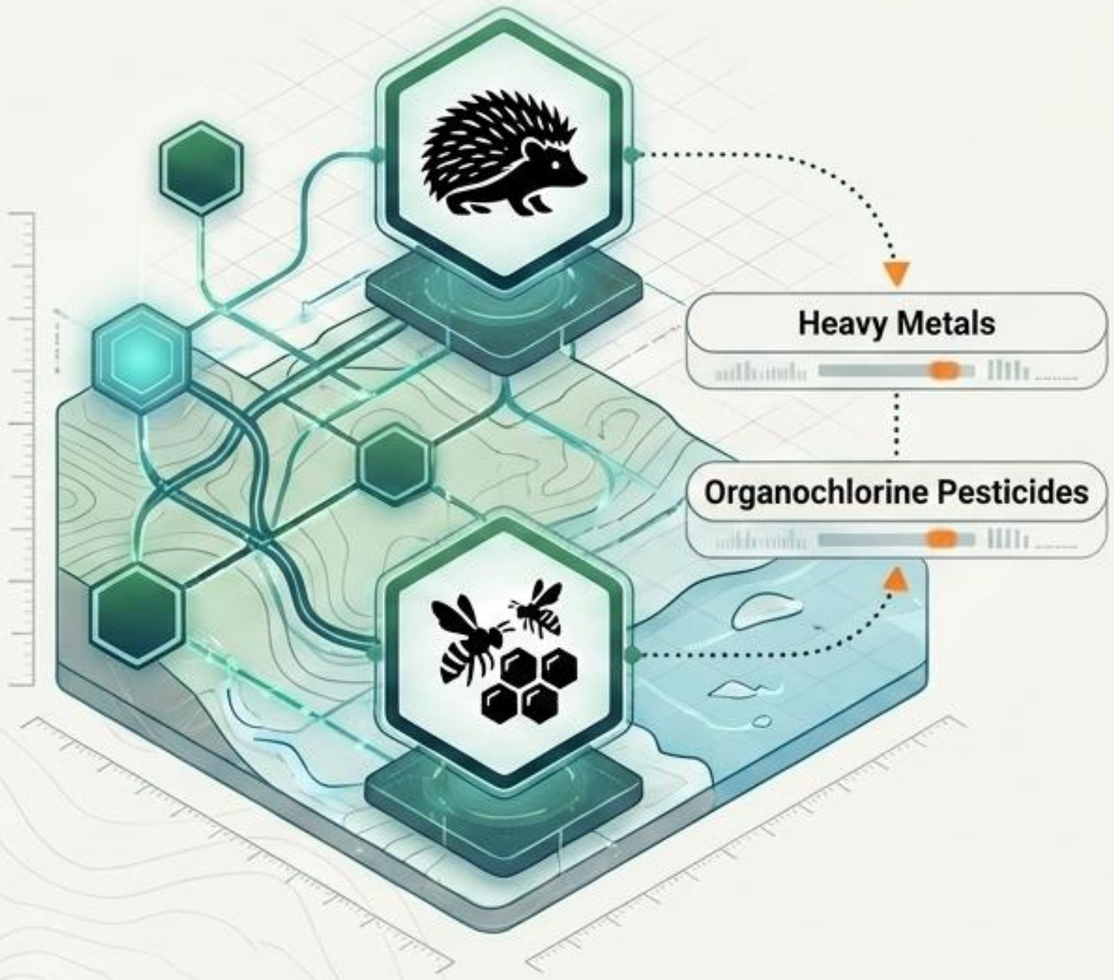
Atypical Dose-Response Curve (EDC)



Endocrine Disrupting Chemicals (EDCs)

Low-dose, mixture-related and non-monotonic effects require dedicated risk-assessment approaches.

Biomonitoring and Sentinel Species



The SSA Model (Sentinel Species Application)

Wild animals act as early detectors of chemical exposure in the entire ecosystem.

Practical Examples

The hedgehog (*Erinaceus europaeus*) proves to be an excellent bioindicator for pollutant accumulation, reflecting contamination in the food web.

Biomonitoring translates ERA theoretical models into real-world field measurements.

Synthesis and Future Perspectives: The New ERA

1. **VICH Regulatory Revision:** Closing the regulatory gap for companion animals and implementation of Phase II tests for spot-ons and collars.

2. **Cumulative Risk:** Overcoming the single-substance model to assess the real impact of chemical mixtures in the environment.

3. **Eco-Sustainable Approach:** Promoting the sustainable use of antiparasitics to protect the entire ecosystem.

ERA is not merely a bureaucratic requirement: it is a One Health tool

ensuring that animal care does not become a source of ecosystem contamination

References

Prof. Domenico Britti

Life Sciences · One Health
Veterinary Medicine

Veterinary Toxicology
Environmental Health
Pesticides · EDCs · AMR

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- *Guideline on environmental impact assessment (EIAS) for veterinary medicinal products — Phase I* (EMA/CVMP/VICH/592/98-FINAL).
- *Guideline on environmental impact assessment for veterinary medicinal products — Phase II* (EMA/CVMP/VICH/790/03-FINAL).
- *Revised guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38* (EMEA/CVMP/ERA/418282/2005-Rev.1).
- *Guideline on the assessment of persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances in veterinary medicinal products* (EMA/CVMP/ERA/52740/2012).
- **Reflection paper on the environmental risk assessment of ectoparasiticidal veterinary medicinal products used in cats and dogs** (EMA/CVMP/ERA/31905/2021).
- **Liebig M. et al. (2010).** *Environmental Risk Assessment of Ivermectin: A Case Study.* Integr Environ Assess Manag.
- **Mancini L. et al. (2020).** *Need for a sustainable use of medicinal products: environmental impacts of ivermectin.* Ann Ist Super Sanità.
- **Kuntz E. (2021).** *Environmental Risk Assessment for Veterinary Medicinal Products.* ECVPT Residency.
- **Diepens N.J. et al. (2023).** *Pet dogs transfer veterinary medicines to the environment.* Sci Total Environ.
- **Fernandez, C. et al.** (2009). Pharmacokinetic profile of ivermectin in cattle dung excretion, and its associated environmental hazard. Soil and Sediment Contamination: An International Journal, 18(5), 564–575.

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