Ecological Indicators 52 (2015) 270–276

Contents lists available at ScienceDirect

Ecological Indicators

journal homepage: www.elsevier.com/locate/ecolind

RANKVET: A new ranking method for comparing and prioritizing the environmental risk of veterinary pharmaceuticals

Valeria Di Nica[a,*], Luca Menaballi[b], Giovanna Azimonti[b], Antonio Finizio[a]

[a] Department of Earth and Environmental Sciences, University of Milano Bicocca, Piazza della Scienza 1, 20126 Milano, Italy
[b] International Centre for Pesticides and Health Risk Prevention (ICPS), Milano, Italy

ARTICLE INFO

Article history:
Received 19 September 2014
Received in revised form
13 November 2014
Accepted 16 December 2014

Keywords:
Veterinary pharmaceuticals
Risk indicators
Risk management
Ranking
Italy

ABSTRACT

In recent years veterinary medicinal products (VMPs) have been recognized as emerging contaminants, giving rise to concerns regarding their environmental impact. Due to the high number of utilized VMPs, it is necessary to develop tools (indicators) for ranking these compounds according to their environmental risk relevance. These indicators can be useful, for example, for setting up monitoring programmes, and more in general for risk management purposes. In this paper we propose a new scoring system method (RANKVET) that enables ranking the risk of VMPs for aquatic and terrestrial organisms. The procedure is fully based on the information required by the EU Directives and Regulations for marketing authorization of VMPs and Veterinary International Conference on Harmonization (VICH) guidelines. According to the latter, if the environmental risk assessment of a VMP indicates an unacceptable risk to the environment, i.e., the risk quotient (RQ) consisting of the ratio of Predicted Environmental Concentration (PEC) to Predicted No Effect Concentration (PNEC) is ≥1, then mitigation measures should be proposed by the applicant in order to reduce the risk to an acceptable level. If a risk mitigation measure does not fulfil the criteria mentioned above then the outcome of the risk assessment is that a serious risk for the environment exists. In accordance with Directive 2001/82/EC (as amended) this risk has to be weighed against the favourable aspects of a marketing authorization. The prioritization scheme is based on a quantitative approach and consist of different phases. First, for each VMP, PECs are calculated using simple exposure models and worst case assumptions. PNECs are calculated for non-target organisms representative of the considered ecosystems (soil or surface water). Then numerical scores are given to the calculated PEC/PNEC ratio. Finally, the obtained score is multiplied with a further score which is based on the relevance of the metabolic rate in animals. RANKVET can be applied for surface water and soil systems and for different farming methods (intensive or pasture) and treated species. As an example of its potential use we applied RANKVET to 48 VMPs largely utilized in Italy.

1. Introduction

Veterinary medicinal products (VMPs) are compounds belonging to several chemical classes that are widely used to treat disease and protect the health of terrestrial and aquatic animals (both for food or non-food animals). In recent years VMPs have been recognized as emerging contaminants due to their widespread occurrence in environmental compartments (Brooks et al., 2007). As a consequence, in the last few years, a greater attention has been addressed to such substances (Jørgensen and Halling-Sørensen, 2000; Stuer-Lauridsen et al., 2000; Kümmerer, 2004). Releases of VMPs into the environment can take place at any step in the life cycle of the product. However, it has been recognized that major contamination routes are the direct application in aquaculture, the wash-off from topical treatments, livestock waste treatment plants, runoff from manure-treated farmlands and from excreta of animals on pasture (Boxall et al., 2003a). Many studies report the presence of VMPs in the environment, especially in surface waters (Boxall et al., 2002; Zuccato et al., 2005; Kemper, 2008; Crane et al., 2009; Iglesias et al., 2014). Although some of these compounds are unlikely to be a risk to the environment because of low concentrations combined with low toxicity, others may pose considerable risks. In fact, in some cases it was found that the detected concentrations of VMPS (e.g. ivermectin and doramectin in dung and monensin in soil) exceeded the effect concentrations (Boxall et al., 2003a) and had an adverse effect such as inhibition of reproduction, endocrine disruption and even potential ecosystem-level responses (Kim et al., 2008).

* Corresponding author. Tel.: +39 3342577792.
E-mail address: v.dinica@campus.unimib.it (V. Di Nica).

http://dx.doi.org/10.1016/j.ecolind.2014.12.021
1470-160X/

To prevent the risks to human health and environment, the European Commission issued several Directives which regulates the use of VMPs in EU (EU Directive 90/676/EEC; Directive 2004/28/EC; Regulation EC/726/2004). According to current legislation, before any new VMP can obtain marketing authorization, a stringent analysis has to be carried out by national and/or European authorities to ensure its efficacy, quality and safety to public health as well as to the environment. For the environmental impact assessment of these substances, the VICH phase I and phase II assessments have been implemented in the EU regulatory scheme (VICH, 2000, 2004). Phase I is an assessment of potential environmental exposure not an assessment of risk. It uses a decision tree approach to decide if exposure is low (not extensive): the basic assumption is that since exposure is so low, magnitude of any hazard has no effect in equation and the product is not expected to pose a significant risk for the environment.

In Phase II, the assessment is based on a risk quotient (RQ) approach which is determined for every non-target test species considered as representative of different ecosystems. The RQ is an exposure-toxicity ratio (ETR) and compares a PEC with a PNEC. The first is obtained by using predictive exposure models, whereas PNEC values are derived from the results of ecotoxicological laboratory tests and using appropriate assessment factors (e.g., by applying a factor between 10 and 1000 to the endpoint of each toxicity test performed on non-target organisms). At the end of the Phase II assessment, a VMP may not be expected to cause a significant harm to the environment or, if the RQ remains $\geq$1, a risk to the environment is assumed. In the latter case, risk mitigation measures have to be implemented to allow the authorization of the product (EMA, 2011).

Since a very large amount of VMPs including antibacterials, parasiticides, hormones, antifungals, are marketed yearly, there is a growing need to develop tools useful to support risk management strategies. For instance, monitoring VMPs in surface water and/or ground water is becoming mandatory; however, before implementing a monitoring programme, it is necessary to identify which VMPs have to be included in the analytical protocols. Therefore, the development of tools such as risk indicators or prioritization schemes allowing to rank and compare VMPs according to their environmental significance (in terms of potential risk) could be very useful to define priority lists. In the last years, these tools have been widely used to objectively identify substances of concern and for risk management actions, since they facilitate the effective targeting of resources for subsequent environmental and human health risk assessment (Capleton et al., 2006). For instance, some scoring and ranking systems have been adopted by authorities and regulatory centres mainly as first screening tools to identify the chemicals with greatest potential for adverse effects (Swanson and Jones, 1994; Huijbregts et al., 2000; Senese et al., 2010). In the field of pesticides, risk indicators are largely used as decision support system tool, to assess the potential environmental or economic consequences of pesticide management systems (Finizio et al., 2001; Kovach et al., 1992; HAIR, 2006) or to monitor temporal pesticide environmental risk trends on different scales (Calliera et al., 2006). At present, still very few risk indicators and prioritization schemes have been developed for VMPs. The first method approaching this topic for VMPs has been tackled by Boxall (Boxall et al., 2003b; Kools et al., 2008), who developed a qualitative prioritization system based on the use of VMPs, the degree of metabolism in the animal and degradation during storage of manure prior to land spreading and the toxicity of the substance to terrestrial and aquatic organisms. These data are used in a prioritization scheme (decision tree matrixes) for identifying VMPs having the potential to impact aquatic and terrestrial systems. A different risk indicator more focused on the potential risks to consumers has been proposed by Capleton and coworkers (Capleton et al., 2006). These authors developed a prioritization scheme of VMPs on the basis of their potential for indirect human exposure via the environment and their toxicity profile.

In this paper we propose a new risk indicator (RANKVET) specifically developed for the ranking of VMPs in terms of their potential environmental risk. RANKVET is a scoring system and is fully based on the VICH guidelines used in the VMPs authorization procedures. RANKVET can be applied to different environmental compartments (surface water and soil), different types of farming (intensively reared animals and pasture) and different treated species. To highlight the potential usefulness in risk management actions, the proposed indicator has been applied to 48 VMPs largely utilized in Italy.

2. Materials and methods

The RANKVET indicator is totally based on the information required by VICH guidelines for placing VMPs on the market. The methodological approach followed to develop RANKVET can be divided in different steps:

(1) compilation of a database of active substances present in VMPs, containing the data needed for the application of RANKVET;
(2) risk characterization (based on the PEC/PNEC ratio);
(3) attribution of scores and final ranking. Each step is described in more detail in the following paragraphs.

An EXCEL electronic page for the calculation of the indicator is available upon request to the authors.

2.1. Collection of data

According to the VICH guidelines, the environmental risk assessment of VMPs must be performed for active substances (a.s.). Therefore the complete list of a.s. was retrieved from the authorized VMPs in Italy. The drugs based on natural substances and microorganisms or those used for non-food animals were excluded from further assessment, in agreement with the VICH guidelines that classify these compounds as less harmful for the environment (VICH, 2000). Fish farm medicines were also excluded because the existing PEC calculation models are too complex for a prioritization approach, and since most of them were built for the Scottish aquacultures they cannot be applied to the Italian case. Data on amounts and/or sales of VMPs in Italy were gathered from the European Medicines Agency (EMA, 2013) and from the Italian Ministry of Health (www.salute.gov.it). This process left 48 a.s. which were included in the database. They belong to different chemical classes and different pharmacological types including antibiotics, ecto/endoparasiticides, or anti-inflammatory drugs and progestogens.

For the selected a.s. information on the animal target groups, dosage, formulations, number of treatments and dosing interval were obtained from a database of the Italian Ministry of Health (http://www.salute.gov.it/farmaciVetWeb/). In addition ecotoxicity data on non-target organisms and data on physical-chemical properties (Koc) were gathered from the *Veterinary Substances DataBase* (VSDB) (http://sitem.herts.ac.uk/aeru/vsdb/index.htm) (Tables S1 and S2 of support information). Finally qualitative information on the metabolism of the selected substance were taken from the work of Boxall and coworkers (2002) and from the VSDB database.

Supplementary Tables S1 and S2 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ecolind.2014.12.021.