Environmental risk determination algorithm for veterinary medicinal products

Algoritm de determinare al riscului de mediu pentru produsele medicinale veterinare

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Cuvinte cheie: mediu, risc, algoritm

Abstract

The environmental risk analysis for veterinary medicinal products is an assessment of their possible evolution, exposures and effects and is structured according to the EMEA/CVMP/ERA/418282/2005-Rev1[1], VICH GL6 (Phase I) and GL38 (Phase II) guides. The three primary components of a quantitative risk assessment are: exposure assessment, effects assessment, and risk characterization. Based on the indication of use of the veterinary medicinal product, the exposure assessment begins with the release of the active substance into the environment, and while taking into account the drug's fate and distribution, develops a predicted environmental concentration (PEC). The effects assessment begins with toxicity data and applies an assessment factor (AF) to it resulting in a predicted no effect concentration (PNEC). The risk characterization includes development of a risk quotient (RQ) that is calculated by dividing the PEC by the PNEC. If RQ ≥1 assessment moves to next tier. The paper presents an algorithm for calculating the initial risk for soil, groundwater, surface water and sediment under the action of the active ingredient in the analyzed veterinary medicinal product. Based on this calculation algorithm, a specialized interactive software has been developed to allow rapid and convenient determination of environmental risk for veterinary medicinal products. It is a very useful tool for environmental risk assessment specialists.

Rezumat

Evaluarea riscului de mediu are la bază caracterizarea științifică sistematică a efectelor adverse potențiale (impacturi) rezultate din expunerea factorilor de mediu la un produs medicinal veterinar și este structurată în doua faze, în conformitate cu ghidurile EMEA/CVMP/ERA/418282/2005-Rev1[1], VICH GL6 (Faza I) și GL38 (Faza II). Cele trei componente principale ale unei evaluări cantitative a riscului sunt: evaluarea expunerii, evaluarea efectelor și caracterizarea riscului. Tinând cont de indicatia de utilizare a produsului medicinal veterinar, evaluarea expunerii începe cu eliberarea substantei active în mediu și, în funcție de impactul produs asupra mediului, se calculeaza o concentratie predictibila de mediu (PEC). Evaluarea efectelor începe cu datele de toxicitate la care se aplică un factor de evaluare (AF), ceea ce duce la o concentrație predictibila fără efect (PNEC). Caracterizarea riscului include determinarea unui coeficient de risc (RQ) care este calculat prin împărțirea PEC la PNEC. Dacă RQ ≥1, evaluarea trece la nivelul următor, (treapta B din faza II). Lucrarea prezinta un algoritm de calcul al riscului initial pentru sol, apa freatica, ape de suprafata si sediment sub acțiunea substanței active din produsul medicinal veterinar analizat. Pe baza acestui algoritm de calcul, a fost elaborat un software original, interactiv specializat , care să permită determinarea rapidă și convenabilă a riscului de mediu pentru produsele medicinale veterinare. Softul este un instrument foarte util pentru specialiștii în evaluarea riscurilor de mediu.

Introduction

The risk assessment is an evaluation of the possible evolution, mode of action and effects of the veterinary medicinal product. Overall, risk assessment is structured around the risk coefficient approach, as described in EMEA / CVMP / ERA / 418282/2005-Rev1 [1],

VICH GL6 (phase I) and GL38 (phase II) guidelines.

The three main components of a quantitative assessment of the initial risk for soil, groundwater, surface waters and sediment under the action of the active ingredient in the analyzed veterinary medicinal product are: exposure assessment, effects assessment and risk characterization (Fig.1).

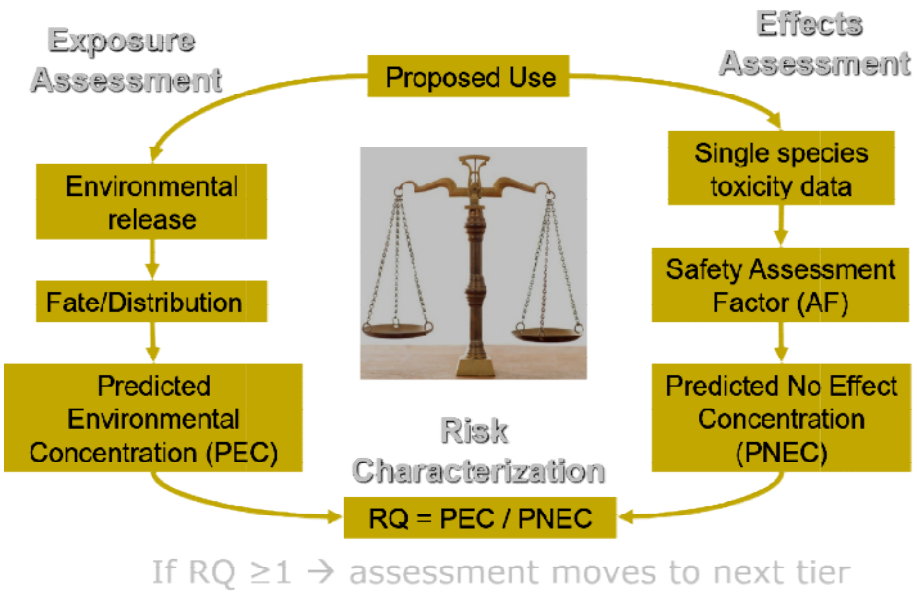


Figure 1. Risk assessment principles

Taking into account the indication of use of the veterinary medicinal product, the exposure assessment starts with the release of the active substance into the environment and, depending on the target species, the mode of administration, the physico-chemical characteristics of the active ingredients and the impact produced by them on the environment, is calculated a predictable environmental concentration (PEC) (Fig.2). [1, 4, 5].

The evaluation of the effects begins with toxicity data to which an evaluation factor (AF) is applied, which leads to a predictable concentration without effect (PNEC) (Fig.3).

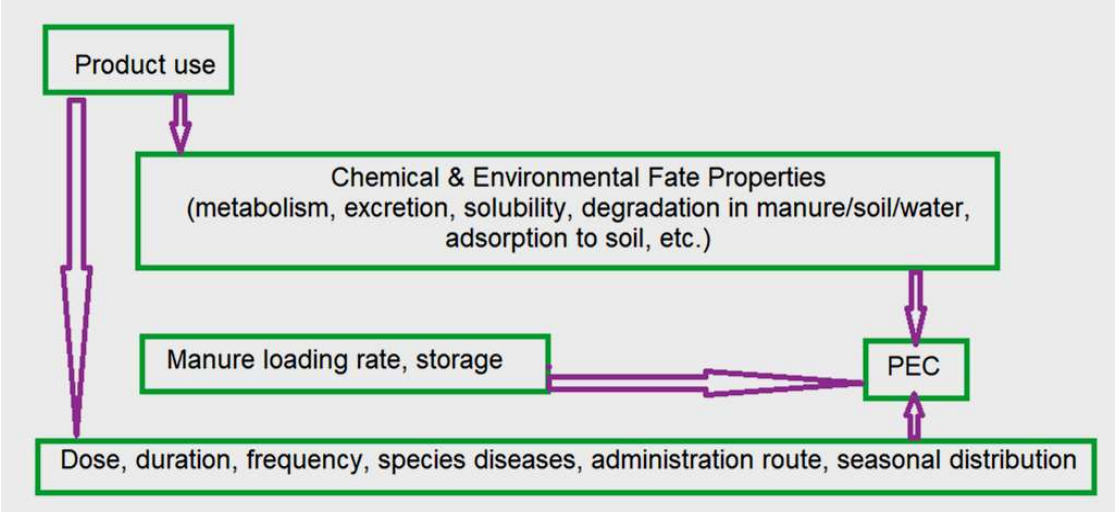


Figure 2. Exposure Assessment

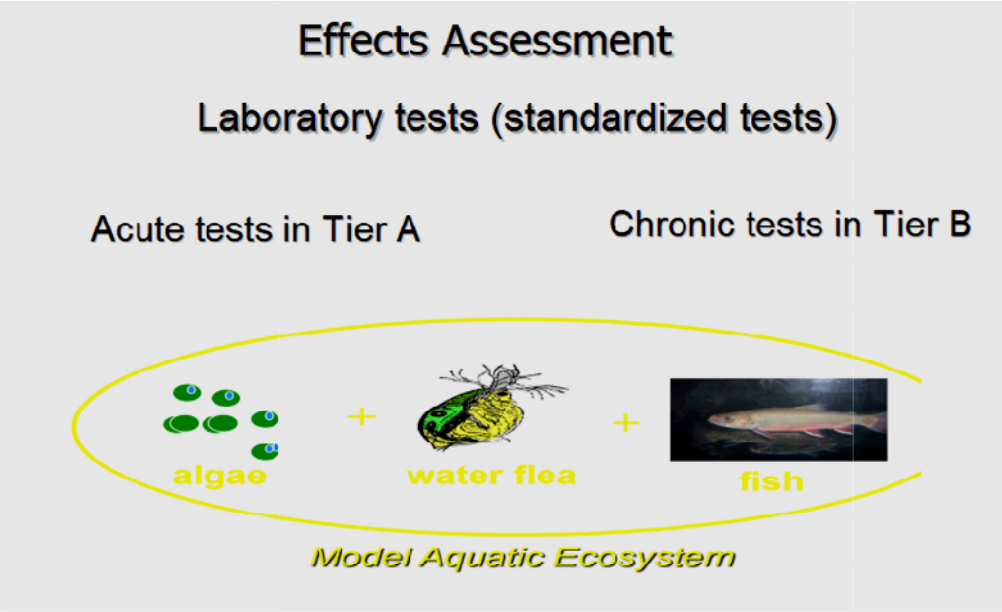
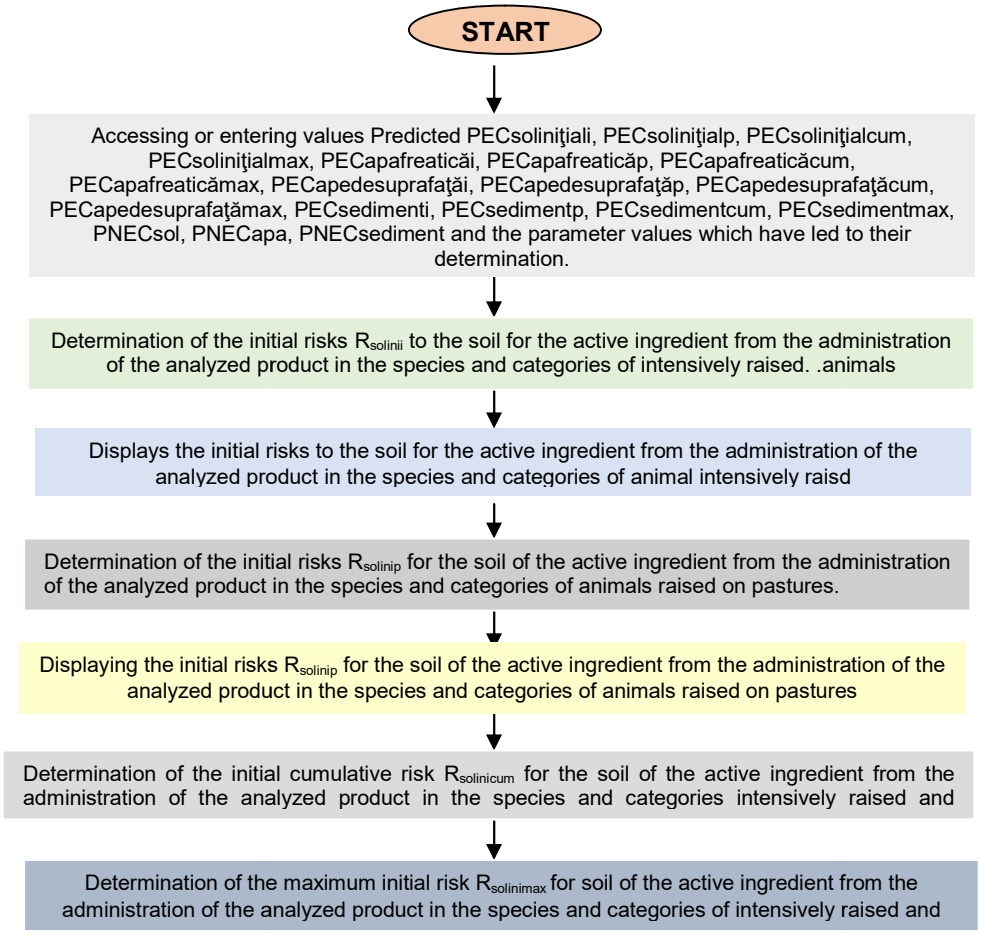


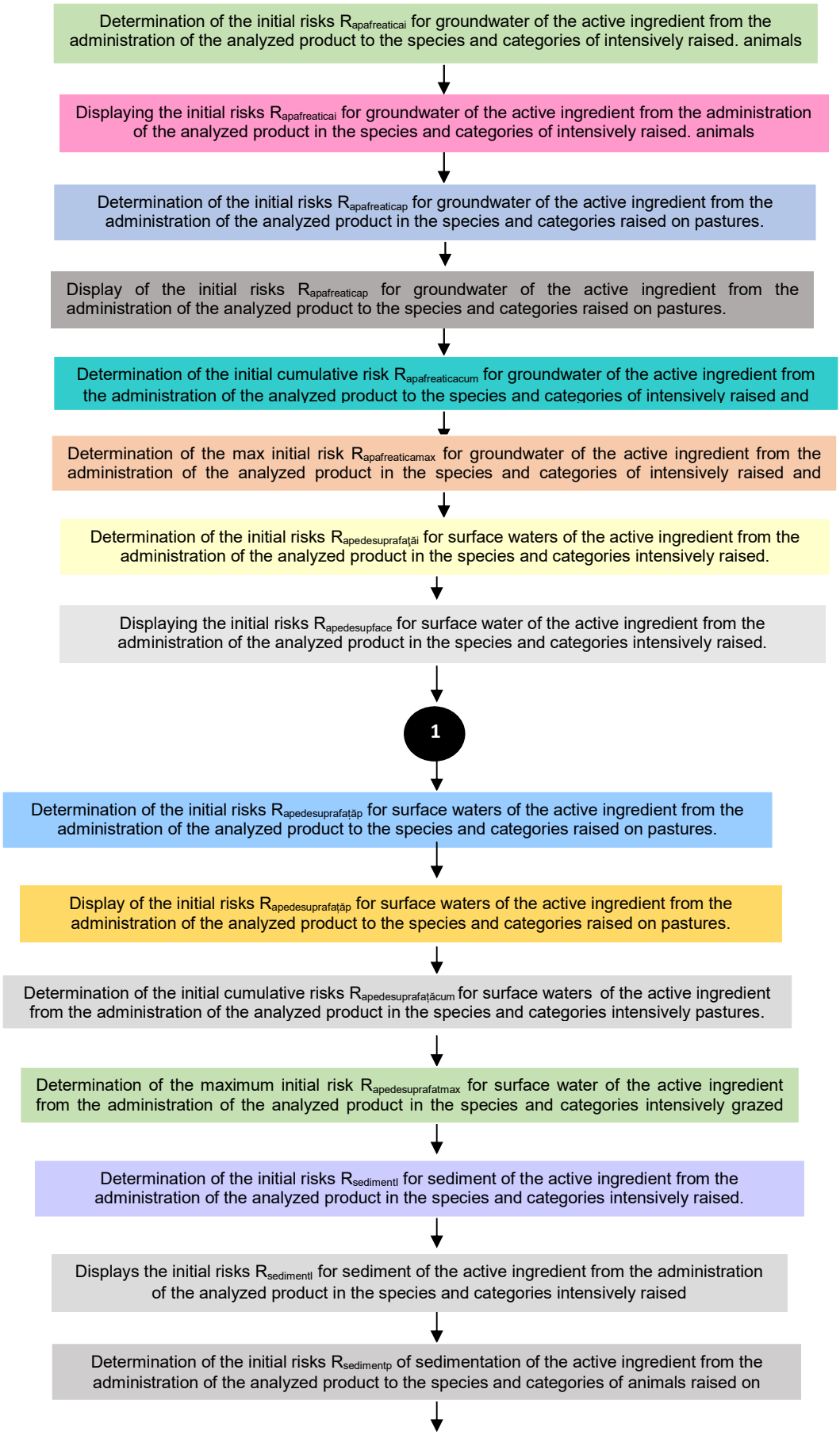
Figure 3. Effects Assessment

Risk characterization includes the development of a risk coefficient (RQ) that is calculated by dividing the PEC by the PNEC. If RQ ≥1 the rating goes to the next level.

The calculated risk coefficient indicates the probability of the adverse effects occurring on the environment [1,2,3,4,5,6].

1. Environmental risk (RQ) calculation algorithm




Determination of the initial risks $R_{apafreaticai}$ for groundwater of the active ingredient from the administration of the analyzed product to the species and categories of intensively raised. animals
Displaying the initial risks $R_{apafreaticai}$ for groundwater of the active ingredient from the administration of the analyzed product in the species and categories of intensively raised. animals
Determination of the initial risks $R_{apafreaticap}$ for groundwater of the active ingredient from the administration of the analyzed product in the species and categories raised on pastures.
Display of the initial risks $R_{apafreaticap}$ for groundwater of the active ingredient from the administration of the analyzed product to the species and categories raised on pastures.
Determination of the initial cumulative risk $R_{apafreaticacum}$ for groundwater of the active ingredient from the administration of the analyzed product to the species and categories of intensively raised and
Determination of the max initial risk $R_{apafreaticamax}$ for groundwater of the active ingredient from the administration of the analyzed product in the species and categories of intensively raised and
Determination of the initial risks $R_{apedesuprafaţăi}$ for surface waters of the active ingredient from the administration of the analyzed product in the species and categories intensively raised.
Displaying the initial risks $R_{apedesupface}$ for surface water of the active ingredient from the administration of the analyzed product in the species and categories intensively raised.
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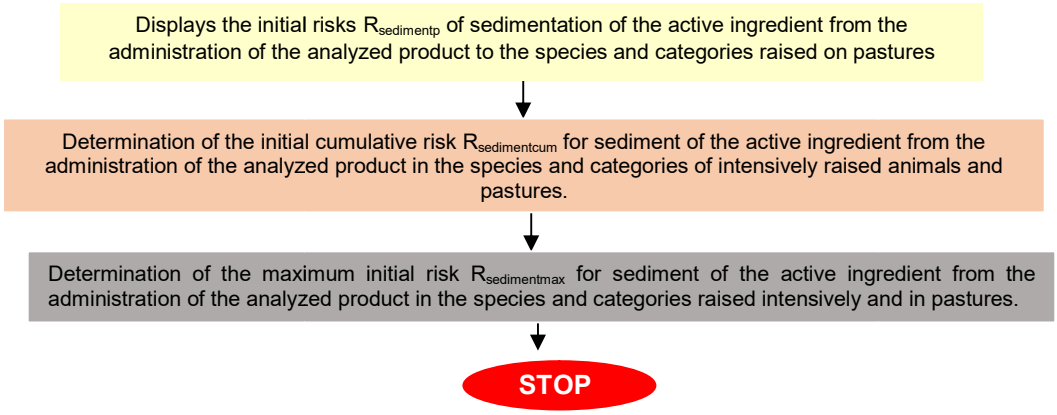
Determination of the initial risks $R_{apedesuprafaţăp}$ for surface waters of the active ingredient from the administration of the analyzed product to the species and categories raised on pastures.
Display of the initial risks $R_{apedesuprafaţăp}$ for surface waters of the active ingredient from the administration of the analyzed product to the species and categories raised on pastures.
Determination of the initial cumulative risks $R_{apedesuprafaţăcum}$ for surface waters of the active ingredient from the administration of the analyzed product in the species and categories intensively pastures.
Determination of the maximum initial risk $R_{apedesuprafatmax}$ for surface water of the active ingredient from the administration of the analyzed product in the species and categories intensively grazed
Determination of the initial risks $R_{sedimentl}$ for sediment of the active ingredient from the administration of the analyzed product in the species and categories intensively raised.
Displays the initial risks $R_{sedimentl}$ for sediment of the active ingredient from the administration of the analyzed product in the species and categories intensively raised
Determination of the initial risks $R_{sedimentp}$ of sedimentation of the active ingredient from the administration of the analyzed product to the species and categories of animals raised on



Appearance of software for assessing the initial risks for soil, groundwater, surface water and sediment of the active ingredient in the veterinary medicinal product (Fig.4) :

Evaluarea riscurilor initiale pentru sol a ingredientului activ de la administrarea produsului analizat este cuantificata prin urmatorii indicatori Rsolinii si Rsolinip, calculati pe baza speciilor si categoriilor de animale crescute intensiv si pe pasuni aflate in tratament, respectiv Rsolinicum si Rsolinimax, calculati pe baza valorilor cumulate, respectiv maxime a diferitelor categorii de concetratii predictibile PECsolinitial determinate anterior:

$i := 0..4$

$j := 0..5$

$$Rsolinii_{i,j} := \frac{PECsolinitiali_{i,j}}{1000 \cdot PNECsol}$$

$$Rsolinii = \begin{pmatrix} 1.354 & 1.015 & 1.593 & 1.843 & 0 & 0 \\ 2.06 & 1.863 & 0.662 & 0 & 0 & 0 \\ 1.002 & 0.117 & 0.222 & 0.063 & 0.499 & 0.699 \\ 0.814 & 0 & 0 & 0 & 0 & 0 \\ 0.819 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Figure 4. Appearance of software

It is to note that:

- the algorithm allows taking into account all species and categories of animals, raised and exploited in intensive system or on pastures that are treated concomitantly with a certain veterinary medicinal product;
- the algorithm allows taking into consideration a particular veterinary medicinal product and its treatment characteristics (daily doses of the active ingredient, the duration of treatment);
- the algorithm requires matrix calculation, because a veterinary medicinal product can be administered concurrently to several species and categories of animals, raised and exploited in intensive system or on pastures;
- for the breeding of animals intensively and on pastures, the species and categories of animals mentioned in the guide are taken into account.
- animal species and categories are the matrix elements (the animal species are found in a row and the animal categories in columns) used to express the matrix calculation in the software.

2. Conclusions

The paper presents an algorithm for calculating the initial risk for soil, groundwater, surface waters and sediment under the action of the active ingredient in the analyzed veterinary medicinal product.

Based on this calculation algorithm, an original, interactive specialized software was developed that will allow the rapid and convenient determination of the environmental risk for veterinary medicinal products.

The software is a very useful tool for environmental risk assessment specialists.

The environmental risk assessment is mandatory for all new products in order to obtain the marketing authorization and aims at environmental protection.

The risk assessment for the environment, an integral part of the authorizations for the veterinary medicinal products, interpreted according to the VICH guides, through the software created, ensures the predictability and transparency of the obtained results.

Bibliography

1. **Guide** EMEA/CVMP/ERA/418282 /2005-Rev1, VICH GL6 (Phase I) and GL38 (Phase II) guides.
2. **ECHA** – Guidance on information requirements and chemical safety assessment - Chapter R10. Characterisation of dose [concentration] – response for environment.
3. **ECHA** – Guidance on information requirements and chemical safety assessment - Chapter R16. Environmental Exposure Estimation.
4. **Silberhorn Eric**. Environmental Impact (Risk) Assessment of Veterinary Pharmaceuticals
5. **Ciuca Viviana, V. V. Safta, Romeo T. Cristina** - Algoritm de calcul al concentraţiilor predictibile (PEC) pentru evalurea riscului de mediu la produse medicinale veterinare. *Medicamentul Veterinar / Veterinary Drug*, 2018, 12(2): 39-45.
6. **Ciuca Viviana, V. V. Safta, Romeo T. Cristina** - Algoritmul de calcul al concentrației predictibile fără efect (PNEC) pentru evaluarea riscului de mediu al produselor medicinale veterinare. *Medicamentul Veterinar / Veterinary Drug*. 2019, 13(1): 53-59.