RESIDUES OF IMIDACLOPRID IN SEWAGE WATER TREATMENT PLANTS AND WATERCOURSES IN SPAIN:

ARE VETERINARY MEDICINAL PRODUCTS A SIGNIFICANT SOURCE OF EMISSION?

MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios

AUTHORS

Irene de la Casa Resino[1], Julia María Villegas Grondona[2], Alejandra Puig Infante[2], Amparo Haro Castuera[1], Arancha Bartolomé Rodríguez[3], Eva Mª Herrera Hernández[3], Cintia Flores Rubio[3], Josep Caixach[3], Ricardo Carapeto García[1].

Cita sugerida: de la Casa-Resino I., Villegas J.M., Puig A., Haro A., Bartolomé A., Herrera E.M., Flores C., Caixach J., Carapeto R. 2022. Residues of imidacloprid in surface water treatment plants and watercourses in Spain: are Veterinary Medicinal Products (VMPs) a significant source of emission? Spanish Agency of Medicines and Medical Devices (AEMPS).

[1] Agencia Española de Medicamentos y Productos Sanitarios (AEMPS).
[2] Dirección General del Agua Ministerio para la Transición Ecológica y el Reto Demográfico (MITECO)
[3] Instituto de Diagnóstico Ambiental y Estudios del Agua (IDAEA-CSIC).

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Calle Campezo, 1, Edificio 8 - E-28022 Madrid
https://www.aemps.gob.es
Fecha de publicación: 4 de julio de 2022
NIPO: 134-22-006-4

SUMMARY

1. RESUMEN EJECUTIVO

El imidacloprid es un insecticida neonicotinoide que ha sido ampliamente utilizado como plaguicida (PPP), biocida (BP) y medicamento veterinario (VMP). Sin embargo, durante los últimos 20 años la legislación europea ha restringido su uso (junto a otros contaminantes) con el fin de reducir la concentración de imidacloprid en el medio acuático.

En España, siguiendo las indicaciones de la Directiva Marco de Aguas (WFD), se ha llevado a cabo la monitorización de imidacloprid desde el año 2018 y se ha extendido hasta (al menos) el año 2021. Se han tomado muestras de diferentes Plantas de Tratamiento de Aguas Residuales (SWTP) y del medio receptor de esas aguas. El principal objetivo de este documento es resumir los resultados obtenidos de la monitorización de imidacloprid en España durante los años 2018 y 2019. Además, se presenta una discusión sobre las posibles fuentes de emisión de los residuos de imidacloprid detectados.

Los resultados obtenidos muestran niveles cuantificables de imidacloprid, que pueden suponer un riesgo para el medio ambiente, en casi todas las SWTP y medios receptores monitorizados durante los años 2018 y 2019. Durante los años 2020 y 2021 también se han tomado muestras, pero los resultados no están disponibles todavía. El uso de imidacloprid como PPP y como MV parecen ser las principales fuentes de emisión. Sin embargo, considerando que el uso como PPP no está actualmente autorizado, cobran importancia los resultados que se obtengan en los próximos años, a fin de establecer una conclusión sobre las principales fuentes de residuos de imidacloprid.

2. EXECUTIVE SUMMARY

Imidacloprid is a commonly used neonicotinoid insecticide that has been authorised as plant protection product (PPP), as biocide (BP) and as Veterinary Medicinal Product (VMP). However, strict regulations have been established in the European Union (EU) during the last two decades to control the concentration levels of imidacloprid (among other water contaminants) in the water environment.

In Spain, monitoring of imidacloprid by following the indications reflected in the Water Framework Directive (WFD) have been performed since 2018 and have been extended until (at least) 2021. Samples in Sewage Water Treatment Plants (SWTP) and watercourses were taken. The main aim of this report is to summarize the results obtained from the monitoring of imidacloprid in Spain during the years 2018 and 2019. Furthermore, a reflection of the possible sources of emission of imidacloprid residues is performed.

Quantifiable levels of imidacloprid, that might suppose a risk for the aquatic environment, were detected in almost all SWTP and watercourses sampled in Spain in 2018 and 2019. Further water samples have been taken during the years 2020 and 2021 although the results are not available yet. It seems that PPP and VMPs might be the main sources of imidacloprid to the aquatic environment. However, as the uses of imidacloprid as PPP are no longer authorised, special attention should be paid to the residues detected in the following years to obtain a more reliable conclusion on which could be the main imidacloprid sources.

3. INTRODUCTION

Imidacloprid IUPAC name: (E)-1-(6-chloro-3-pyridinylmethyl)-N-nitroimidazolidin-2-ylideneamine) (Pubchem, 2020) is a commonly used neonicotinoid insecticide. Its insecticide effects are exerted by binding irreversibly to the nicotinic acetylcholine receptors (nAChRs), interfering with the transmission of nerve impulses in insects (EMA 2021). Neonicotinoids are very soluble in water and persistent in soils and sediment (Wood and Goulson 2017; Bonmatin et al. 2015; Sharlow 2017). **Their popularity is largely due to their high toxicity to invertebrates, the ease and flexibility with which they can be applied, their long persistence, and their systemic distribution and action in plants**. However, these properties also increase the probability of environmental contamination and exposure of non-target organisms (Bonmatin et al. 2015).

Environmental contamination with imidacloprid occurs via a number of sources as products containing this substance have been authorised as Plant Protection Products (PPP; according to Regulation [EC] 1107/2009), **as biocidal products (BPs**; according to Regulation (EU) 528/2012) **and as Veterinary Medicinal Products (VMPs**; according to Directive 2001/82/EC). Strict regulations have been established in the European Union (EU) during the last two decades to control the concentration levels of imidacloprid (among other water contaminants) in the water environment. In this sense, the Water Framework Directive (WFD, Directive 2000/60/EC) entered into force on 22 December 2000 with the aim of achieving a good chemical status for all water bodies in Europe. Article 16 of the **WFD requires the Commission to identify Priority Substances among those presenting significant risk to or via the aquatic environment**, and to set EU Environmental Quality Standards (EQS) for those substances in water, sediment and/or biota. Furthermore, Directive 2008/105/EC provides a legal framework for the establishment of a Watch List of substances for which Union-wide monitoring data are to be gathered for the purpose of supporting future prioritisation exercises in accordance with Article 16 of Directive 2000/60/EC. In 2015, the first Watch List was published including imidacloprid among the seven substances that should be monitored during the next two years (Decision (EU) 2015/495). In 2018 the second Watch List was published repealing the first one (Decision (EU) 2018/840). In this list, although there were some changes in the included substances, the monitoring of imidacloprid was maintained as it was considered that the quality of the data gathered was not satisfactory (Loos et al. 2018). The third watch list repealing the second one was published in 2020 (Decision (EU) 2020/1161) in which the substances that have been in the list since 2015 (including imidacloprid) were not included as it was considered that enough quality data was already obtained to perform a risk assessment.

In 2014, the European Food Safety Authority (EFSA) published the peer review report of the pesticide risk assessment for aquatic organisms for the active substance imidacloprid (EFSA, 2014) in which the Regulatory Acceptable Concentrations (RAC) of imidacloprid were discussed (Table 1). **The report concluded that**

the most sensitive organisms are the aquatic invertebrates, and specifically, insects are more sensitive than crustaceans. Furthermore, it also stablished the RAC that should be used for the risk assessment, indicating that "tier-1 RACs have to be considered as less conservative because they did not cover more sensitive species than the standard tested species, therefore they are not appropriate for risk assessment. The tier-2 RACs cover the species that according to the scientific information available were more sensitive. However, they can only be considered as provisional due to the qualitative and quantitative limitations of the data set. No tier-3 RACs could be derived".

Furthermore, The Predicted No-Effect Concentration (PNEC) considered in the Review of the 1st Watch List under the Water Framework Directive and recommendations for the 2nd Watch List to determine if there was enough quality data for imidacloprid was 0.009 µg/L (Loos et al., 2018).

In Spain, monitoring of imidacloprid by following the indications reflected in the WFD has been performed since 2018 and extended until (at least) 2021. In this sense, the main aim of this report is to summarize the results obtained from the monitoring of imidacloprid in Spain during the years 2018 and 2019. Furthermore, a reflection of the possible sources of emission of imidacloprid residues is performed.

TABLE 1 Summary on the Regulatory Acceptable Concentrations (RACs) for imidacloprid. Adapted from EFSA (2014).

	Acute RAC (µg a.s./L)	Chronic RAC (µg a.s./L)
Tier 1	0.341	0.209
Tier 2 (SSD)	0.098* To be used only as provisional for risk assessment***	0.009** To be used only as provisional for risk assessment***
Tier 3	Not available	Not available

a.s: active substance; SSD: Standard Sensitivity Distribution.

*Based on a median HC5 (and 95% confidence interval) of 0.49 (0.098-1.38) µg/L and AF of 5.

**Based on an HC5 value (and 95% confidence interval) of 0.027 (0.0031-0.092) µg/L and AF of 3.

*** To be used only as provisional for risk assessmentdue to the lack of data.

4. MATERIAL AND METHODS

4.1 Study areas

Imidacloprid monitoring in Spain according to Directive (EU) 2000/60 was performed by the Ministry of Environment (MITECO, Ministerio para la Transición Ecológica y el Reto Demográfico). **Spain has 25 river basin districts, out of which 8 are international sharing watercourses with France to the northeast and Portugal to the west** (Figure 1). Samples of Imidacloprid were taken in the effluents of 16 Sewage Water Treatment plants (SWTP) and 20 watercourses downstream the SWTP of ten river basin districts in Spain (Table 2).

RIVER BASIN DISTRICTS IN SPAIN

Figure 1

TABLE 2 River Basin districts and sampling points of imidacloprid.

River Basin District	Code	Sampling point	Sampling date 2018	Sampling date 2019
CUENCAS INTERNAS DE CATALUÑA	ES100_01_EDAR	SWTP Prat	26/04/2018	07/10/2019
	ES100_02_MR	WC: Llobregat river	26/04/2018	07/10/2019

River Basin District	Code	Sampling point	Sampling date 2018	Sampling date 2019
CANTABRICO OC-CIDENTAL	ES018_01_EDAR	SWTP center of Asturias	16/04/2018	08/10/2019
	ES018_02_MR	WC: Nora river	16/04/2018	08/10/2019
SEGURA	ES070_01_EDAR	SWTP Murcia (east)	23/04/2018	23/10/2019
	ES070_02_MR	MR: Segura river	23/04/2018	23/10/2019
GUADIANA	ES040_01_EDAR	SWTP Badajoz	11/04/2018	01/10/2019
	ES040_02_MR	WC: Guadiana river	11/04/2018	01/10/2019
	ES040_03_MR	WC: Guadiana river	05/04/2018	01/10/2019
EBRO	ES091_01_EDAR	SWTP Zaragoza	03/04/2018	01/10/2019
	ES091_02_MR	WC: Ebro river	03/04/2018	01/10/2019
	ES091_03_EDAR	SWTP Vitoria	09/04/2018	25/09/2019
	ES091_04_MR	WC: Zadorra river	09/04/2018	25/09/2019
GUADALQUIVIR	ES050_01_EDAR	SWTP Córdoba	03/04/2018	01/10/2019
	ES050_02_MR	WC: Guadalquivir river	03/04/2018	01/10/2019
	ES050_03_MR	WC: Guadalbullón river	09/04/2018	07/10/2019
MIÑO-SIL	ES010_01_EDAR	SWTP Reza	04/04/2018	23/09/2019
	ES010_02_MR	WC: Miño river	04/04/2018	23/09/2019
	ES010_03_EDAR	SWTP Villadepalos	10/04/2018	25/09/2019
	ES010_04_MR	WC: Sil river	10/04/2018	25/09/2019
	ES010_05_MR	WC: Miño river	17/04/2018	30/09/2019
DUERO	ES020_01_EDAR	SWTP León	02/04/2018	24/09/2019
	ES020_02_MR	WC: Bernesga river	02/04/2018	24/09/2019
	ES020_03_EDAR	SWTP Valladolid	10/04/2018	24/09/2019
	ES020_04_MR	WC: Pisuerga river	10/04/2018	24/09/2019

River Basin District	Code	Sampling point	Sampling date 2018	Sampling date 2019
JÚCAR	ES080_01_EDAR	SWTP Cuenca del Carraixet	17/04/2018	16/10/2019
	ES080_02_MR	WC: Barranco del Carraixet	17/04/2018	16/10/2019
	ES080_03_MR	WC: Turia river	24/04/2018	10/10/2019
	ES080_04_EDAR	SWTP Teruel	24/04/2018	10/10/2019
	ES080_05_MR	WC: Canal de Mª Cristina	25/04/2018	01/10/2019
	ES080_06_EDAR	SWTP Valle del Vinalopó	19/04/2018	28/10/2019
	ES080_07_MR	WC: Vinalopó river	19/04/2018	28/10/2019
TAJO	ES030_01_EDAR	SWTP Sur Oriental	18/04/2018	21/10/2019
	ES030_02_MR	WC: Jarama river	18/04/2018	21/10/2019
	ES030_03_EDAR	SWTP Santa María de Benquerencia	25/04/2018	24/09/2019
	ES030_04_MR	WC: Tajo river	25/04/2018	24/09/2019

SWTP: Sewage Water Treatment Plant; WC: Watercourse.

4.2 Standards and reagents

All solvents used (analytical or high-performance LC/MS) were supplied by Merck (Darmstadt, Germany). Methanol (MeOH) SupraSolv; acetonitrile (ACN) and water (H2O) LiChroSolv; formic acid (HCOOH) (98-100%). The native standard Imidacloprid was provided by Dr. Ehrenstorfer. Isotopically labelled (Imidacloprid-d4) was purchased from A2S (Analytical Standard Solution).

4.3 Solid-Phase extraction (SPE)

For the SPE procedure, OASIS HLB cartridges (200 mg, 6 mL) and a vacuum extraction manifold were used. 100mL of sample was spiked with d4-Imidacloprid as internal standard, in order to obtain concentration of 50 ng/L. The cartridge was conditioned with 6 mL of acetonitrile and 6 mL of ultrapure water. After the sample was loaded, the cartridge was rinsed with 6mL of ultrapure water/methanol (65:35) and was dried under vacuum aspiration for 20 min. Imidacloprid was eluted with 6 mL of acetonitrile. The extract was evaporated until 100 µL. Finally, the extract was filtered through 0.22 µm polytetrafluoroethylene (PTFE) syringe filter.

4.4 LC–ESI–HRMS AnalIsYs

Orbitrap-Exactive HCD (Thermo Fisher Scientific, Bremen, Germany) mass spectrometer equipped with heated electrospray source (H–ESI II), a Surveyor MS Plus pump and an Accela Open AS autosampler kept at 5.5 °C (Thermo Fisher Scientific, San Jose, California) was used.

The chromatographic separation was performed on a reversed phase Luna C18 column (150 × 2mm, 5µm, Phenomenex, Torrance, CA, USA) preceded by an C18 guard column (4 x 2.0mm, Phenomenex, Torrance, CA, USA). The mobile phase was composed of 0.1 % of HCOOH in water as solvent A and 0.1 % of HCOOH in ACN as solvent B at a flow rate of 200µL min-1. The linear gradient elution program was: 5% up to 95% ACN in 15min. This percentage was then maintained for 1min and after that the LC system returns to initial conditions for 9min. The injection volume was 10 µL.

The MS analyses were carried out in ESI positive ionisation mode. N2 was used as a sheath gas, ion sweep gas and auxiliary gas at flow rates of 40 psi, 0 and 10 a.u. (arbitrary units), respectively.

Otherwise, for LC–ESI–HRMS analysis, data were acquired in full-scan mode in a mass range of *m/z* 50-1,000. Optimum tube lens voltage was selected as −135 V for entire range of masses. The resolution was 50,000 (*m/z* 200, Full Width at Half Maximum, FWHM) at a scan rate 2 Hz and with an accuracy in the measurement of the mass <5 ppm with external calibration. The automatic gain control (AGC) was set as “balanced” (1e6) with a maximum injection time of 250 ms. Data acquisition was performed with Xcalibur Software (Thermo Fisher Scientific, Bremen, Germany).

4.5 Quality assurance and quality control

Identification and quantification were carried out by isotope dilution method. The imidacloprid was identified according to the following criteria: the ratio of the retention time of the analyte to that of the internal standard, shall correspond to that of the calibration solution at a tolerance of ±2.5 %; maximum mass accuracy of 5 ppm; score of isotopic pattern >80 % and the area of chromatographic peak >10^4.

The quantification was performed using six-level calibration curve in the 2-250 ng/L range.

Method and instrumental blanks were measured to check background level.

Method accuracy and precision were evaluated by analysing a spiking sample (n=4) with a known concentration of the analyte (50 ng/L). Recoveries were ranged between 91 and 109 %. Standard deviation of calculated concentrations was 4 %.

Limit of detection (LOD) of 1 ng/L was estimated as the concentration equivalent to a signal-to-noise ratio equal to 3 from the chromatograms of the samples spiked at the lowest validated level. Limit of quantification (LOQ) was considered the lowest validated level of the linear range, 2 ng/L.

5. RESULTS

5.1 Residues of imidacloprid in SWTP and watercourses in Spain

Residues of imidacloprid were determined in 16 effluents of SWTP and 20 samples of fresh water in different river basin areas along Spain. Results are summarized in Table 3.

TABLE 3 Imidacloprid residues detected in SWTP and watercourses in 2018 and 2019 in Spain.

River Basin District	Code	Sampling point	Imidacloprid (µg/L) per year	
			2018	2019
CUENCAS INTERNAS DE CATALUÑA	ES100_01_EDAR	SWTP	0.120	0.073
	ES100_02_MR	WC	0.012	0.036
CANTABRICO OCCIDENTAL	ES100_01_EDAR	SWTP	<LOQ	0.054
	ES018_02_MR	WC	<LOQ	0.043
SEGURA	ES070_01_EDAR	SWTP	0.111	0.090
	ES070_02_MR	WC	0.055	0.074
GUADIANA	ES040_01_EDAR	SWTP	0.044	0.086
	ES040_02_MR	WC	<LOQ	0.045
	ES040_03_MR	WC	<LOQ	0.037
EBRO	ES091_01_EDAR	SWTP	0.110	0.070
	ES091_02_MR	WC	<LOQ	0.007
	ES091_03_EDAR	SWTP	0.024	0.044
	ES091_04_MR	WC	<LOQ	0.019
GUADALQUIVIR	ES050_01_EDAR	SWTP	0.063	0.078
	ES050_02_MR	WC	0.007	0.006
	ES050_03_MR	WC	0.006	0.010
MIÑO-SIL	ES010_01_EDAR	SWTP	0.015	0.050
	ES010_02_MR	WC	<LOQ	<LOQ
	ES010_03_EDAR	SWTP	0.009	0.007
	ES010_04_MR	WC	<LOQ	<LOQ
	ES010_05_MR	WC	<LOQ	<LOQ

River Basin District	Code	Sampling point	Imidacloprid (µg/L) per year	
			2018	2019
DUERO	ES020_01_EDAR	SWTP	<LOQ	0.044
	ES020_02_MR	WC	<LOQ	0.006
	ES020_03_EDAR	SWTP	<LOQ	0.042
	ES020_04_MR	WC	<LOQ	0.003
JÚCAR	ES080_01_EDAR	SWTP	0.372	0.354
	ES080_02_MR	WC	0.087	0.049
	ES080_03_MR	WC	0.011	<LOQ
	ES080_04_EDAR	SWTP	0.195	0.071
	ES080_05_MR	WC	0.053	0.058
	ES080_06_EDAR	SWTP	0.075	0.098
	ES080_07_MR	WC	0.059	0.077
TAJO	ES030_01_EDAR	SWTP	0.078	0.016
	ES030_02_MR	WC	0.015	0.051
	ES030_03_EDAR	SWTP	0.185	0.037
	ES030_04_MR	WC	0.020	0.023

SWTP: Sewage Water Treatment Plant; WC: Watercourse.

5.2 Risk characterization

In order to determine if the detected residues may imply a risk for the aquatic environment a risk characterization was performed. It was performed according to VICH (International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Products) guidelines (GL) 6 and 38 (VICH GL6, 2000; VICH GL38, 2005). A risk quotient (RQ) approach was considered as described in VICH GL38 guideline, which is the ratio of the predicted environmental concentration (PEC) and the predicted no effect concentration (PNEC) on non-target organisms. The RQ (PEC/PNEC) is compared against a value of one. A value less than one indicates that no risk for the environment is expected. In this case, the acute RAC of 0.098 µg/L and the chronic RAC of 0.009 µg/L stablished by EFSA (2014) were considered as PNEC (Table 1). The results obtained are summarized in Table 4 and Table 5. For the purposes of risk characterization in those cases were the residues obtained were below the LOQ, a value half of the LOQ was considered (i.e. 0.001 µg/L).

TABLE 4 Risk assessment based on comparison of tier-2 RACs with the residues obtained for imidacloprid in the year 2018.

River Basin District	Code	Sampling point	Imidacloprid (µg/L)	Acute RQ	Chronic RQ
CUENCAS INTERNAS DE CATALUÑA	ES100_01_EDAR	SWTP	0.1202	1.2	13.4
	ES100_02_MR	WC	0.0116	0.1	1.3
CANTABRICO OCCIDENTAL	ES018_01_EDAR	SWTP	0.0010	0.0	0.1
	ES018_02_MR	WC	0.0010	0.0	0.1
SEGURA	ES070_01_EDAR	SWTP	0.1107	1.1	12.3
	ES070_02_MR	WC	0.0549	0.6	6.1
GUADIANA	ES040_01_EDAR	SWTP	0.0440	0.4	4.9
	ES040_02_MR	WC	0.0010	0.0	0.1
	ES040_03_MR	WC	0.0010	0.0	0.1
EBRO	ES091_01_EDAR	SWTP	0.1099	1.1	12.2
	ES091_02_MR	WC	0.0010	0.0	0.1
	ES091_03_EDAR	SWTP	0.0237	0.2	2.6
	ES091_04_MR	WC	0.0010	0.0	0.1
GUADALQUIVIR	ES050_01_EDAR	SWTP	0.0631	0.6	7.0
	ES050_02_MR	WC	0.0069	0.1	0.8
	ES050_03_MR	WC	0.0062	0.1	0.7
MIÑO-SIL	ES010_01_EDAR	SWTP	0.0148	0.2	1.6
	ES010_02_MR	WC	0.0010	0.0	0.1
	ES010_03_EDAR	SWTP	0.0086	0.1	1.0
	ES010_04_MR	WC	0.0010	0.0	0.1
	ES010_05_MR	WC	0.0010	0.0	0.1
DUERO	ES020_01_EDAR	SWTP	0.0010	0.0	0.1
	ES020_02_MR	WC	0.0010	0.0	0.1
	ES020_03_EDAR	SWTP	0.0010	0.0	0.1
	ES020_04_MR	WC	0.0010	0.0	0.1

River Basin District	Code	Sampling point	Imidacloprid (µg/L)	Acute RQ	Chronic RQ
JÚCAR	ES080_01_EDAR	SWTP	0.3720	3.8	41.3
	ES080_02_MR	WC	0.0872	0.9	9.7
	ES080_03_MR	WC	0.0115	0.1	1.3
	ES080_04_EDAR	SWTP	0.1952	2.0	21.7
	ES080_05_MR	WC	0.0528	0.5	5.9
	ES080_06_EDAR	SWTP	0.0752	0.8	8.4
	ES080_07_MR	WC	0.0587	0.6	6.5
TAJO	ES030_01_EDAR	SWTP	0.0778	0.8	8.6
	ES030_02_MR	WC	0.0146	0.1	1.6
	ES030_03_EDAR	SWTP	0.1848	1.9	20.5
	ES030_04_MR	WC	0.0202	0.2	2.2

SWTP: Surface Water Treatment Plant: WC: Watercourse. Values in red denotes those cases in which the ratio (PEC/PNEC) was above one, i.e. a risk for the environment is identified.

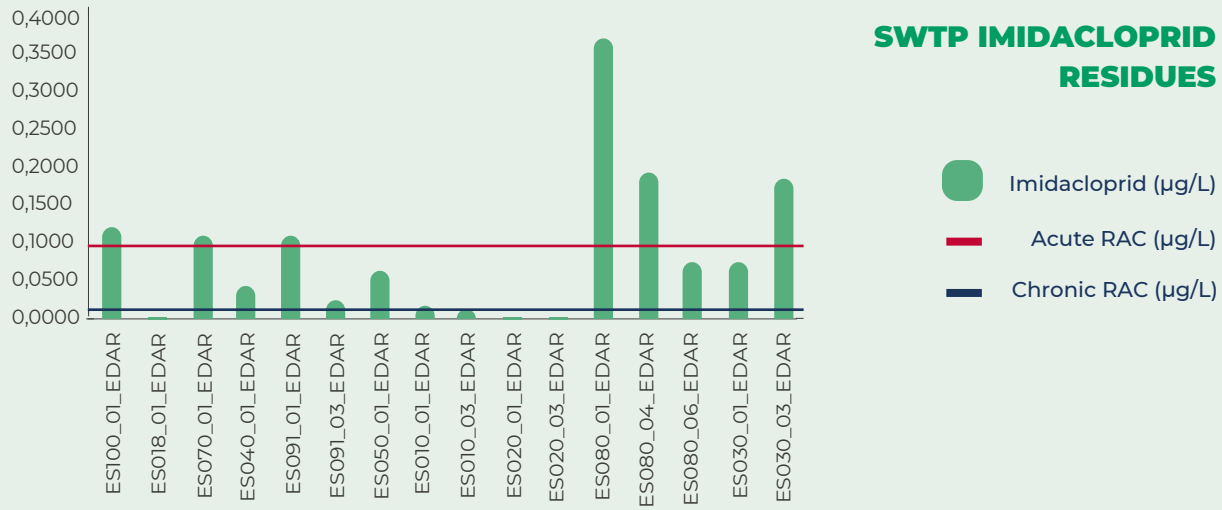

Figure 2
Imidacloprid residues detected in the effluents of each SWTP sampled in 2018. RAC: Regulatory Acceptable Concentration. EDAR: SWTP.

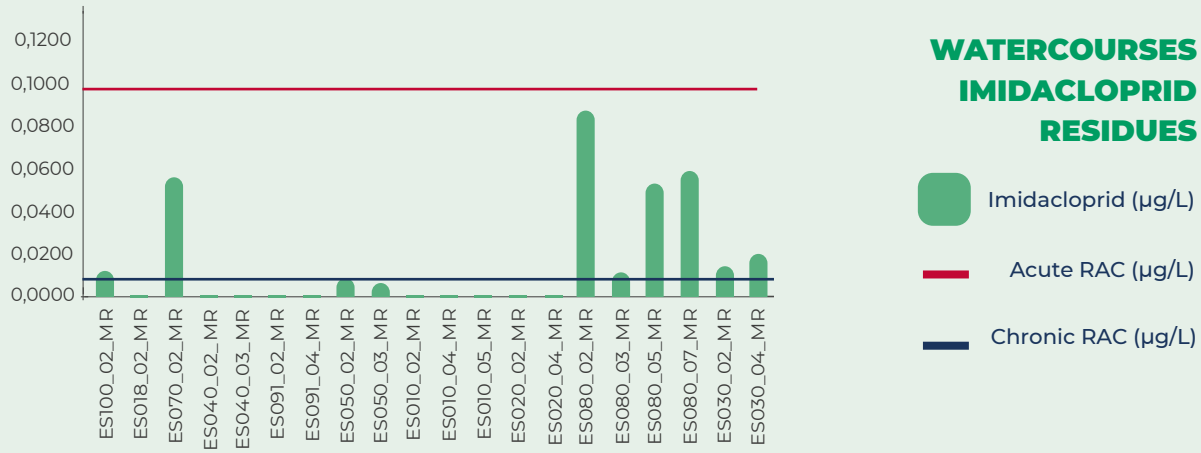

Figure 3
Imidacloprid residues detected in watercourses downstream of each SWTP sampled in 2018. RAC: Regulatory Acceptable Concentration; MR: watercourse.

TABLE 5

Risk assessment based on comparison of tier-2 RACs with the residues obtained for imidacloprid in the year 2019.

River Basin District	Code	Sampling point	Imidacloprid (µg/L)	Acute RQ	Chronic RQ
CUENCAS INTERNAS DE CATALUÑA	ES100_01_EDAR	SWTP	0.0728	0.7	8.1
	ES100_02_MR	WC	0.0364	0.4	4.0
CANTABRICO OCCIDENTAL	ES018_01_EDAR	SWTP	0.0538	0.5	6.0
	ES018_02_MR	WC	0.0431	0.4	4.8
SEGURA	ES070_01_EDAR	SWTP	0.0903	0.9	10.0
	ES070_02_MR	WC	0.0738	0.8	8.2
GUADIANA	ES040_01_EDAR	SWTP	0.0855	0.9	9.5
	ES040_02_MR	WC	0.0451	0.5	5.0
	ES040_03_MR	WC	0.0367	0.4	4.1
EBRO	ES091_01_EDAR	SWTP	0.0702	0.7	7.8
	ES091_02_MR	WC	0.0065	0.1	0.7
	ES091_03_EDAR	SWTP	0.0439	0.4	4.9
	ES091_04_MR	WC	0.0186	0.2	2.1
GUADALQUIVIR	ES050_01_EDAR	SWTP	0.0777	0.8	8.6
	ES050_02_MR	WC	0.0061	0.1	0.7
	ES050_03_MR	WC	0.0095	0.1	1.1

River Basin District	Code	Sampling point	Imidacloprid (µg/L)	Acute RQ	Chronic RQ
MIÑO-SIL	ES010_01_EDAR	SWTP	0.0498	0.5	5.5
	ES010_02_MR	WC	0.0010	0.0	0.1
	ES010_03_EDAR	SWTP	0.0069	0.1	0.8
	ES010_04_MR	WC	0.0010	0.0	0.1
	ES010_05_MR	WC	0.0010	0.0	0.1
DUERO	ES020_01_EDAR	SWTP	0.0442	0.5	4.9
	ES020_02_MR	WC	0.0058	0.1	0.6
	ES020_03_EDAR	SWTP	0.0417	0.4	4.6
	ES020_04_MR	WC	0.0031	0.0	0.3
JÚCAR	ES080_01_EDAR	SWTP	0.3536	3.6	39.3
	ES080_02_MR	WC	0.0491	0.5	5.5
	ES080_03_MR	WC	0.001	0.0	0.1
	ES080_04_EDAR	SWTP	0.0706	0.7	7.8
	ES080_05_MR	WC	0.0579	0.6	6.4
	ES080_06_EDAR	SWTP	0.0980	1.0	10.9
	ES080_07_MR	WC	0.0768	0.8	8.5
TAJO	ES030_01_EDAR	SWTP	0.0157	0.2	1.7
	ES030_02_MR	WC	0.0506	0.5	5.6
	ES030_03_EDAR	SWTP	0.0370	0.4	4.1
	ES030_04_MR	WC	0.0226	0.2	2.5

SWTP: Sewage Water Treatment Plant: WC: Watercourse. Values in red denotes those cases in which the ratio (PEC/PNEC) was above one, i.e. a risk for the environment is identified.

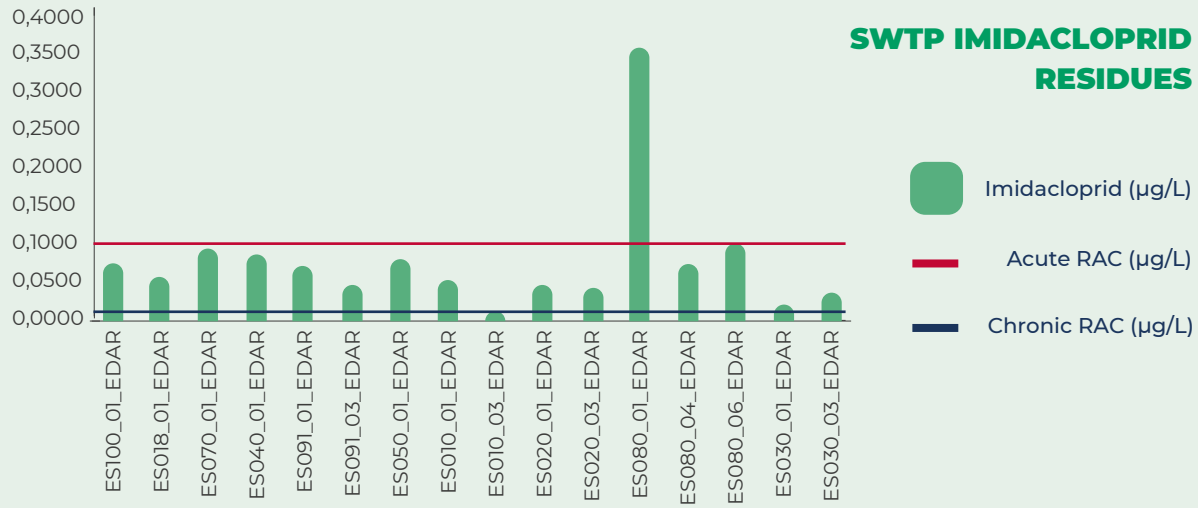

Figure 4

Imidacloprid residues detected in the effluents of each SWTP sampled in 2019. RAC: Regulatory Acceptable Concentration. EDAR: SWTP.

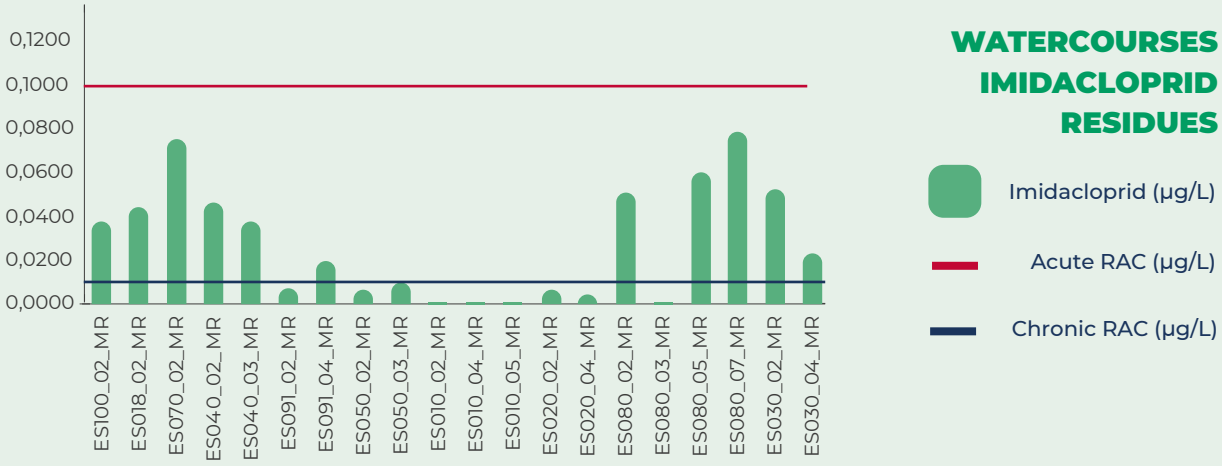

Figure 5

Imidacloprid residues detected in watercourses downstream of each SWTP sampled in 2019. RAC: Regulatory Acceptable Concentration; MR: watercourse.

An acute risk was identified in 6 out of 16 SWTP in 2018 and in 1 out of 16 SWTP in 2019. No acute risk was identified in the WC sampled in 2018 or 2019. Regarding the chronic risk, values above 1 were identified in 12 out of 16 SWTP and in 8 out of 20 WC in 2018 and in 15 out of 16 SWTP and in 12 out of 20 WC in 2019. Especially significant is the chronic risk identified in almost all effluents of SWTP sampled in 2019 (Table 4, Table 5, Figure 2, Figure 3, Figure 4 and Figure 5).

6. DISCUSSION

As summarized above, residues of imidacloprid in the effluents of SWTP and in watercourses downstream of the SWTP were detected (Table 3). Furthermore, these residues may imply an acute and chronic risk for the environment (Table 4, Table 5, Figure 2, Figure 3, Figure 4, Figure 5). In order to allow the management of the identified risks for the environment, a reflection about the potential sources of imidacloprid residues is necessary.

As indicated above, in Spain imidacloprid is a component of products used as PPP, BPs, and VMPs.

6.1 Uses as Plant Protection Products (PPP).

Imidacloprid was included in Annex I to Directive 91/414/EEC on 1 August 2009 by Commission Directive 2008/116/EC and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. The peer review leading to the approval of imidacloprid was finalised on 29 May 2008 (EFSA, 2008).

In 2013, the Commission prohibits the use of imidacloprid in bee-attractive crops (including maize, oilseed rape and sunflower); the uses in greenhouses, treatments of some outdoor crops after flowering and winter cereals was still permitted (Regulation (EU) 485/2013). At the same time, the applicant was obliged to provide further data (so-called "confirmatory information") in order to confirm the safety of the uses still allowed. The EFSA conclusions on the risk assessment of these confirmatory data were published in the EFSA website on November 2016 (EFSA, 2016). Following the assessment of this confirmatory information, The Commission and the Member States concluded that the remaining outdoor uses could no longer be considered safe due to the identified risks to bees (honeybee, bumblebee and solitary bee). Therefore, the Commission proposed to completely ban the outdoor uses of imidacloprid. This proposal was supported by a qualified majority of Member States in the Regulatory Committee on 27 April 2018. As a result, **all outdoor uses of imidacloprid were banned** and only the use in permanent greenhouses or in seeds intended to be used only in permanent greenhouses remained possible. The resulting crop must stay within a permanent greenhouse during its entire life cycle (Regulation (EU) 2018/783). In the light of these restrictions, the applicant for the renewal of approval of imidacloprid withdrew its application. Consequently, the approval of imidacloprid expired on 1 December 2020. Therefore, **currently the use of imidacloprid as PPP is not authorised in the EU** (Regulation (EU) 2020/1643), so since 2020 no emission is expected for this use.

The professional use as a PPP implies a direct emission to the environment, but there might be also an indirect emission to the environment after a consumer eats vegetables with residues of imidacloprid under the Maximum Residue Levels (MRLs) legally allowed. The only authorised use during the years 2018 and 2019 was in greenhouses (foliar and seed application). Therefore, during these years the

consumer exposure to imidacloprid was possible when eating fruits or leafs produced in permanent greenhouses. The foliar application is poorly absorbed by the plant (EFSA et al., 2019) and there might be residues on the surface of the fruits or leafs to which the consumer could be exposed to. The seed application follows an intense metabolisation by the plant, so it is expected that there would be less residues in the fruits or leafs in this use. A MRL for each crop was stablished due to the possibility of consumer exposure (EFSA et al. 2019).

After exposure of the consumer to residues through food, imidacloprid is rapidly absorbed, metabolized in the liver, and excreted, primarily via the urine. There are two main routes of metabolism in mammals. The first one, through oxidative cleavage to imidazolidine and 6-chloronicotinic acid, and the second one that involves hydroxylation of the imidazolidine ring, followed by the elimination of water and formation of an unsaturated metabolite. More than 90% of the dose is eliminated within 24 h, with total excretion by 48 h; 80% of the dose is excreted via the urine, with 20% eliminated via the feces. There is no information available on the amounts of parent compound excreted (Sheets 2001).

The stablished acceptable daily intake (ADI) for imidacloprid is 0.06 mg/kg body weight (EFSA et al. 2019). Therefore, this value can be used as an upper threshold of exposure of consumers to imidacloprid. It can be assumed that a maximum of 0.06 mg imidacloprid/kg body weight/day could be consumed through food. However, the percentage of imidacloprid that could be excreted unchanged (i.e. not metabolised and, therefore, active) and that could reach the SWTP cannot be precisely calculated due to the lack of metabolism data.

Furthermore, imidacloprid may reach the aquatic environment while rinsing vegetables before consumption. However, the percentage of imidacloprid that would reach watercourses through this route is difficult to quantify.

6.2 Uses in Biocide Products (BPs)

According to ECHA there were 34 BPs containing imidacloprid authorised in Spain (ECHA, 2021; Table A1). **The products are authorised for professional and non-professional users to be used indoors and outdoors mainly as baits against cockroaches, ants and flies**. Due to this type of uses, it is not likely that imidacloprid could reach watercourses in high quantities as they BP authorised are designed for being included in limited spaces with limited access to water.

Therefore, the environmental exposure due to the use of imidacloprid as biocide is expected to be low due to the formulations design.

6.3 Veterinary Medicinal Products (VMPs)

According to the Spanish database CIMA-Vet (CIMA-Vet, 2021) there are 49 products authorised containing imidacloprid. **As imidacloprid has a pronounced insecticide effect, but no acaricide effect, it is also used in combination with other parasiticides with acaricide effect. All of them are formulated as spot-on or collars for dogs and cats** (Table A2). The Spanish College of Veterinary Surgeons (OCV; Organización Colegial Veterinaria Española), recommends to prevent and protect pets against external parasite during the whole year (Colvet 2021).

According to Sharlow (2017) imidacloprid from VMPs may reach surface water (1) by the rain falling onto whatever habitat the

animal is on, (2) when the animal or its bedding is washed (Jacobs et al. 2001), or (3) direct pollution when the animal enters watercourses. Furthermore, imidacloprid in dogs and cats may be excreted in urine after the absorption through the skin (Craig et al. 2005; Wang et al. 2015; Sharlow 2017).

The environmental exposure of VMPs used in pets has always been considered diffuse and not very important in size. Indeed, VMPs for use in non-food animals is considered to be associated with fewer environmental concerns than the use of VMPs in food-producing animals simply because there is less total amount of product used on the individual animals. Therefore, no in deep risk assessment is required when the product is used in companion animals (VICH GL6 2000). Nevertheless, the changes in the population uses and customs (over 10 million dogs and cats in Spain in 2020 and the figure grows every year (FEDIAF 2020)) have led to a very significant amount of pets that might be treated with parasiticides. Sporadic treatment to these animals will probably have no impact to the environment, but continuous treatment (as currently recommended by professional associations), can end up posing a significant emission of active substances with insecticidal activity ready to affect to non-target organisms in the environment. In this sense, the Committee for Medicinal Products for Veterinary Use (CVMP) adopted in 2020 a concept paper to develop a reflection paper, on whether the current approach for the environmental risk assessment of VMPs containing antiparasitics used in companion animals remains scientifically justified. The reflection paper will also aim to explore the need and feasibility of mitigation measures for such products (EMA 2020). The reflection paper is a work currently ongoing.

In summary, the contribution of VMPs to the imidacloprid residues detected in the effluents of SWTP and watercourses cannot be disregarded.

7. CONCLUSIONS

Quantifiable levels of imidacloprid, that might suppose a risk for the aquatic environment, were detected in almost all SWTP and watercourses sampled in Spain in 2018 and 2019. It seems that PPP and VMPs could be the main sources of imidacloprid to the aquatic environment, as on those dates the use of imidacloprid as PPP was still allowed in permanent greenhouses. Nevertheless, the use of imidacloprid as PPP is not authorised since December 2020. Consequently, the presence of imidacloprid in SWTP and downstream watercourses after 2020 would confirm with a high level of certainty the relevance of the VMP source. Additional sampling efforts are therefore necessary to discard or confirm the risk of the use of pets' parasiticides containing imidacloprid and to apply appropriate risk mitigation measures if necessary.

8. REFERENCES

Bonmatin, J-M, C Giorio, V Girolami, D Goulson, D P Kreutzweiser, C Krupke, M Liess, et al. 2015. Environmental Fate and Exposure; Neonicotinoids and Fipronil. Environmental Science and Pollution Research International 22 (1): 35–67. https://doi.org/10.1007/s11356-014-3332-7.

CIMA-Vet, 2021. Medicamentos veterinarios. https://cimavet.aemps.es/cimavet/publico/home.html. Consulted on October 2021.

Colvet. 2021. La OCV destaca la importancia de prevenir y proteger a los animales domésticos frente a parásitos externos durante todo ell año. http://www.colvet.es/node/10414. Consulted on November 2021.

Craig, MS, RC Gupta, TD Candery, and DA Britton. 2005. Human Exposure to Imidacloprid from Dogs Treated with Advantage(R)." Toxicology Mechanisms and Methods 15 (4): 287–91. https://doi.org/10.1080/15376520590968842.

Decision (EU) 2015/495. Commission Implementing Decision (EU) 2015/495 of 20 March 2015 Establishing a Watch List of Substances for Union-Wide Monitoring in the Field of Water Policy Pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Official Journal of the European Union L78/40 (C(2015) 1756): 20–30.

Decision (EU) 2018/840. Commission Implementing Decision (EU) 2018/840 of 5 June 2018 Establishing a Watch List of Substances for Union-Wide Monitoring in the Field of Water Policy. Official Journal of the European Union L 141 (March 2015): 9–12.

Decision (EU) 2020/1161. Commission Implementing Decision (EU) 2020/1161 of 4 August 2020 Establishing a Watch List of Substances for Union-Wide Monitoring in the Field of Water Policy Pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Official Journal of the European Union L 257: 32–35.

Directive 2000/60/EC. Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 Establishing a Framework for Community Action in the Field of Water Policy. Official Journal of the European Communities L327: 1-72.

Directive 2001/82/EC. 2001. Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Veterinary Medicinal Products. Official Journal of the European Union L311: 1–66.

Directive 2008/105/EC. 2008. Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on Environmental Quality Standards in the Field of Water Policy, Amending and Subsequently Repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC. Official Journal of the European Union L348: 84–97.

ECHA (European Chemicals Agency), 2021. Information on biocides. https://echa.europa.eu/es/information-on-chemicals/biocidal-products. Consulted on October 2021.

EFSA (European Food Safety Authority), 2014. Conclusion on the Peer Review of the Pesticide Risk Assessment for Aquatic Organisms for the Active Substance Imidacloprid. EFSA Journal 12 (10): 49. https://doi.org/doi:10.2903/j.efsa.2014.3835.

EFSA (European Food Safety Authority), 2016. Conclusion on the peer review of the pesticide risk assessment for the active substance imidacloprid in light of confirmatory data submitted. EFSA Journal 2016; 14(11): 4607. doi:10.2903/j.efsa.2016.4607.

EFSA (European Food Safety Authority), Himdata Abdourahime, Maria Anastassiadou, Alba Brancato, Daniela Brocca, Luis Carrasco Cabrera, Chloe De Lentdecker, et al. 2019. Review of the Existing Maximum Residue Levels for Imidacloprid According to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 17 (1): e05570. https://doi.org/https://doi.org/10.2903/j.efsa.2019.5570.

EMA. 2000. "Guideline on Environmental Impact Assessment (EIAs) for Vetinary Medicinal Products (VMPs) - Phase I." The European Agency for the Evaluation of Medicinal Products.

EMA, 2020. Concept Paper the Environmental Risk Assessment Framework for Companion Animals. EMA/CVMP/ERA/55512/2020." www.ema.europa.eu/contact.

EMA, 2021. "Committee for Medicinal Products for Veterinary Use European Public MRL Assessment Report (EPMAR)." www.ema.europa.eu/contact.

FEDIAF. 2020. The European Pet Food Industry. Facts and Figures 2020 European Overview. https://www.nvg-diervoeding.nl/assets/files/fediaf-facts-and-figures-2020.pdf.

Jacobs, D E, M J Hutchinson, D Stanneck, and N Mencke. 2001. Accumulation and Persistence of Flea Larvicidal Activity in the Immediate Environment of Cats Treated with Imidacloprid. Medical and Veterinary Entomology 15 (3): 342–45. https://doi.org/10.1046/j.0269-283x.2001.00320.x.

Loos, Robert, Dimitar Marinov, Isabella Sanseverino, Dorota Napierska, and Teresa Lettieri. 2018. Review of the 1st Watch List under the Water Framework Directive and Recommendations for the 2nd Watch List. Joint Research Center. https://doi.org/10.2760/614367.

Regulation (EU) 2018/783. European Commission Implementing Regulation (EU) 2018/783 of 29 May 2018 Amending Implementing Regulation (EU) No 540/2011 as Regards the Conditions of Approval of the Active Substance Imidacloprid. Official Journal of the European Union, L132:31-34.

Regulation (EU) 2020/1643. Commission Implementing Regulation (EU) 2020/1643 of 5 November 2020 Amending Implementing Regulation (EU) No 540/2011 as Regards the Approval Periods of the Active Substances Calcium Phosphide, Denathonium Benzoate, Haloxyfop-P, Imidacloprid, Pencycuron. Official Journal of the European Union, L370: 18-20.

Regulation (EU) 485/2013. Commission Implementing Regulation (EU) No 485/2013 of 24 May 2013 Amending Implementing Regulation (EU) No 540/2011, as Regards the Conditions of Approval of the Active Substances Clothianidin, Thiamethoxam and Imidacloprid, and Prohibiting the Use and Sale of Seeds Treated With Plant Protection Products Containing Those Active Substances. L139: 12-26. https://doi.org/10.2903/j.efsa.2013.3067.

Regulation (EU) 528/2012. Regulation (EU) 528/2012 of the European Parliament and of the Council of 22 May 2012 Concerning the Making Available on the Market and Use of Biocidal Products. Official Journal of the European Union, L167: 1-123.

Regulation (EC9 1107/2009. 2009. Regulation 1107/2009/EC of the European Parliament and of the Council of 21 October 2009 Concerning the Placing of Plant Protection Products on the Market and Repealing Council Directives 79/117/EEC and 91/414/EEC. Official Journal of the European Union. L 309: 1:50.

Sharlow, M. 2017. Neonicotinoids Insecticides in British Freshwaters. 2016 Water Framework Directive Watch List Monitoring Results and Recommendations Saving the Small Things That Run the Planet. https://cdn.buglife.org.uk/2019/10/QA-Neonicotinoids-in-water-in-the-UK-final-2-NI.pdf. Consulted on January 2022.

Sheets, Larry. 2001. Chapter 95 - Imidacloprid: A Neonicotinoid Insecticide. Hayes' Handbook of Pesticide Toxicology (Third Edition), Robert Krieger (Ed). Academic Press, ISBN 9780123743671.

VICH GL6, 2000. Environmental impact assessment (EIAS) for veterinary medicinal products - Phase I. CVMP/VICH/592/98-FINAL.

VICH GL38, 2005. Guideline on environmental impact assessment for veterinary medicinal products—Phase II. CVMP/VICH/790/ 03-FINAL.

Wang, Lei, Tianzhen Liu, Fang Liu, Junjie Zhang, Yinghong Wu, and Hongwen Sun. 2015. Occurrence and Profile Characteristics of the Pesticide Imidacloprid, the Preservative Parabens, and Their Metabolites in Human Urine from Rural and Urban China. Environmental Science & Technology 49. https://doi.org/10.1021/acs.est.5b04037.

Wood, Thomas James, and Dave Goulson. 2017. The Environmental Risks of Neonicotinoid Pesticides: A Review of the Evidence Post 2013. Environmental Science and Pollution Research 24 (21): 17285–325. https://doi.org/10.1007/s11356-017-9240-x.

9. ANNEX

TABLE 1 List of biocides products containing imidacloprid authorised in SPAIN (ECHA, 2021)

TRADE NAME	ACTIVE SUBSTANCE	FIELD OF USE	USER CATEGORY	TARGET ORGANISM	APPLICATION METHOD
ANTIHORMIGAS GEL | EC GEL HORMIGAS | ECOGEL HORMIGAS | TRAMPA DE HORMIGAS CARREFOUR X3 | TRAMPA HORMIGAS DIA | X GEL HORMIGAS	imidacloprid	Outdoor/ Indoor	Non-profesional	Ants	Bait application
ECOPRO HORMIGAS	imidacloprid	Outdoor/ Indoor	Non-profesional	Ants	Bait application
MAXFORCE TRAMPA HORMIGAS	imidacloprid	Outdoor/ Indoor	Profesional	Ants	Bait application
BAYTHION GEL | PROTECT HOME Anti-hormigas gel	imidacloprid	Outdoor/ Indoor	Non-profesional	Ants	Bait application
MAXFORCE QUANTUM	imidacloprid	Outdoor/ Indoor	Profesional	Ants	Bait application
ECOPRO CUCARACHAS FUSION | MAGNUM GEL NOA | MAGNUM GEL OPTIMUM	imidacloprid	Indoor	Profesional	Cockroaches	Bait application
-	S-Methoprene | imidacloprid	Outdoor/ Indoor	Both	Ants	Bait application
VICTOR GEL HORMIGAS	imidacloprid	Outdoor/ Indoor	Both	Ants	In bait boxes
MAGNUM GEL CUCARACHAS	imidacloprid	Indoor	Both	Cockroaches	Open application of a gel bait applied as a drops from a syringe

TRADE NAME	ACTIVE SUBSTANCE	FIELD OF USE	USER CATEGORY	TARGET ORGANISM	APPLICATION METHOD
EC GEL CUCARACHAS IGR | Ecogel Cucarachas IGR | X GEL IGR CUCARACHAS	S-Methoprene | imidacloprid	Indoor	Both	Cockroaches	Bait application
ABAGEL BLATTA | BIOGEL | BLATTATHOR | CIMEX IMIDAGEL | DEFENS GEL CUCARACHAS | EUROGEL CUCARACHAS | GEL CUCARACHAS PLUS | IMIDASCET ROACH TRAP | IMIDASECT | KELT GEL CUCARACHAS | LETAL GEL CUCARACHAS | MELOCAR CUCARACHAS | MKI IMIDAGEL | PREVALIEN CUCARACHAS | ROACH OVER GEL | SUPER GEL CUCARACHAS | TRX GEL CUCARACHAS | TRX TRAMPA ANTICUCARACHAS | ZUM GEL CUCARACHAS PLUS	imidacloprid	Outdoor/ Indoor	Both	Cockroaches	In bait boxes
ADVER GEL | ARTEMISA GEL | CERES GEL | GENGEL | IMIDASECT PLUS | MELOCAR PLUS | STOP CUCARACHAS | TRX GEL CUARACHAS PLUS	imidacloprid	Outdoor/ Indoor	Both	Cockroaches	In bait boxes
ANTICUCARACHAS GEL | EC GEL CUCARACHAS | ECOGEL CUCARACHAS | EFI PROTECT TRAMPA MATACUCARACHAS | TRAMPA MATACUCARACHAS CARREFOUR X6 | X GEL CUCARACHAS	imidacloprid	Indoor	Non-professional	Cockroaches	In bait boxes

TRADE NAME	ACTIVE SUBSTANCE	FIELD OF USE	USER CATEGORY	TARGET ORGANISM	APPLICATION METHOD
MAGNUM GEL CUCARACHAS IGR | Magnum Gel Cucarachas IGR PLUS	S-Methoprene | imidacloprid	Indoor	Both	Cockroaches	Bait application
AQUILES CUCARACHAS | VICTOR GEL	imidacloprid	Indoor	Both	Cockroaches	Open system
MAXFORCE PRIME	imidacloprid	Indoor	Profesional	Cockroaches	Bait application as a drops from a syringe
TRAMPA CEBO ACTIVO BOSQUE VERDE MATACUCARACHAS USO DOMÉSTICO	S-Methoprene | imidacloprid	Indoor	Non-professional	Cockroaches	Bait application
TRAMPA MATACUCARACHAS BOSQUE VERDE	imidacloprid	Indoor	Non-professional	Cockroaches	In bait boxes
MAXFORCE WHITE IC	imidacloprid	Indoor	Profesional	Cockroaches	Bait application
ECOPRO CUCARACHAS	imidacloprid	Indoor	Non-professional	Cockroaches	Manual application in bait boxes
CUCAL TRAMPA CUCARACHAS	imidacloprid | pyriproxyfen	Indoor	Non-professional	Cockroaches	In bait boxes
ABAGEL FORMICA | ANTS OVER GEL | BIOGEL ANTS | DEFENS GEL HORMIGAS | EUROGEL HORMIGAS | FORMITHOR | FRAMEX GEL HORMIGAS | GEL HORMIGAS PLUS | HORMIFIN IMIDAGEL | IMIDAGEL HORMIGAS | LETAL GEL HORMIGAS | MELOCAR HORMIGAS | PREVALIEN HORMIGAS | SUPER GEL HORMIGAS | TRX GEL HORMIGAS | ZUM GEL HORMIGAS PLUS	imidacloprid	Outdoor/ Indoor	Both	Ants	Opens system in bait boxes

TRADE NAME	ACTIVE SUBSTANCE	FIELD OF USE	USER CATEGORY	TARGET ORGANISM	APPLICATION METHOD
MAGNUM GEL HORMIGAS PLUS	imidacloprid	Outdoor/ Indoor	Both	Ants	Bait applicatin in gel with syringe in bait boxes
TRAMPA CEBO ACTIVO BOSQUE VERDE PARA HORMIGAS USO DOMÉSTICO	S-Methoprene | imidacloprid	Indoor	Non-profesional	Ants	Bait application
BAYTHION GR | PROTECT HOME CEBO ANTIHORMIGAS GRANULADO	imidacloprid	Outdoor/ Indoor	Non-profesional	Ants	Bait application
CEBO PARA HORMIGAS IMD | DX3 GEL | DX3 GEL BOX HORMIGAS | DX3 GEL HORMIGAS | EFFECT CEBO PARA HORMIGAS | KAMAZIL GEL | KAMAZIL GEL BOX HORMIGAS | KAMAZIL GEL HORMIGAS | KAPTER GEL BOX HORMIGAS | KAPTER GEL HORMIGAS | KELT GEL BOX HORMIGAS | KELT GEL HORMIGAS | SKULD GEL BOX HORMIGAS | SKULD GEL HORMIGAS	imidacloprid	Outdoor/ Indoor	Both	Ants	- | - | - | -
TRAMPA CONTRA HORMIGAS BOSQUE VERDE	imidacloprid	Outdoor/ Indoor	Non-profesional	Ants	In bait boxes
SPIRA TOC TRAMPA HORMIGAS NUEVA FORMULACION	imidacloprid	Indoor	Non-profesional	Ants	In bait boxes
IMIDAFLY | IMIFLY BAIT | KELT FLY BAIT | LETAL GR 05 | MAX FLY | Sharda Fly Bait | SOFAST | TRX MOSCAS LISTO PARA SU USO	cis-tricos-9-ene (Muscalure) | imidacloprid	Indoor	Profesional	Flies	In bait boxes

TRADE NAME	ACTIVE SUBSTANCE	FIELD OF USE	USER CATEGORY	TARGET ORGANISM	APPLICATION METHOD
QUICK BAYT WG | QUICK BAYT WG10	cis-tricos-9-ene (Muscalure) | imidacloprid	Indoor	Profesional	Flies	Manual application
GEL LETAL LZ CUCARACHAS | KAPTER FLUOGEL | PESTNET Fluogel | PREBEN GEL CUCARACHAS IMD | Protect Home Gel Anti-Cucarachas | SKULD FLUOGEL | TX3 GEL	imidacloprid	Indoor	Both	Cockroaches	Bait application in drops in bait boxes
CUCAL PROFESIONAL	imidacloprid	Indoor	Non-profesional	Cockroaches	Manual application
MAXFORCE QUANTUM PORTACEBO	imidacloprid	Outdoor/ Indoor	Both	Ants	In bait boxes
BAYTHION TRAMPA GEL | PROTECT HOME Trampa Hormigas	imidacloprid	Outdoor/ Indoor	Both	Ants	In bait boxes

TABLE 2 List of VMPs authorised in Spain containing imidacloprid (CIMA-Vet, 2021).

TRADE NAME	ACTIVE SUBSTANCE
Advantage 40 para gatos	IMIDACLOPRID
Advantix solucion spot-on para perros de mas de 25 hasta 40 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros hasta 4 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros hasta 4 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros hasta 4 kg	IMIDACLOPRID,PERMETRINA
Ataxxa 500 mg/100 mg solucion para uncion dorsal puntual para perros de mas de 4 kg hasta 10 kg	IMIDACLOPRID,PERMETRINA
Poli-ecto solucion spot-on para perros de mas de 4 hasta 10 kg	IMIDACLOPRID,PERMETRINA (40 CIS/60 TRANS)
Poli-ecto solucion spot-on para perros de mas de 25 hasta 40 kg	IMIDACLOPRID,PERMETRINA (40 CIS/60 TRANS)

TRADE NAME	ACTIVE SUBSTANCE
Poli-ecto solucion spot-on para perros de mas de 40 kg hasta 60 kg	IMIDACLOPRID,PERMETRINA (40 CIS/60 TRANS)
Poli-ecto solucion spot-on para perros de mas de 10 hasta 25 kg	IMIDACLOPRID,PERMETRINA (40 CIS/60 TRANS)
Poli-ecto solucion spot-on para perros hasta 4 kg	IMIDACLOPRID,PERMETRINA (40 CIS/60 TRANS)
Ataxxa 1250 mg/250 mg solucion para uncion dorsal puntual para perros de mas de 10 kg hasta 25 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros de mas de 10 hasta 25 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros de mas de 4 hasta 10 kg	IMIDACLOPRID,PERMETRINA
Seresto collar 1,25 g+0,56 g para perros + 8 kg	IMIDACLOPRID,FLUMETRINA
Ataxxa 2000 mg/400 mg solucion para uncion dorsal puntual para perros de mas de 25 kg	IMIDACLOPRID,PERMETRINA
Ataxxa 200 mg/40 mg solucion para uncion dorsal puntual para perros de hasta 4 kg	IMIDACLOPRID,PERMETRINA
Advantix solución spot-on para perros de mas de 40 kg hasta 60 kg	IMIDACLOPRID,PERM
Prinocate 80 mg /8 mg solucion para uncion dorsal puntual para gatos grandes	IMIDACLOPRID,MOXIDECTINA
Prinocate 40 mg /4 mg solucion para uncion dorsal puntual para gatos pequeños y hurones	IMIDACLOPRID,MOXIDECTINA
Prinocate 40 mg /10 mg solucion para uncion dorsal puntual para perros pequeños	IMIDACLOPRID,MOXIDECTINA
Advantix solucion spot-on para perros de mas de 4 hasta 10 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros de mas de 10 hasta 25 kg	IMIDACLOPRID,PERMETRINA
Advantix solucion spot-on para perros de mas de 25 hasta 40 kg	IMIDACLOPRID,PERMETRINA
Advocate 40 mg + 4 mg solucion para uncion dorsal puntual para gatos pequeños y hurones	MOXIDECTINA,IMIDACLOPRID
Seresto collar 1,25 g+0,56 g para perros ¿ 8 kg	IMIDACLOPRID,FLUMETRINA
Seresto collar 4,50 g+2,03 g para perros > 8 kg	IMIDACLOPRID,FLUMETRINA

TRADE NAME	ACTIVE SUBSTANCE
Advocate 80 mg + 8 mg solucion para uncion dorsal puntual para gatos grandes	IMIDACLOPRID,MOXIDECTINA
Advocate 40 mg + 10 mg solucion para uncion dorsal puntual para perros pequeños	MOXIDECTINA,IMIDACLOPRID
Advocate 100 mg + 25 mg solucion para uncion dorsal puntual para perros medianos	IMIDACLOPRID,MOXIDECTINA
Advocate 250 mg + 62,5 mg solucion para uncion dorsal puntual para perros grandes	MOXIDECTINA,IMIDACLOPRID
Advocate 400 mg + 100 mg solucion para uncion dorsal puntual para perros muy grandes	MOXIDECTINA,IMIDACLOPRID
Prinocate 100 mg /25 mg solucion para uncion dorsal puntual para perros medianos	IMIDACLOPRID,MOXIDECTINA
Prinocate 250 mg /62,5 mg solucion para uncion dorsal puntual para perros grandes	IMIDACLOPRID,MOXIDECTINA
Prinocate 400 mg /100 mg solucion para uncion dorsal puntual para perros muy grandes	IMIDACLOPRID,MOXIDECTINA
Advantage 40 para perros	IMIDACLOPRID
Advantage 100 para perros	IMIDACLOPRID
Advantage 250 para perros	IMIDACLOPRID
Prinovox 250 mg + 62,5 mg solucion para uncion dorsal puntual para perros grandes	IMIDACLOPRID,MOXIDECTINA
Prinovox 400 mg + 100 mg solucion para uncion dorsal puntual para perros muy grandes	IMIDACLOPRID,MOXIDECTINA
Prinovox 40 mg + 10 mg solucion para uncion dorsal puntual para perros pequeños	IMIDACLOPRID,MOXIDECTINA
Prinovox 40 mg + 4 mg solucion para uncion dorsal puntual para gatos pequeños y hurones	IMIDACLOPRID,MOXIDECTINA
Prinovox 80 mg + 8 mg solucion para uncion dorsal puntual para gatos grandes	IMIDACLOPRID,MOXIDECTINA
Prinovox 100 mg + 25 mg solucion para uncion dorsal puntual para perros medianos	IMIDACLOPRID,MOXIDECTINA
Seresto collar 1,25 g+0,56 g para perros ¿ 8 kg y gatos	IMIDACLOPRID,FLUMETRINA
Seresto collar 4,50 g+2,03 g para perros > 8 kg	IMIDACLOPRID,FLUMETRINA

TRADE NAME	ACTIVE SUBSTANCE
Advantage 400 para perros	IMIDACLOPRID
Advantage 80 para gatos	IMIDACLOPRID
Seresto collar 1,25 g+0,56 g para gatos	IMIDACLOPRID,FLUMETRINA