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Interference and dual legislation of veterinary medicinal products in the EU, PFAS restriction

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Sectoral legislation: VMP Regulation 2019/6 - stated aims

Forthcoming EU Regulation for VMPs - Objectives -

- Guarantee a **high level of public health protection**
- Ensure **high quality & safety standards**
- Enhance the **availability of VMPs**
- Support an **optimal functioning of the internal market**
- Put in place an **up-to-date legal framework, tailored to VMPs**
- **Simplify procedures** for obtaining **a marketing authorisation**
- Review **incentives for breakthrough medicines**

⇨ Strengthen the **fight against AMR**

European Commission

Julie SAINZ & Wolfgang TRUNK
DG Health and Food Safety

AMR One-Health Network Meeting
Brussels, 26 October 2018

Health and Food Safety

Sectoral legislation: basic principles

Veterinary Medicial Products (VMP) authorisation under Reg 2019/6 – a solid legal framework

- EMA as the responsible Agency
- Thorough product assessment ensures:
    - Quality, including assessment and inspection of manufacturing process and facilities
    - Efficacy
    - Safety for: worker/user, consumer, target animal, ***AND*** environment
        - Requirements similar to those under REACH, consumer safety as an additional data set
        - Irrespective of projected volumes or tonnages
- Approval based on a *thorough benefit/risk assessment* of each product *prior to authorisation and market entry*
- Manufacturing process part of product approval, thoroughly assessed and inspected by regulatory authorities
- Post-authorisation: continued monitoring of quality, safety and efficacy through pharmacovigilance

Sector needs regulatory stability and predictability

- Time from discovery to product ready for evaluation: 10 – 15 years; regulatory authorisation 1.5 – 2 years
- Any changes in approved product composition require renewed testing and approval – once more a process of years
- "Substitution" of the active ingredient in a product is not possible; either there is a product with a therapeutic effect driven by the active ingredient, or there is not

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Interference from other legislation

Impact on veterinary medicines

Interferences with Veterinary Medicinal Products (VMP) Regulation

- **Substances required for manufacturing being restricted or banned (REACH)**
  - Triton-X, aprotic solvents N-Methylpyrrolidone, Dimethylformamide and Dimethylacetamide
  - New restriction proposal envisaged for PFAS with the broadest scope possible (Chemical Strategy (CSS)/REACH):
    - PFAS used in manufacturing, quality control, diagnostics
    - Materials and equipment used in manufacturing containing PFAS

- **VMPs themselves risk to be banned (new PFAS restriction proposal under CSS/REACH)**
  - Parasiticides, inhalation anaesthetics, NSAIDs
    - More detail later in this presentation

- **Additional labelling and new reporting requirements are imposed (REACH, CLP)**
  - Microplastics in medicinal formulations (REACH)
  - Hazard labelling proposed for CLP-revision (proposal to delete exemptions for medicines and VMPs)

Interferences with Veterinary Medicinal Products (VMP) Regulation

- **Critical component of tablet formulations no longer allowed (Food Additive Regulation)**
  - Titanium dioxide TiO2 - EFSA
    - Impacting 100,000's of human and veterinary marketing authorisations
    - No suitable alternatives on the shelf
    - Limited timeframe (3 years) largely insufficient to investigate TiO2 and alternative's safety

- **New packaging and waste legislation**
  - Risks imposing additional restrictions/labelling/other (Product Packaging and Waste Directives)
    - National requirements differ – hampering multilingual packs
    - Potential effect on availability in some markets

- **One substance, one assessment**
  - Direct interference with the concept of the EMA and NCAs as directed by law
  - VMR regulates ***products, not substances*** – very specific sectoral rules

Our perspectives

VMP authorisation under Reg 2019/6 – a solid legal framework

- EMA as the responsible Agency
- Approval ensures quality, efficacy and worker/user, consumer, environmental and target animal safety
- Based on a thorough benefit/risk assessment of each product ***prior to authorisation***
- "Substitution" of an API is not possible

Sector needs regulatory stability and predictability

- Interference is now stifling innovation and investment in the EU
- Manufacturing in the EU is becoming unsustainable (despite Pharmaceutical Strategy aims)

EMA and NCAs need to safeguard the longer term strategic perspective

- Focus (understandably) on short-term VMR implementation issues **BUT**
- Chemical Strategy and other legislative initiatives risk to completely destabilising the medicines sector

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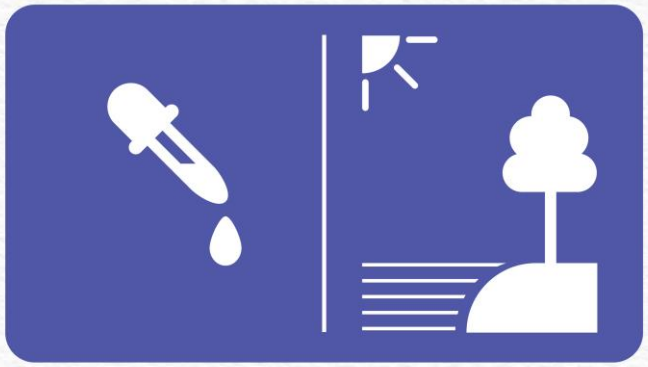
PFAS restriction and the essential use concept

Impact on veterinary medicines

Evaluating hazards, risks and benefit/risk

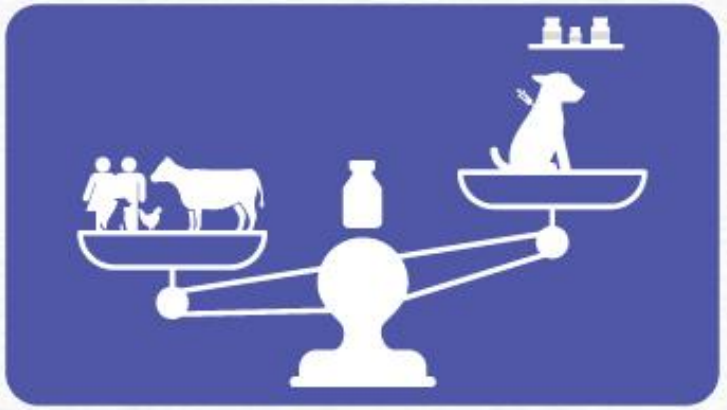
Generic Risk Assessment (GRA): Hazard approach

A hazard is something that has the potential to cause harm.



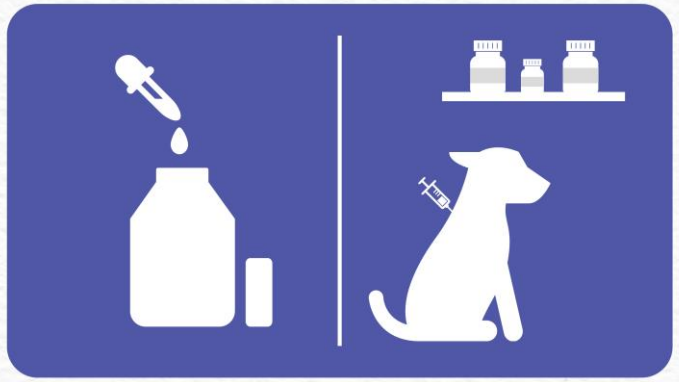
Benefit/risk approach

Measuring whether the potential benefits outweigh any risks identified.



Risk assessment approach

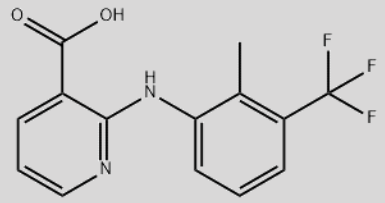
Risk is the likelihood of a hazard causing harm, taking exposure into account .



Interferences of REACH/CSS with VMP Regulation - consequences

- **Substances required for manufacturing being restricted or banned (REACH/CSS/PFAS ban)**
  - New restriction proposal envisaged for PFAS with the broadest scope possible (Chemical Strategy (CSS)/REACH):
    - PFAS used in manufacturing, quality control, diagnostics (irrespective of exposure control?)
    - Materials and equipment used in manufacturing or packaging containing PFAS

- **VMPs themselves risk to be banned (new PFAS restriction proposal under CSS/REACH)**
  - Marginally qualifying as PFAS under the very broad definition used in the restriction proposal (terminal –CF2 or –CF3 group(s) in larger molecules, no long-chain CF like e.g. PFOA)
  - Exposure: low volumes – not to be compared with industrial chemicals
  - Therapeutic areas affected: (novel) parasiticides, inhalation anaesthetics, anti-inflammatory agents



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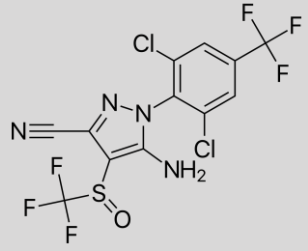

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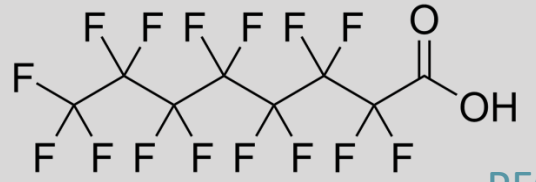
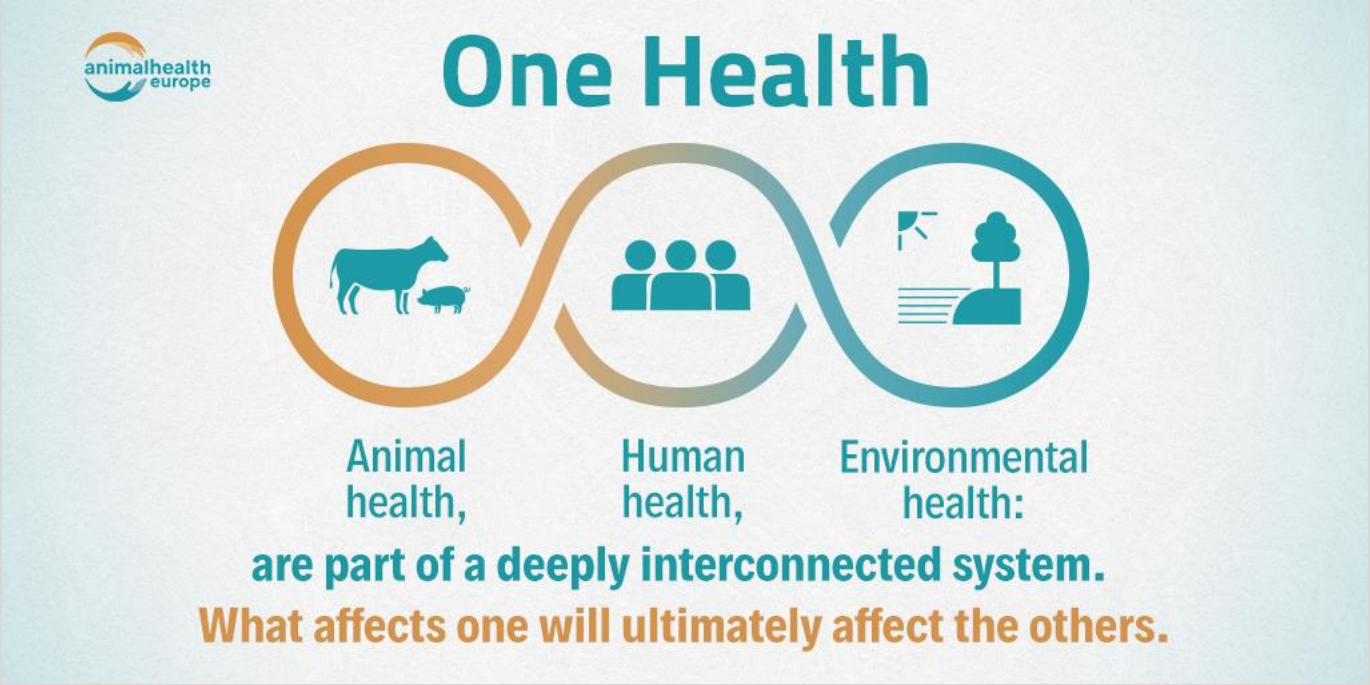


PFOA

The importance of veterinary medicines for public health



- Some of the animal diseases/infestations can affect human health (zoonoses)
- Examples include fleas, ticks and other parasites which may infest humans, and the diseases they carry (Lyme disease, tick encephalitis, Babesiosis, cat scratch disease,....)
- Adequate treatment of animals greatly reduces the risks for public health

Absence of regulatory stability and predictability

- **Consequences:**
  - Interference from REACH/CSS/PFAS ban is now stifling innovation and investment in the EU
    - Alternatives are not readily available and may even never be found
    - Indiscriminative PFAS ban would put veterinary medicine 30+ years back in time in affected therapeutic areas
    - What and when will be the next restriction? Not predictable
    - Lengthy development and approval times (10-15 years + 1.5-2 years) require stability, predictability for industry to be able to invest
  - Manufacturing in the EU risks becoming unsustainable (despite Pharmaceutical Strategy aims)
  - Competitiveness of the EU region is seriously hampered:
    - Unpredictable restrictions – investment focus to other regions
    - Reduced treatment options – potential impact on animal and public health
    - Manufacturing (currently being brought back to the EU) having to relocate out again

The essential use concept

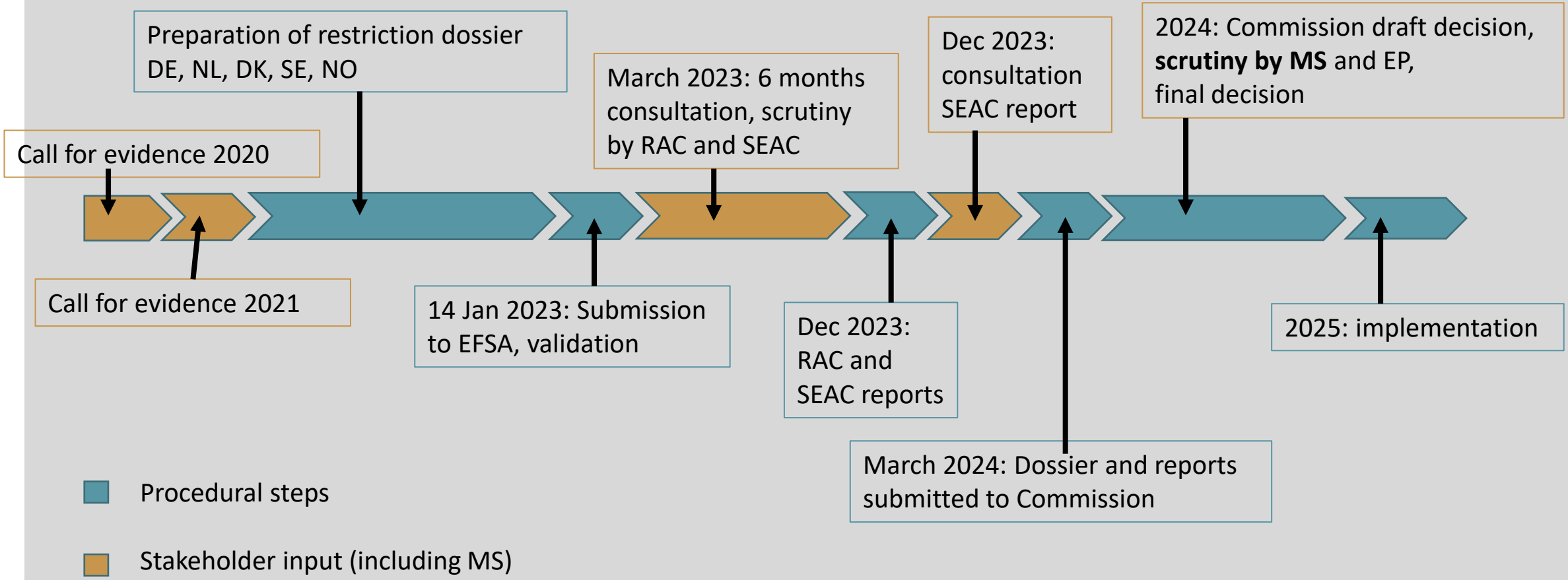
Our understanding of the basic principles (criteria under development):

- Strictly necessary for ensuring a high level of protection of the environment or health OR
- The ceasing of that use has **critical consequences** on the functioning of the society AND
- No technically or economically feasible alternatives are available.
- Temporary in nature and subject to periodic review

Specifics related to veterinary medicines

- Benefit/risk assessment guiding authorisation
- Necessary to safeguard animal health and welfare
- Playing an important role in protecting human health
- Human-animal bond: role in society (affinty and emotional wellbeing; food safety and security)
- Need different alternatives to treat a given condition:
    - Individual/breed/species sensitivity (e.g.,Collie-like dogs, Duroc pig breeds, cats vs dogs,...)
    - Resistance development to e.g. parasiticides
    - Regional differences and needs
- Currently there are already issues with availability of VMPs – see stated aims for Regulation 2019/6
    - Diverse animal species and diseases – market segmentation - affordability
- In view of long development and approval times: need stability and predictability

Timelines for the PFAS restriction procedure



Way forward

Safeguard objectives of Regulation 2019/6

- Maintain focus on thorough risk assessment and the benefit/risk approach of products, not substances
- Ensure continued availability of VMPs and safeguard innovation
- Maintain production in the EU

Proposal to ensure coherence of legislation with other DGs

- Regulation 2019/6 takes priority; EMA/NCA as the responsible Agencies
- Acknowledgement of the comprehensive risk/benefit assessment for VMPs as appropriate to meet CSS objectives
- Exemption from REACH restrictions – urgent in the case of PFAS
- Exempt manufacturing process and materials as these are thoroughly assessed and inspected prior to authorisation
- Recognition of veterinary medicines as “essential use” under the Chemical Strategy for Sustainability

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