

SUPPORTING INFORMATION FOR

RETROSPECTIVE SCREENING OF HIGH RESOLUTION MASS

SPECTROMETRY ARCHIVED DIGITAL SAMPLES CAN IMPROVE

ENVIRONMENTAL RISK ASSESSMENT OF EMERGING CONTAMINANTS: A

CASE STUDY ON ANTIFUNGAL AZOLES

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Section 1. Sampling sites

Table S1. List of sampling sites and additional information related to land use and sampling campaigns

Site	Matrices* (number of samples)	Main land use	Year	Sampling period	New samples
Aadorf	FW (7), Effluent (3), Gamm. (4)	Urban	2014-2015	Various	
Aesch	GW (1)	Woods	2017	May	
Ag	FW (9)	Arable	2012	Various	
Aphtal	Soil (1)	Arable	2005	June	
Heimberg	Soil (1)	Mix	2017	Various	
Avusy	GW (1)	Arable	2017	May	
Baar	GW (1)	Woods	2017	May	
Basel	Sed (2)	Mix	2017	June, Sept	✓
MoosKanal	FW (1)	Arable	2015	Various	
Binningen	Soil (1)	Woods	2005	June	
Birmensdorf	FW (7), Effluent (3), GW (1)	Woods	2014 or 2017	Various	
Birs	GW (1)	Meadows	2013	Dec	
Weierbach	FW (64)	Arable	2015	Various	
Buttisholz	FW (6), Biof (6), Eff (2), sed (4)	Arable	2014-2016	Various	✓
Bützelgraben	Sed (2)	Meadows	2016	Nov	✓
Cheseaux	GW (1)	Arable	2017	Mai	
Colombier	FW (2)	Mix	2014	Feb	
Corcells	GW (1)	Meadows	2014	May	
Daillens	GW (1)	Arable	2017	May	
Disentis	Soils (1)	Unproduct.	2005	June	✓
Duernten	FW (1)	Meadows	2014	Feb	
Durton	FW (2)	Urban	2014	Heb	
Egliswill	GW (1)	Mix	2017	May	
Elgg	Eff (3), FW (11), Gamm (4)	Urban	2014, 2015, 2017	Jan	
Emmen	GW (1)	Urban	2017	Mai	
Epende	Soil (1)	Arable	1994	June	
Ergolz	GW (1)	Woods	2013	Dec	
Faellen	Eff (1)	Urban	2014	May	
Fischbach	GW (1)	Arable	2017	May	
Frauenfeld	GW (1)	Arable	2017	May	
Frenke	GW (1)	Mix	2013	Dec	
Fribourg	Sed (2)	Meadows	2017	June, Sept	✓
Glattfelden	GW (1)	Mix	2017	May	
Goldach	FW (2)	Unproduct.	2014	Jul	
Goldingen	GW (1)	Meadows	2017	Mai	
Greiffensee	Sed (14)	Mix	2015, 2016	Feb	✓
Härkingen	Soil (1)	Arable	2005	June	
Herisau	Eff (4), FW (18), Biof (8), Gamm (4), Fish (16)	Mix	2014, 2015, 2016	Various	
Hochdorf	Eff (2), FW (7), Sed(2), Biof (8)	Mix	2014, 2016	Various	✓
Hornmussen	FW (2)	Woods	2014	Feb	
Hünenberg	GW (1)	Arable	2017	May	
Jona	Sed (2)	Unproduct.	2016	Setp	✓
Jussy	Soil (1)	Arable	2005	June	
Kloten	GW (1)	Mix	2017	May	

Knonau	Eff (3), FW (7), Gamm (4)	Woods	2014, 2015	Jan	
Kuzacker	Soil (1)	Mix	2017	Various	✓
Lake Geneva	Sed (8)	Mix	2015, 2017	Mai, October	✓
Lange	Sed (2)	Mix	2016	Sept	✓
Lavigny	GW (1)	Arable	2017	May	
Löhningen	GW (1)	Woods	2017	May	
Lugano	Soil (1)	Woods	2005	June	✓
Marthalen	Eff (3), FW (7), Gamm (4)	Arable	2014, 2015	Jan	
Method	GW (1)	Arable	2017	May	
Messen	FW (2)	Woods	2014	Feb	
Montmagny	GW (1)	Arable	2017	Feb	
Muri	Eff (3), FW (7)	Arable	2014	May	
Murten	GW (1)	Arable	2017	May	
Neerach	GW (1)	Arable	2017	May	
Niederdorf	FW (2)	Arable	2014	Feb	
Niederönz	GW (1)	Arable	2017	May	
Novaggio	Soil (1)	Woods	2005	June	
Ollon	GW (1)	Woods	2017	May	
Panoram	Soil (1)	Mix	2017	Various	
Rapperswil	GW (1)	Arable	2017	May	
Reinach	Eff, FW	Urban	2014	July	
Reichenburg	Sed (2)	Woods	2016	Oct	✓
Rifferwil	Soil (1)	Mix	2005	Oct	
Romont	FW (2)	Woods	2014	Feb	
Rothenturm	FW (2)	Woods	2014	Feb	
Saint-Ursanne	Sed (4)	Woods	2016	Sept	✓
Schaffhausen	Sed (2)	Unproduct	2017	June	✓
Seuzach	GW (1)	Arable	2017	May	
Sevarey	Eff (3), FW (7)	Woods	2014	March	
So	FW (8)	Arable	2012	April	
Stans	GW (1)	Meadows	2017	May	
Steinach	Eff (1), FW (5), Biof (2), Fish (33)	Unproduct	2014, 2015	Various	✓
Tegerfelden	GW (1)	Woods	2017	May	
Eschelisbach	FW (19)	Arable	2012	Various	
Thurgau	Sed (2)	Arable	2017	June	✓
Canal di piano	FW (42)	Arable	2015	Various	
Trüllikon	GW (1)	Arable	2017	May	
Unterhrendingen	Eff (3), FW (7), Gamm (4)	Mix	2014, 2015	Various	
Val de ruz	Eff (2), FW (4), Gamm (4)	Arable	2014, 2015	Various	
Vd	FW (6)	Arable	2012	Various	
Venoge	Sed (3)	Mix	2014	Oct	✓
Villeret	Eff (3), FW (7), gamm (4)	Meadows	2014, 2015	Sept	
Tsatonire	FW (44)	Arable	2015	April	
Wald	Soil (1)	Arable	2005	June	
Wäldi	GW (1)	Arable	2017	May	
Winterthur	Soil (1)	Mix	2005	June	
Zermec	Soil (1)	Reference	2005	June	
Zh	FW (8)	Mix	2012	April	
Zufikon	GW (1)	Mixl	2017	May	
Zulwill	Eff (3), FW (6), Gamm (4)	Woods	2015	Jan	
Zürich	Soil (1)	Mix	2005	Sept	

*FW, surface water; GW, Groundwater; Eff, Wastewater effluent; Sed, sediment; Biof, biofilms; n.d., not defined. Unproduct., unproductive area. Check marks indicate biofilms and sediment samples newly investigated in the present study.

Section 2. Sample preparation and chemical analyses

Surface waters, effluents, groundwaters, gammarids, soils and fish were previously extracted and analyzed in Spycher et al. 2018 [1], Munz et al. 2017 [2], Hollender et al. 2018 [3], Kiefer et al. 2019 [4], Munz et al. 2018 [5], Chiaia-Hernandez et al. 2017 [6], and Fischer et al (in prep), respectively. Here the methods used for the extraction and the analysis in the respective studies are described whereas extraction and analysis of sediments and biofilms were performed in this study.

Archive of fresh surface waters and effluents

Surface water and effluents samples were analysed using online solid phase extraction liquid chromatography coupled to LC-Q-Exactive-HRMS system as described in [2]. Briefly, all samples were filtered (GF/F, 0.7 µm, 47 mm, Whatman, UK) and spiked with internal standards prior to enrichment. Then, 20 mL of filtrated surface water or 20 mL of 4 times diluted filtered effluents were loaded on a self-prepared multilayered cartridge filled with 9 mg of Oasis HLB and 9 mg of a mixture of Strata XAW, Strata XCW and isolate ENV+. The cartridge was eluted with methanol supplemented with 0.1 of formic acid (FA) while the chromatographic separation was performed on an Atlantis T3 column (5µm, 3 x 150 mm) using a mixture of nanopure water and methanol supplemented with 0.1% of FA through the following gradient: 85:15 (A:B) at 0 to 5 min, to 5:95 at 20 min, then held until 29 min, and back to 85:15 from 29.5 to 35 min, at a flow rate of 300 µl/min and a column temperature of 30 °C.

The detection was performed on a Q-Exactive-hybrid mass detector equipped with an ESI source operated in positive ionization (+4 kV). For the low flow condition samples, full scan acquisition was performed for a m/z range 100-1000 at a resolution of 70'000 (at m/z 200) followed by data independent MS/MS acquisition (DIA) in 5 isolation windows at a resolution of 17'500 (at m/z 200) with stepped normalized collision energies (m/z isolation windows (mean collision energy): 95 – 180 (100), 170 – 255 (70), 245 – 330 (40) as described in [2]. For small streams in high flow condition, the detection was completed in full scans with a mass resolution (R) of 140'000 (at m/z 200) and data-dependent MS/MS (R = 17 500, Top 5) with separate runs for positive and negative electrospray ionization as described in [1].

Archive of groundwater samples

Groundwater samples were from two studies [3, 4]. Groundwaters from 2013 were filtered through a glass microfiber filter (GF/F, 47mm, 0.7 µm) before the SPE extraction. This was then followed by injection to LC-HRMS/MS system as described in [3]. The analytes were separated using a reversed phase column (XBridge™ C18 column, 3.5 um, 2.1 × 50 mm, Waters) coupled with a pre-column (3.5 um, 2.1 × 10 mm, same material). The mobile phase consisted of water and methanol both acidified with formic acid (0.1%) and a gradient from 10 to 95% methanol was applied. The injection volume was 20 mL, and the mobile phase flow was 0.2 m/min. Detection was performed using Q-Exactive™ hyrid quadrupole-Orbitrap mass spectrometer with an ESI probe performed in two separate runs for the positive and negative ionization modes each. Full scan accurate mass spectra were acquired from 100 to 1000 m/z with a nominal resolving power of 70'000 referenced at m/z 200. The automated gain control (AGC) was set to 500'000 and the maximal injection time was 200 ms with a mass accuracy of ±5 ppm. Data-independent high-resolution product ion spectra (HR-MS/MS) were recorded at a resolving power of 17'500 at m/z 200, AGC set to 200'000 and maximal injection time to 100 ms.

Groundwaters from May 2017 were enriched with Büchi as described in [4]. A volume of 100 mL, corresponding to 15 mL of the original water sample was then injected on a reverse phase C18 column (Atlantis® T3 3 um, 3.0 x 150 mm; Waters, Ireland). The gradient started with

100% eluent A (water þ 0.1% concentrated formic acid). Then eluent B (methanol þ 0.1% concentrated formic acid) was increased from 1.5 to 18.5 min to 95%, held for 10 min, and lowered again to the starting conditions. The column was re-equilibrated for 4 min. The flow rate was 0.3 mL/min. As described in [4], the detection consisted with electrospray ionization with (spray voltage 4/-3 kV) and an MS1 full-scan (m/z 100e1000, mass resolution 140 000 at m/z 200) followed by five data-dependent fragmentation experiments (mass resolution 17 500 at m/z 200) using higher energy collision-induced dissociation (HCD). MS/MS acquisition was triggered by the m/z of the target ions with normalised collision energies (NCE) 15e120 depending on the m/z . Isolation window was 1 Da. If no target ion was detected, the most intense ions in the MS1 were fragmented at NCE 15, 60, and 105.

Archive of soils and new sediment samples

Freeze-dried soils and sediment were extracted and purified using pressurized liquid extraction based on the method of Chiaia-Hernandez et al. 2017 dedicated to the analysis of semi-polar to polar pesticides. Briefly, 4 g of dry weight sediment were spiked with internal standards, mixed with 0.5 g of hydromatrix and put into 10 mL stainless steel accelerated solvent extraction (ASE) cells filled with a 27-mm glass fiber filter, a 16.2-mm cellulose filter (Dionex, Olten, Switzerland), ~1 g of activated Florisil (60/100 mesh, Supelco, Bellefonte, USA), and an additional cellulose filter. Extraction and in-cell purification were performed on an ASE-350 system through two 5 min static cycles at 80°C, a rinsing volume of 60% followed by 100 s of purging with nitrogen using a mixture of ethyl-acetate/acetone (70:30; v:v). The extracts were evaporated to approximately 1 mL at a temperature of 45°C with an automated evaporator system (Syncore® Polyvap from Büchi, Flawil, Switzerland). Additional evaporation to almost dryness was performed under N₂ at 40°C (Turbovap, Biotage). Final extracts were reconstituted in 1.5 mL of methanol and stored at -20°C prior analysis.

Analysis of the compounds was performed on a LC-HRMS systems, as reported in Chiaia-Hernandez et al. 2017. Briefly, chromatographic separation was based on X-Brigde C18 column (3.5 μ m, 2.1 \times 50 mm, Waters) equipped with a 2.1 \times 10 mm C18 security guard cartridge at 35 °C at a flow rate of 200 μ L/min using the following gradient (Table S2).

Table S2. Elution gradient used for the analysis of sediment, soil and biofilms samples

Time (min)	Flow Rate (mL/min)	A (%)	B (%)	C (%)
0.00	0.20	95	5	0
0.02	0.32	95	5	0
0.50	0.20	95	5	0
1.00	0.20	90	10	0
4.00	0.20	50	50	0
18.00	0.20	0	0	100
30.00	0.20	95	5	0
30.01	0.20	95	5	0
38.00	0.20	95	5	0

A nanopure water with 0.1% formic acid; *B* methanol with 0.1% formic acid; *C* 100% isopropanol

The detection was based on Q-Exactive-hybrid mass detector equipped with an ESI source. Data used for the retrospective analysis were acquired with positive electrospray ionization in data independent acquisition (DIA) mode whereas new samples were acquired in both DIA and data dependent acquisition (DDA) modes. DIA consisted in a full-scan with a mass to charge (m/z) range of 100-800 with a resolution of 140,000 followed by MS2 acquisition on nine different mass ranges (mass range = inclusion window \pm isolation window) with a

resolution of 17,500, corresponding high-energy collisional dissociation (HCD) energies and scan windows (mass range over which the MS2 spectrum were recorded). The 9 isolation windows with specific HCD were : 95-155 m/z (100), 150-190 m/z (90), 185-225 m/z (80), 220-260 m/z (60), 255-295 m/z (50), 290-330 m/z (30), 325-365 m/z (20), 360-400 (15) m/z and 395-1005 m/z (15). DDA measurements where completed in full-scan mode (100-800 m/z), followed by MS2 acquisition based on an inclusion list based on the analysis of the DIA measurement. Additionally, the 5 most intense peaks were also acquired.

For the generation of product ions by higher energy collision dissociation (HCD), the normalized collision energies were set to 95%, 100% and 105%. The electrospray, source fragmentation and capillary voltage were set to 5 kV, 15 V and 25 V in positive ion mode. The capillary temperature and tube lens were set at 300°C and 60 V in positive mode. The sheath and auxiliary gas flow were set at 50 and 20 arbitrary units, respectively.

Biota samples: Archive of fish and gammarids , new biofilm samples

Biota have been extracted as described in Munz et al. 2018 [5] with some modification for the biofilms. Briefly, 500 mg of wet gammarids or fish muscle were transferred into 2 mL microcentrifuge tubes and spiked with 80 µL internal standard mixture (1 mg/L) and was stored overnight at 4°C. Then, 500 mg of 1 mm zirconia/silica beads (Biospec Products, Inc., U.S.A.), 500 µL of acetonitrile (ACN) and 500 µL of water were added. Homogenization was performed using a Fast Prep bead beater (MP Biomedicals, Switzerland) through two cycles of 15s at 6 m/s with cooling in ice between. Samples were centrifuged for 6 min at 10 000 rpm at 20 °C. Then, 800 µL of the supernatant were transferred to 2 mL microcentrifuge tubes containing 300 mg of QuEChERS salts (4:1, MgSO₄:NaCl, Agilent Technologies), quickly vortexed and centrifuged (6 min, 10000 rpm, 20°C). The supernatant was transferred in a new 2 mL tube. The whole procedure was repeated by adding 500 µL of ACN to the first homogenate. A last clean-up was performed to remove the lipids by adding 500 µL of heptane to the final vial containing approximately 800 µL of ACN. After vortexing and centrifugation, almost 400 µL of heptane was transferred in a glass vial. This clean-up was performed two times leading to two vials, one containing 800 µL of heptane and one containing 800 µL of ACN. For the gammarids and fish extract, ACN vials were filled with methanol to a final volume of 2 mL prior to storage and online injection. 200 µL of the extracts were added to 20 mL of nanopure water in online vials. Chromatographic separation and HRMS based detection was performed as described above for the surface water and the effluents (i.e. DIA acquisition with 5 isolation windows).

For the biofilms, 100 mg of freeze-dried samples was used for the extraction performed as described above. However, they were analyzed in the same way as the sediments (i.e. 50 µL offline injection). Here, the ACN fraction was exchanged to a mixture of methanol/nanopure water.

Data analysis under Compound Discoverer (CD) 2.1 software

HRMS raw data were first analyzed under CD2.1 by using both “Expected Compounds” and “Unknown Compounds” workflows (WFs) ([Figure S3](#)).

In the “expected” WF, we screened for both parents and predicted biotransformation products based on known biotransformation reactions. Here, we defined a list of 61 antifungal azoles ([Table S3](#)) including the exact mass, the formula and the structure based on Chemspider® database. In particular, we set dealkylation and dearylation reaction as true while we allowed maximal three transformation reactions in series. In these transformation reactions, in addition to usual phase I and phase II reactions, we have added transformation pathways identified by Rösch et al. in gammarids [7] ([Figure S2](#)). In the “unknown” WF, we based the identification on search mass lists including a list of parental antifungal azoles and their known

transformations products from the literature (e.g. PPDB, Envipath PPS), listed on [Tables S3](#) and [S4](#) respectively. The workflow parameters are detailed in [Figure S3](#).

Name	Leaving Group	Arriving Group	Leaving Modification	Arriving Modification	ΔM [Da]	Phase	Max Occurrence
Aa	Aa	Aa	Aa	Aa	=	Aa	=
Loss of dioxolane	C5 H8 O		C5 H8 O		-84.05751	Other	1
Loss of dioxolane + further oxidation	C5 H10 O		C5 H10 O		-86.07316	Other	1
Phosphate conjugation		H O3 P		H O3 P	79.96633	Other	1
Imidazole ring oxidation		H2 O2		H2 O2	34.00548	Other	1
Loss of imidazole ring and CO	C4 H2 N2 O		C4 H2 N2 O		-94.01671	Other	1
Partial loss of hydroxylated imidazole	C2 H N	O	C2 H N	O	-23.01598	Other	1
Imidazole ring loss + aliphatic hydro + further oxy	C3 H4 N2	O	C3 H4 N2	O	-52.04253	Other	1
Partial loss of imidazole ring	C3 H N		C3 H N		-51.01090	Other	1
loss of imidazole ring + CO hydroxy	C4 H2 N2 O	O	C4 H2 N2		-78.02180	Other	1
loss of imidazole ring + cysteine product	C3 H2 N2	C3 H5 N O2 S	N	H3 O2 S	52.98230	Other	1
Remaining chlorophenyl moiety and C2H5NO	C7 H8 N2 O		C7 H8 N2 O		-136.06366	Other	1
Acetylation at CO-imid ring NH4+ adduct		C2 H2 O		C2 H2 O	42.01056	Other	1
Arom hydro + glucose and sulf conjugaison		C6 H10 O9 S		C6 H10 O9 S	258.00455	Other	1
Loss of imidazole ring	C3 H2 N2		C3 H2 N2		-66.02180	Other	1
Loss of propyl side chain	C3 H6		C3 H6		-42.04695	Other	1

Figure S1. List of transformation reactions added in the suspect workflow (WF) (from CD2.1).

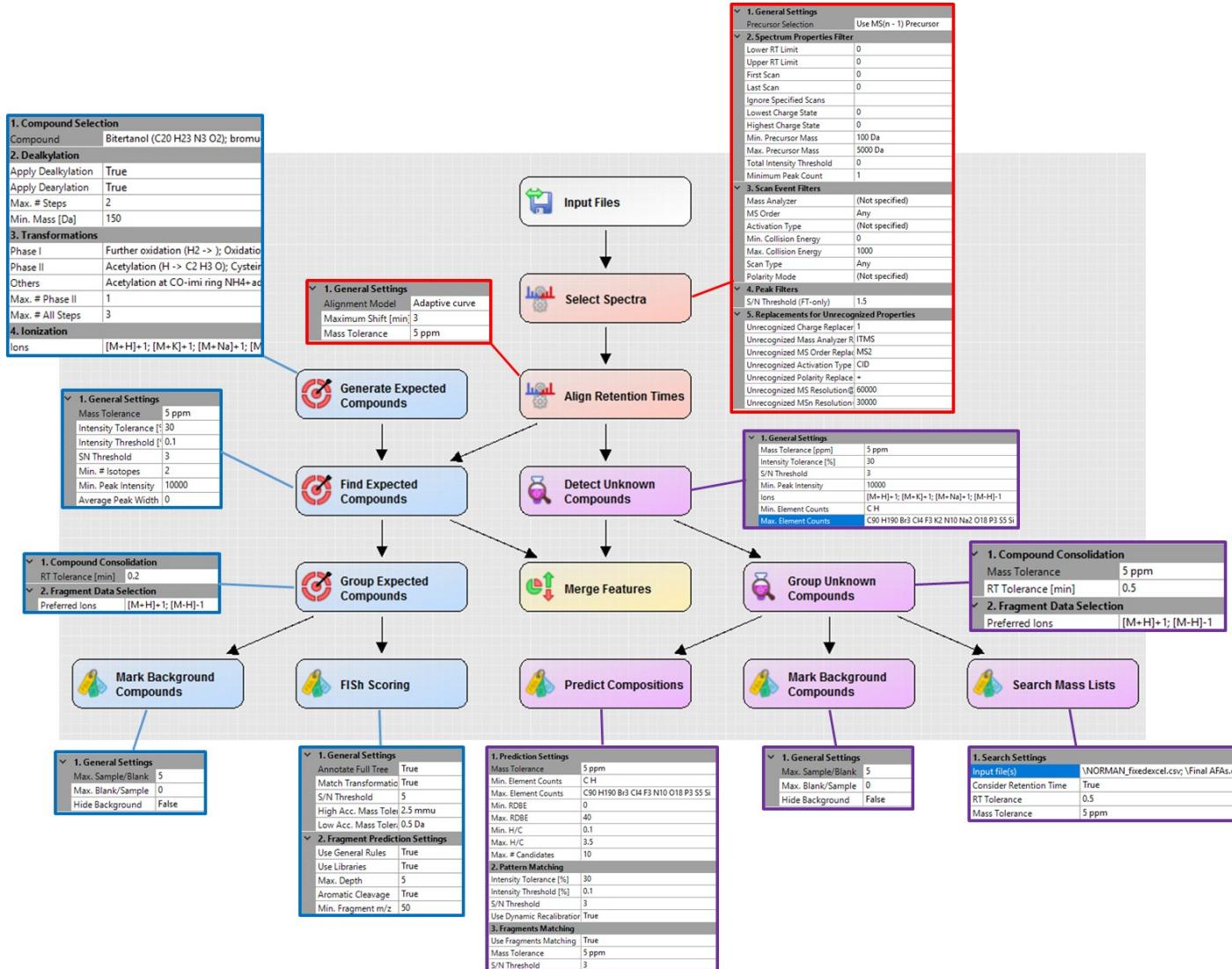


Figure S2. Compound Discoverer 2.1™ workflow used for the analysis of antifungal azoles.

Table S3. Suspect Mass List of antifungal azoles used in Compound Discoverer (CD) 2.1 software.

	Compounds	Chemical Classes	CAS	Chemical Formula	Molecular Weight	Monoisotopic Mass ^a
Pesticides	Azaconazole	Triazole	60207-31-0	C12H11Cl2N3O2	300.14	299.022827
	Bitertanol	Triazole	55179-31-2	C20H23O2N3	337.42	337.179027
	Bromuconazole	Triazole	116255-48-2	C13H12BrCl2N3O	377.07	374.954071
	Cyproconazole	Triazole	94361-06-5	C15H18CIN3O	291.78	291.113831
	Difenoconazole	Triazole	119446-68-3	C19H17Cl2N3O3	406.26	405.064697
	Diniconazole	Triazole	83657-24-3	C15H17Cl2N3O	326.22	325.07486
	Epoxiconazole	Triazole	133855-98-8	C17H13ClFN3O	329.76	329.07312
	Etaconazole	Triazole	60207-93-4	C14H15Cl2N3O2	328.19	327.054138
	Fenamidone	Triazole	161326-34-7	C17H17N3OS	311.40	311.1092329
	Fenbuconazole	Triazole	114369-43-6	C19H17CIN4	336.82	336.114166
	Fluquinconazole	Triazole	136426-54-5	C16H8Cl2FN5O	376.17	375.009003
	Flusilazole	Triazole	85509-19-9	C16H15F2N3Si	315.39	315.100342
	Flutriafol	Triazole	76674-21-0	C16H13F2N3O	301.29	301.102661
	Fuberidazole	Triazole	3878-19-1	C11H8N2O	184.19	184.0636629
	Furconazole	Triazole	112839-33-5	C15H14Cl2F3N3O2	396.19	395.041504
	Hexaconazole	Triazole	79983-71-4	C14H17Cl2N3O	314.21	313.07486
	Imazalil	imidazole	35554-44-0	C14H14Cl2N2O	297.18	296.048309
	Imibenconazole	Triazole	86598-92-7	C17H13Cl3N4S	411.73	409.992645
	Ipconazole	Triazole	125225-28-7	C18H24ClN3O	333.86	333.160797
	Ipfentrifluconazole	Triazole	1417782-08-1	C19H17ClF3N3O2	411.81	425.111786
	Mefentrifluconazole	Triazole	1417782-03-6	C18H15ClF3N3O2	397.78	397.080475
	Metconazole	Triazole	125116-23-6	C17H22ClN3O	319.83	319.145142
	Myclobutanil	triazole	88671-89-0	C15H17CIN4	288.78	288.114166
	Oxoconazole	imidazole	134074-64-9	C19H24ClN3O2	361.87	361.155701
	Paclobutrazol	Triazole	76738-62-0	C15H20ClN3O	293.79	293.12949
	Penconazole	Triazole	66246-88-6	C15H15Cl2N3	284.19	283.064301
	Prochloraz	imidazole	67747-09-5	C15H16Cl3N3O2	376.67	375.030823
	Propiconazole	Triazole	60207-90-1	C15H17Cl2N3O2	342.22	341.069794
	Prothioconazole	Triazole	178928-70-6	C14H15Cl2N3OS	344.26	343.031281
	Quinconazole	Triazole	103970-75-8	C16H9Cl2N5O	358.18	357.018402
	Simeconazole	Triazole	149508-90-7	C14H20FN3OSi	293.42	293.135956
	Tebuconazole	Triazole	107534-96-3	C16H22ClN3O	307.82	307.145142
	Tetraconazole	Triazole	112281-77-3	C13H11Cl2F4N3O	372.15	371.021515
	Triadimefon	Triazole	43121-43-3	C14H16ClN3O2	293.75	293.093109
	Triadimenol	Triazole	55219-65-3	C14H18ClN3O2	295.77	295.108765
	Triflumizole	imidazole	99387-89-0	C15H15ClF3N3O	345.75	345.085571
	Triticonazole	Triazole	131983-72-7	C17H20ClN3O	317.81	317.129486
	Uniconazole	triazole	83657-22-1	C15H18ClN3O	291.78	291.113831
Pharmaceuticals	ALBACONAZOLE	Triazole	187949-02-6	C20H16ClF2N5O2	431.83	431.096069
	BIFONAZOLE	imidazole	60628-96-8	C22H18N2	310.40	310.147003
	BUTOCONAZOLE	imidazole	64872-77-1	C19H17Cl3N2S	411.77	410.017792
	CLIMBAZOLE	imidazole	38083-17-9	C15H17ClN2O2	292.76	292.09787
	CLOTRIMAZOLE	imidazole	23593-75-1	C22H17CIN2	344.84	344.108032
	ECONAZOLE	imidazole	27220-47-9	C18H15Cl3N2O	381.68	380.024994
	EFINAConazole	Triazole	164650-44-6	C18H22F2N4O	348.40	348.176178
	FENTICONAZOLE	imidazole	72479-26-6	C24H20Cl2N2OS	455.40	454.067352
	FLUConazole	triazole	86386-73-4	C13H12F2N6O	306.27	306.104065
	ISOCONAZOLE	imidazole	27523-40-6	C18H14Cl4N2O	416.12	413.986023
	ITRAConazole	imidazole	84625-61-6	C35H38Cl2N8O4	705.64	704.239319
	KETOCONAZOLE	imidazole	65277-42-1	C26H28Cl2N4O4	531.43	530.148743
	LULICONAZOLE	imidazole	187164-19-8	C14H9Cl2N3S2	354.27	352.961487
	MICONAZOLE	imidazole	22916-47-8	C18H14Cl4N2O	416.12	413.986023
	OMOCOMAZOLE	imidazole	74512-12-2	C20H17Cl3N2O2	423.72	422.036
	OXICONAZOLE	imidazole	64211-45-6	C18H13Cl4N3O	429.12	426.981262
	POSAConazole	Triazole	171228-49-2	C37H42F2N8O4	700.79	700.329712
	RAVUCONAZOLE	Triazole	182760-06-1	C22H17F2N5OS	437.47	437.112183
	SERTACONAZOLE	imidazole	99592-32-2	C20H15Cl3N2OS	437.76	435.99707
	SULCONAZOLE	imidazole	61318-90-9	C18H15Cl3N2S	397.74	396.002167
	TIOCONAZOLE	imidazole	65899-73-2	C16H13Cl3N2OS	387.70	385.981415
	VORICONAZOLE	Triazole	131983-72-7	C17H20ClN3O	317.81	349.115051

^a, from Envipat website (<https://www.envipat.eawag.ch/index.php>)

Table S4. Suspect mass list of antifungal fungal transformation products (TPs) used under Compound Discoverer (CD) 2.1.

Parents	Name Compound	Chemical Formula	Mono-isotopic Mass ^a
Bromuconazole	LS 860551	C13H13Cl2N3O2	309.0516
	LS802050	C10H7Cl2N3O	254.9966
	LS860976	C14H15Cl2N3O2	327.0541
	LS861590	C13H11Cl2N3O2	311.0228
	LS-870353	C13H11Cl2N3O2	311.0228
	MWt 257	C10H9Cl2N3O	257.0123
	RPA 401527	C13H9Cl2N3O2	309.0072
Cyproconazole	1,2,4 triazole	C2H3N3	69.0327
	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
	CP_M308a	C15H18CIN3O2	307.1088
	CP_M308b	C15H18CIN3O2	307.1088
	CP_M308c	C15H18CIN3O2	307.1088
	Hydroxy-Triazole	C2H3N3O	85.02761
	1,2,4 triazole	C2H3N3	69.0327
Difenoconazole	CGA 189138	C13H8Cl2O3	281.985
	CGA 205374	C16H11Cl2N3O2	347.0228
	CGA 205375	C16H13Cl2N3O2	349.0385
	1-[2-chloro-4-(4-chlorophenoxy) phenyl]-2-(1H-1,2,4-triazol-1-yl)ethanol	C16H13Cl2N3O2	349.0385
	1-[2-chloro-4-(4-chlorophenoxy) phenyl]-2-(1H-1,2,4-triazol-1-yl)ethanone	C14H10Cl2O2	280.0058
	1,2,4 triazole	C2H3N3	69.0327
	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
Epoxiconazole	BF 480 alcohol	C17H15CIFN3O	331.0888
	BF 480 entriazol	C17H13CIFN3	313.0782
	BF 480-11	C17H15CIFN3O2	347.0837
	EP_637	C27H30CIFN6O7S	636.1569
	EP_M346	C17H13CIFN3O2	345.068
	EP_M424	C17H13CIFN3O5S	425.0248
	EP_M449	C20H18CIFN4O3S	448.0772
	EP_M451	C20H20CIFN4O3S	450.0929
	EP_M467	C20H20CIFN4O4S	466.0878
	Hydroxy-Triazole	C2H3N3O	85.02761
	Triazole alanine	C5H8N4O2	156.0647
	1,2 dihydro-triazolone	C2H3N3O	85.02761
Fenbuconazole	1,2,4 triazole	C2H3N3	69.0327
	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
	Hydroxy Fenbuconazole	C19H17CIN4O	352.1091
	Hydroxy-Triazole	C2H3N3O	85.02761
	RH-6467 4-(4-chlorophenyl)-2-(methyl-1H-1,2,4-triazole)-4-oxo-2-phenyl butane nitrile	C19H15CIN4O	350.0934
	RH-6468 "iminolactone"	C19H17CIN4O	352.1091
	RH-9129 cis-5-(4-chlorophenyl) dihydro-3-phenyl-3-(1H-1,2,3-triazol-1-yl)methyl-2(3H)-furanone	C19H16CIN3O2	353.0931
	Triazole alanine	C5H8N4O2	156.0647
	1,2 dihydro-triazolone	C2H3N3O	85.02761
	1,2,4 triazole	C2H3N3	69.0327
Fluquinconazole	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382

	Dione	C14H7Cl2FN2O2	323.9869
	SN 617406	C15H9Cl2FN2O2	338.0025
	Triazole alanine	C5H8N4O2	156.0647
Fuberidazole	M01 2-Carboxybenzimidazole	C8H6N2O2	162.0429
	M11 2-Acetylbenzimidazole	C9H8N2O	160.0637
Imazalil	R014821	C11H10Cl2N2O	256.017
Ketoconazole	KET_M565	C26H30Cl2N4O6	564.1542
Metconazole	CL 382389	C17H20CIN3O2	333.1244
Myclobutanil	butyric acid	C13H11CIN4O2	290.0571
	butyric diacid	C13H12CIN3O4	313.0385
	1,2,4 triazole	C2H3N3	69.0327
Penconazole	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
	CGA 179944	C11H9Cl2N3O2	285.0072
	BTS 44 595	C12H15Cl3N2O2	324.0199
	BTS 44 596	C13H15Cl3N2O3	352.0148
	BTS 45 186	C6H3Cl3O	195.9249
	Imidazole	C3H4N2	68.03745
	N-propyl-N-(2-(2,4,6-trichlorophenoxy)ethyl)-urea	C12H15Cl3N2O2	324.0199
	N-propyl-N-2-(2,4,6-trichlorophenoxy)-ethylamine	C11H14CL3NO	281.0141
	PRZ_M239	C8H8Cl3NO	238.9671
	PRZ_M282	C11H14Cl3NO	281.0141
	PRZ_M298	C11H14Cl3NO2	297.009
	PRZ_M310	C12H14Cl3NO2	309.009
Prochloraz	PRZ_M323a	C12H12Cl3NO3	322.9883
	PRZ_M323b	C12H12Cl3NO3	322.9883
	PRZ_M325	C12H15Cl3N2O2	324.0199
	PRZ_M353	C13H15Cl3N2O3	352.0148
	PRZ_M382	C14H18Cl3N3O3	381.0414
	PRZ_M392a	C15H16Cl3N3O3	391.0257
	PRZ_M392b	C15H16Cl3N3O3	391.0257
	PRZ_M429	C15H19Cl3N2O4S	428.0131
	PRZ_M469	C15H16Cl3N3O6S	470.9825
	PRZ_M477	C18H22Cl2N4O5S	476.0688
	PRZ_M573	C19H23Cl3N4O8S	572.0302
	PRZ_M632a	C21H26Cl3N3O11S	633.0354
	PRZ_M632b	C21H26Cl3N3O11S	633.0354
	PRP_M256	C10H7Cl2N3O	254.9966
	PRP_M258	C10H9Cl2N3O	257.0123
	PRP_M358a	C15H17Cl2N3O3	357.0647
	PRP_M358b	C15H17Cl2N3O3	357.0647
Propiconazole	1,2,4 triazole	C2H3N3	69.0327
	M01 prothioconazole-s-methyl	C15H17Cl2N3OS	357.0469
	M02 2-chlorobenzoic acid	C7H5ClO2	155.9978
	M02 prothioconazole-sulfonic acid	C14H15Cl2N3O4S	391.016
	M03 prothioconazole-trizolinone	C14H15Cl2N3O2	327.0541
	M04 prothioconazole-desthio	C14H15Cl2N3O	311.0592
	M14 prothioconazole-3-hydroxy-desthio	C14H15Cl2N3O2	327.0541
	M17 prothioconazole-6-hydroxy-desthio	C14H15Cl2N3O2	327.0541
Tebuconazole	1,2,4 triazole	C2H3N3	69.0327
	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
	HWG 1608-4-hydroxy (M05)	C16H22CIN3O2	323.1401
	HWG 1608-5-enol (M08)	C16H20CIN3O2	321.1244

	HWG 1608-5-keto (M09)	C16H20CIN3O2	321.1244
	HWG 1608-desbutyl (M15)	C12H14CIN3O	251.0825
	HWG 1608-ketodesbutyl (M16)	C12H12CIN3O	249.0669
	HWG 1608-lactone (M17)	C11H17N3O2	223.1321
	HWG 1608-pentanoic acid	C11H19N3O3	241.1426
	HWG 1608-triazole-pinacoline (M18)	C8H13N3O	167.1059
	Hydroxy-triazole (M29)	C2H3N3O	85.02761
	Triazole alanine	C5H8N4O2	156.0647
	3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butan-2-one	C8H13N3O	167.1059
	TEB_M324a	C16H22CIN3O2	323.1401
	TEB_M324b	C16H22CIN3O2	323.1401
	TEB_M324c	C16H22CIN3O2	323.1401
	TEB_M388	C16H23CIN3O4P	387.1115
	TEB_M404	C16H23CIN3O5P	403.1064
Thiabendazole	5-Hydroxy-thiabendazole	C10H7N3OS	217.031
	Benzimidazole	C7H6N2	118.0531
Triadimenol	1,2,4 triazole	C2H3N3	69.0327
	1,2,4 triazole acetic-acid	C4H5N3O2	127.0382
	KWG1640 (M02)	C14H16CIN3O4	325.0829
	KWG1732(M03)	C11H10CIN3O4	283.036
	P02	C5H5N3O4	171.028
	P03	C4H3N3O3	141.0174
	P04	C3H6O5	122.0215
	P05	C3H4O4	104.011
	P06	C3H4O5	120.0059
	P07	C5H5N3O4	171.028
	P08	C4H5N3O3	143.0331
	P09	C3H5N3O	99.04326
	P-chloro-phenol	C6H5ClO	128.0029
	Triadimefon (M01)	C14H16CIN3O2	293.0931
	Triazole alanine (M06)	C4H6N4O2	142.0491
	Triazolyl-glycerine acid	C5H7N3O4	173.0437
Triticonazole	Metabolite 1 (RPA 404766)	C17H19CIN3O2	332.1166
	Metabolite 3 (RPA 406341)	C17H20CIN3O2	333.1244

^a, from Envipath website (<https://www.envipat.eawag.ch/index.php>)

Quantification in Trace Finder 4.1

Quantification of antifungal azoles was performed using TraceFinder 4.1 (Thermo Fisher Scientific) using internal standards (ISTD) and an external calibration curve. Briefly, mixture of reference standards dissolved in methanol/nanopure water (50/50; v/v) were used to obtain calibration curves, which consisted of 10 points (0.1, 0.25, 0.5, 1, 2.5, 5, 10, 25, 50, and 100 µg/L). The calibration curves were plotted as analyte to ISTD mean peak area ratio vs. analyte to ISTD concentration ratio. Calibrations were measured twice (at the beginning and at the end of the batch). The average and the standard deviation were then calculated and used to plot the compound-specific calibration curves, as well as to calculate the concentrations. The linear dynamic range was found with values of $R^2 > 0.99$ for the curves with 10 calibration points (3 orders of magnitude). Instrument blanks containing only the solvents (50% methanol and 50% nanopure water) were used to check for carry-over and contamination, while matrix blanks were employed to detect the presence of contamination during the sample preparation procedure. For the quantification of chemicals in archived samples, the closest-matching ISTD according to retention time and structure was used for the chemicals without their own

internal standard (Table S5). The injection of a broad mixture of reference standards and ISTD allowed us to establish the calibration curves in parallel of the samples used to build the HRMS data archive, thereby allowing the retrospective quantification. Also, for the newly extracted samples (i.e. sediments and biofilms) the quantification was done on both DIA and DDA-based data to compare both approaches. For both, positive detection of at least three fragments were set as a criteria for quantification. The DDA inclusion list is provided in the Table S6.

Table S5. Relative recoveries using internal standards

Standard	Internal standard	Relative Recovery	
		Average	STDV
Climbazole	Epoxiconazole d4	101%	6%
Cyproconazole	Myclobutanol d4	86%	8%
Difenoconazole	Propiconazole d5	89%	6%
Epoxyconazole	Epoxiconazole d4	95%	3%
Fenamidone	Myclobutanol d4	83%	20%
Fenbuconazole	Prochloraz d7	110%	15%
Fluconazole	Fluconazole d4	89%	8%
Flusilazole	Prochloraz d7	88%	11%
Fuberidazole	Fluconazole d4	99%	13%
Imazalil	Epoxiconazole d4	88%	18%
Ketoconazole	Epoxiconazole d4	90%	22%
Metconazole	Metconazole d6	94%	5%
Myclobutanol	Myclobutanol d4	88%	8%
Paclobutrazol	Epoxiconazole d4	87%	14%
Penconazole	Propiconazole d5	89%	9%
Pro. BTS 40348	Epoxiconazole d4	70%	16%
Pro. BTS 44595	Metconazole d6	100%	10%
Prochloraz	Prochloraz d7	92%	4%
Propiconazole	Propiconazole d5	105%	6%
Prothio desthio	Prochloraz d7	92%	8%
Tebuconazole	Propiconazole d5	99%	16%
Triadimenol	Epoxiconazole d4	90%	9%
Triflumizole	Metconazole d6	76%	12%

Where relative recovery is calculated as follows:

$$\text{Relative recovery} = \frac{C_i \text{ in spiked sample} - C_i \text{ in unspiked sample}}{C_i \text{ spiked}}$$

Where C_i is the concentration of the compound i

Table S6. Inclusion list of antifungal azoles for data-dependent acquisition (DDA) analysis as a second step

	Compounds	Chemical classes	CAS	chemical formula	[M+H] ⁺ ^a
Pesticides	Azaconazole	Triazole	60207-31-0	C12H11Cl2N3O2	300.03011
	Bitertanol	Triazole	55179-31-2	C20H23O2N3	338.1863
	Bromuconazole	Triazole	116255-48-2	C13H12BrCl2N3O	375.96133
	Cyproconazole	Triazole	94361-06-5	C15H18CIN3O	292.12112
	Difenoconazole	Triazole	119446-68-3	C19H17Cl2N3O3	406.07197
	Epoxiconazole	Triazole	133855-98-8	C17H13ClFN3O	330.08039
	Fenamidone	Triazole	161326-34-7	C17H17N3OS	312.11651
	Fenbuconazole	Triazole	114369-43-6	C19H17CIN4	337.12145
	Fluquinconazole	Triazole	136426-54-5	C16H8Cl2FN5O	376.01627
	Flusilazole	Triazole	85509-19-9	C16H15F2N3Si	316.10761
	Fuberidazole	Triazole	3878-19-1	C11H8N2O	185.07094
	Imazalil	imidazole	35554-44-0	C14H14Cl2N2O	297.0556
	Metconazole	Triazole	125116-23-6	C17H22CIN3O	320.15242
	Myclobutanil	triazole	88671-89-0	C15H17CIN4	289.12145
	Oxoconazole	imidazole	134074-64-9	C19H24CIN3O2	362.12769
	Paclobutrazol	Triazole	76738-62-0	C15H20CIN3O	294.13677
	Penconazole	Triazole	66246-88-6	C13H15Cl2N3	284.07158
	Prochloraz	imidazole	67747-09-5	C15H16Cl3N3O2	376.03809
	Prochloraz BTS40348	imidazole	67747-01-7	C11H14Cl3NO	282.0213
	Prochloraz BTS44595	imidazole	139520-94-8	C12H15Cl3N2O2	325.0271
	Propiconazole	Triazole	60207-90-1	C15H17Cl2N3O2	342.07706
	Prothioconazole	Triazole	178928-70-6	C14H15Cl2N3OS	344.03856
	Prothio.-desthio	Triazole	120983-64-4	C14H15Cl2N3O	312.0664
	Tebuconazole	Triazole	107534-96-3	C16H22CIN3O	308.15242
	Triadimenol	Triazole	55219-65-3	C14H18CIN3O2	346.09285
	Triflumizole	imidazole	99387-89-0	C15H15ClF3N3O	296.11604
	Triticonazole	Triazole	131983-72-7	C17H20CIN3O	318.13677
Pharmaceuticals	Climbazole	imidazole	38083-17-9	C15H17CIN2O2	293.10513
	Clotrimazole	imidazole	23593-75-1	C22H17CIN2	345.1153
	Fluconazole	triazole	86386-73-4	C13H12F2N6O	307.11134
	Ketoconazole	imidazole	65277-42-1	C26H28Cl2N4O4	531.15604

^a, from Envipat website (<https://www.envipat.eawag.ch/index.php>)

Quality control and analytical performance

Quality control and analytical performance were established for all the matrix on a new set of samples spiked with the selected antifungal azoles in parallel of the investigation of newly extracted samples of biofilms and sediments.

Extraction recovery of each chemicals was established by spiking the samples with regular standards prior the extraction and with ISTD after extraction. Recovery was then calculated as follows:

$$\text{Ext. recovery (\%)} = \frac{C_i \text{ in spiked sample (actual)} - C_i \text{ in unspiked sample (actual)}}{C_i \text{ spiked (theoretical)}} \times 100$$

Where Ci is the concentration of the compound i

The limit of quantification (LOQ) was first estimated for the reference standards dissolved in methanol/nanopure water (50/50; v/v) (LOQsolvent). This was done by using the signal-to-noise ratio (S/N), where a S/N of 10 was employed. The LOQ in the solvent was calculated as follows.

$$LOQ_{\text{solvent}} = \frac{C \text{ in standard}}{\frac{S}{N} \text{ in standard}} \cdot 10$$

The LOQ specific to the different matrices was calculated by using the absolute recoveries as described below:

$$LOQ_{matrix} = \frac{LOQ_{solvent}}{\text{Absolute recovery}} \cdot \text{enrichment factor}$$

$$\text{where } \% \text{Absolute recovery} = \frac{(\text{Area spiked} - \text{Area unspiked})}{\text{Area standard}} \cdot 100$$

Where Area spiked, Area unspiked , and Area standard are the areas of the spiked and unspiked samples, and the standard of the same amount dissolved in the solvent, respectively.

Recoveries and LOQs are reported in the table S7.

Table S7. Absolute recovery (%), extraction recovery (%), and LOQ matrix (ng/g or ng/L) of the antifungal azoles

	Sediment/Soil						Biofilms						Gammarids					
	Ab. Reco.		Ext. Reco.		LOQ		Ab. Reco.		Ext. Reco.		LOQ		Ab. Reco.		Ext. Reco.		LOQ	
	Average	STDV	Average	STDV	Average	STD	Average	STDV	Average	STDV	Average	STDV	Average	STDV	Average	STDV	Average	STDV
Bromuconazole	42%	10%	67%	10%	0.35	0.18	33%	20%	61%	13%	3.58	2.60	43%	13%	80%	9%	4.00	1.21
Climbazole	9%	1%	10%	1%	0.23	0.07	42%	14%	59%	13%	0.75	0.54	101%	1%	57%	23%	0.90	0.56
Clotrimazole	< 5%	-	< 5%	-	-	-	18%	3%	56%	13%	15.80	4.12	69%	19%	49%	8%	23.73	6.21
Cyproconazole	54%	12%	70%	11%	0.33	0.17	50%	18%	67%	17%	2.41	2.39	45%	16%	78%	19%	2.91	2.45
Difenconazole	43%	6%	67%	6%	0.61	0.35	48%	12%	70%	11%	3.73	4.52	59%	29%	72%	19%	7.20	2.14
Epoxyconazole	63%	9%	75%	8%	0.15	0.09	38%	1%	73%	11%	1.52	0.94	62%	17%	80%	5%	1.59	0.46
Fenamidone	64%	8%	76%	7%	0.10	0.07	58%	8%	52%	11%	1.91	1.45	72%	34%	88%	8%	1.91	1.52
Fenbuconazole	56%	9%	75%	9%	0.32	0.20	32%	2%	77%	11%	3.37	1.90	48%	18%	74%	6%	3.88	0.73
Fluconazole	< 5%	1%	20%	1%	4.31	3.10	76%	14%	79%	11%	3.65	2.38	95%	5%	96%	13%	4.42	0.23
Fluquinconazole	57%	15%	81%	14%	0.59	0.39	40%	8%	63%	10%	5.04	3.87	32%	21%	49%	13%	4.38	-
Flusilazol	69%	11%	75%	9%	0.26	0.19	30%	5%	79%	15%	1.93	1.67	56%	19%	84%	17%	2.22	1.69
Fuberidazol	30%	3%	36%	3%	0.07	0.04	99%	11%	67%	17%	0.29	0.24	43%	27%	53%	24%	0.32	0.01
Imazalil	6%	0%	7%	0%	0.37	0.13	35%	18%	47%	13%	0.90	0.73	102%	9%	84%	0%	0.69	0.05
Ketoconazole	< 5%	-	< 5%	-	7.28	-	54%	10%	59%	17%	0.79	-	82%	1%	71%	7%	7.48	0.23
Metconazole	51%	8%	58%	6%	0.19	0.11	38%	0%	69%	10%	1.62	0.97	55%	6%	85%	8%	1.55	0.27
Myclobutanyl	63%	9%	85%	6%	0.22	0.14	39%	3%	71%	5%	2.90	1.98	47%	19%	90%	2%	3.64	1.85
Paclolutrazol	64%	15%	70%	15%	0.11	0.07	43%	12%	59%	14%	2.39	2.78	28%	11%	58%	19%	3.20	2.79
Penconazole	57%	14%	72%	14%	0.15	0.09	34%	5%	66%	11%	1.82	1.09	69%	17%	74%	8%	1.79	0.39
Pr. BTS40348	< 5%	-	< 5%	-	3.30	-	44%	19%	53%	15%	4.09	2.59	66%	13%	69%	13%	3.54	1.21
Pr. BTS44595	35%	2%	49%	2%	0.22	0.08	57%	15%	81%	17%	2.04	1.41	74%	18%	98%	15%	1.96	0.59
Prochloraz	42%	11%	23%	3%	0.38	0.18	40%	11%	62%	14%	3.31	2.41	61%	19%	51%	7%	3.47	0.46
Propiconazole	61%	13%	74%	12%	0.21	0.14	36%	4%	72%	13%	2.37	1.46	70%	19%	84%	15%	2.43	0.48
Prothioconazole	-	-	-	-	-	-	22%	3%	39.3%	12.6%	25.80	4.63	32%	2%	51%	3%	18.0	2.3
Prothio.desethio	65%	10%	67%	13%	0.17	0.10	40%	18%	53%	17%	2.31	1.80	52%	19%	68%	17%	2.67	0.41
Tebuconazole	59%	17%	74%	16%	0.51	0.31	39%	2%	74%	13%	3.56	2.95	64%	17%	81%	4%	4.71	1.92
Triadimenol	65%	19%	79%	16%	0.19	0.12	49%	11%	73%	20%	1.98	1.26	50%	-	78%	-	3.43	-
Triflumizole	42%	4%	52%	4%	0.12	0.06	31%	8%	62%	10%	0.99	0.78	53%	16%	73%	7%	1.01	0.05

Table S7. Continued

	Fish						Water					
	Ab. Reco.		Ext. Reco.		LOQ		Ab. Reco.		Ext. Reco.		LOQ	
	Average	STDV	Average	STDV	Average	STDV	Average	STDV	Average	STDV	Average	STDV
Bromuconazole	25%	-	10%	-	35.1	-	83%	-	-	-	0.1	-
Climbazol	46%	-	21%	-	1.3	-	63%	-	117%	-	0.1	-
Clotrimazol	< 5%	-	-	-	-	-	-	-	-	-	-	-
Cyproconazole	31%	-	14%	-	0.7	-	42%	-	45%	-	0.8	-
Difenoconazole	38%	-	16%	-	10.5	-	65%	-	108%	-	0.8	-
Epoxyconazole	43%	-	8%	-	2.0	-	95%	-	95%	-	0.2	-
Fenamidone	26%	-	11%	-	10.0	-	71%	-	77%	-	0.2	-
Fenbuconazole	20%	-	17%	-	9.0	-	59%	-	77%	-	0.6	-
Fluconazole	12%	-	144%	-	53.7	-	94%	-	113%	-	0.4	-
Fluquinconazole	25%	-	7%	-	12.3	-	76%	-	77%	-	0.8	-
Flusilazol	35%	-	32%	-	0.7	-	86%	-	110%	-	0.4	-
Fuberidazol	39%	-	36%	-	32.9	-	57%	-	64%	-	0.1	-
Imazalil	51%	-	12%	-	5.8	-	95%	-	98%	-	0.1	-
Ketoconazole	41%	-	18%	-	17.1	-	103%	-	105%	-	0.7	-
Metconazole	31%	-	9%	-	3.2	-	84%	-	103%	-	0.2	-
Myclobutanyl	22%	-	13%	-	13.2	-	73%	-	79%	-	0.4	-
Paclobutrazol	35%	-	7%	-	13.1	-	98%	-	91%	-	0.1	-
Penconazole	27%	-	12%	-	4.5	-	87%	-	137%	-	0.2	-
Pr. BTS40348	38%	-	11%	-	7.2	-	46%	-	131%	-	0.6	-
Pr. BTS44595	41%	-	9%	-	5.7	-	63%	-	76%	-	0.3	-
Prochloraz	35%	-	29%	-	31.8	-	90%	-	110%	-	0.4	-
Propiconazole	32%	-	13%	-	4.6	-	91%	-	114%	-	0.3	-
Prothioconazole	9%	-	16%	-	152.4	-	< 5%	-	9%	-	1.7	-
Prothio.desethio	34%	-	21%	-	27.9	-	115%	-	103%	-	0.1	-
Tebuconazole	30%	-	16%	-	6.6	-	78%	-	134%	-	0.7	-
Triadimenol	24%	-	4%	-	10.6	-	81%	-	77%	-	0.3	-
Triflumizole	37%	-	12%	-	25.2	-	64%	-	77%	-	0.2	-

Section 3. Retrospective screening of all the matrices

Table S8. List of antifungal azoles identified through the retrospective analysis under Compound Discoverer (CD) 2.1.

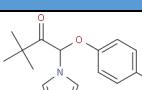
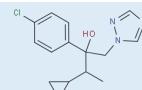
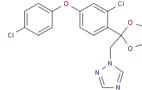
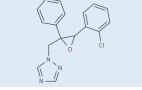
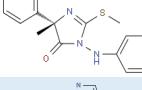
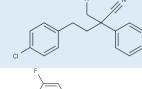
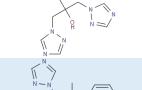
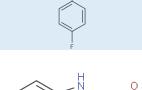
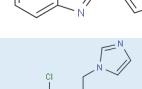
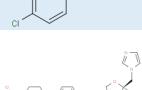
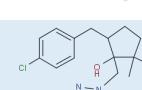
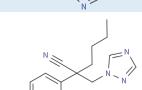
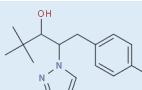
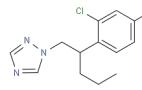
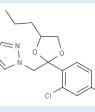
	Name	Structure	Formula	Molecular Weight	ΔMass [Da]	ΔMass [ppm]	RDBE	H/C	Rank	# Matched Iso.	# Missed Iso.	SFit [%]	Pattern Cov. [%]	MS Cov. [%]
1	Climbazole		C15 H17 Cl N2 O2	292.09786	-0.00007	-0.23	8	1.1	1	8	0	76	100	100
2	Cyproconazole		C15 H18 Cl N3 O	291.11384	-0.00005	-0.17	8	1.2	1	7	1	74	99.21	100
3	Difenoconazole		C19 H17 Cl2 N3 O3	405.0647	-0.00017	-0.43	12	0.9	2	5	0	83	96.17	100
4	Epoxiconazole		C17 H13 Cl F N3 O	329.07312	0.00007	0.23	12	0.8	1	6	0	83	99.45	100
5	Fenamidone		C17 H17 N3 O S	311.10923	0	0.01	11	1	1	5	0	78	99.17	96.52
6	Fenbuconazole		C19 H17 Cl N4	336.11417	-0.00041	-1.22	13	0.9	1	8	0	80	99.93	99.97
7	Fluconazole		C13 H12 F2 N6 O	306.10407	-0.00004	-0.14	10	0.9	1	4	0	78	99.73	100
8	Flusilazole		C16 H15 F2 N3 Si	315.10033	0.0001	0.32	11	0.9	3	7	0	76	100	99.96
9	Fuberidazole		C11 H8 N2 O	184.06366	-0.00009	-0.48	9	0.7	1	2	0	96	98.51	83.26
10	Imazalil		C14 H14 Cl2 N2 O	296.04832	-0.00005	-0.18	8	1	2	5	0	87	97.72	100
11	Ketoconazole		C26 H28 Cl2 N4 O4	530.14876	-0.00016	-0.29	14	1.1	3	8	0	76	99.66	99.52
12	Metconazole		C17 H22 Cl N3 O	319.14514	-0.00003	-0.1	8	1.3	1	8	0	77	100	99.92
13	Myclobutanil		C15 H17 Cl N4	288.11417	0.00002	0.08	9	1.1	1	5	1	74	96.15	77.81
14	Paclobutrazol		C15 H20 Cl N3 O	293.12949	-0.00031	-1.07	7	1.3	1	8	0	73	100	99.97
15	Penconazole		C13 H15 Cl2 N3	283.0643	0.00011	0.37	7	1.2	1	10	1	77	99.55	99.97

Table S8. Continued

	Name	Structure	Formula	Molecular Weight	Δ Mass [Da]	Δ Mass [ppm]	RDBE	H/C	Rank	# Matched Iso.	# Missed Iso.	SFit [%]	Pattern Cov. [%]	MS Cov. [%]
16	Prochloraz		C15 H16 Cl3 N3 O2	375.03081	0.00051	1.36	8	1.1	1	9	0	87	98.57	100
17	Propiconazole		C15 H17 Cl2 N3 O2	341.06978	0.00014	0.42	8	1.1	3	8	2	74	98.72	100
18	Tebuconazole		C16 H22 Cl N3 O	307.14514	0.0001	0.31	7	1.4	1	8	0	74	100	100
19	Triadimenol		C14 H18 Cl N3 O2	295.10875	-0.00031	-1.05	7	1.3	1	8	0	75	100	100
20	Triflumizole		C15 H15 Cl F3 N3 O	345.08557	0.00007	0.2	8	1	1	8	0	69	100	99.85

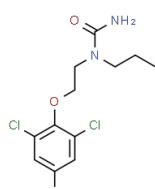
Δ Mass is the difference between the theoretical mass and the measured mass in dalton or ppm ; **RDBE** (ring and double-bond equivalents) is the number of unsaturated bonds in a compound ; **H/C** is the minimum hydrogen-to-carbon ratio ; **Rank** is the rank order of each composition; **# Matched Iso.** (isotope) is the number of matching isotopes ; **# Miss Iso.** is the number of isotopes that were missing in the measured isotope pattern as compared to the theoretical pattern for the predicted composition; **SFit** is the spectral similarity score between the theoretical and the measured isotope pattern as a percentage; **Pattern Cov** (pattern covariance) is the summed intensity of the matching isotope peaks on the measured MS1 spectrum relative to the summed intensity of the theoretical isotope pattern. It provides a quantitative measure of how well the measured isotope pattern matches the theoretical isotope pattern; **MS Cov** (MS covariance) is the summed intensity of matching isotope peaks in the measured pattern relative to the summed intensity of all the peaks in the measured pattern.

Table S9. List of antifungal azole (bio)transformation products (TPs) potentially occurring in all investigated samples

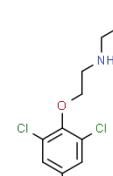
Compartment	[M+H] ⁺	Fromula	Molecular weigh	ΔMass	ΔMass	RDBE	H/C	Rank	Match Iso	Miss Iso	Sfit	Pattern Cov	MS cov	Tentative Name	Parent compound
Surface water	168.11320	C8 H13 N3 O	167.10586	2E-05	0.13	4	1.6	1	5	0	82	99.85	99.6	HWG 1608 triazole pinacoline M18	Tebuconazole
														3,3-Dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butane	
														2-dimethylamino-56-dimethyl-pyrimidin-4-ol	
	312.06620	C14 H15 Cl2 N3 O	311.05922	-0.0003	-0.98	8	1.1	1	11	1	62	99.47	100	Prothioconazole-desthio	Prothioconazole
Biota	350.05490	C16 H13 Cl2 N3 O2	349.03848	-8E-05	-0.24									CGA 205375	Difenconazole
	256.00380	C10 H7 Cl2 N3 O	254.99662	4E-05	0.15	8	0.7	1	5	0	73	97.83	100	LS802050	Bromuconazole
	258.01950	C10 H9 Cl2 N3 O	257.01227	-0.0001	-0.39	7	0.9	1	5	0	71	97.83	100	MWt 257	Bromuconazole
	168.11290	C8 H13 N3 O	167.10586	-0.0001	-0.83	4	1.6	1	3	0	90	99.37	98.77	2-dimethylamino-56-dimethyl-pyrimidin-4-ol	Tebuconazole
Sediment	326.09170	C14 H16 Cl N3 O4	325.08293	0.0011	3.43	8	1.1	1	4	0	94	97.97	100	KWG1640 M02	Triadimenol
	312.06610	C14 H15 Cl2 N3 O	311.05927	-0.0003	-0.98	8	1.1	1	11	1	62	99.47	100	Prothioconazole-desthio	Prothioconazole
	339.00950	C15 H9 Cl2 F N2 O2	338.00251	-0.0002	-0.58	11	0.6	3	4	0	86	92.53	100	SN617406	Fluquinconazole
	282.02120	C11 H14 Cl3 N O	281.0141	-0.0004	-1.32	4	1.3	1	5	0	60	93.29	86.09	BTS 40348	Prochloraz
	282.02148	C11 H14 Cl3 N O	281.0141	9E-05	0.31	4	1.3	1	5	0	38	99.19	100	BTS 40348	Prochloraz
	325.02771	C12 H15 Cl3 N2 O2	324.01991	-0.0005	-1.66	4	1.2	1	5	0	41	97.69	89.8	BTS 44595	Prochloraz
	312.06778	C14 H15 Cl2 N3 O	311.05922	-0.001	-3.36	8	1.1	1	11	1	57	98.33	87.3	Prothioconazole-desthio	Prothioconazole
	358.05423	C15 H17 Cl2 N3 O S	357.04694	-5E-05	-0.13	8	1.1	1	5	0	85	96.66	100	M01 prothioconazole smethyl	Prothioconazole

*based on Schymanski et al. 2014 [8]. Table heading names are explained in Table S8.

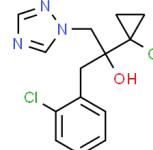
The structure of those confirmed at level 1 are presented below



Prochloraz BTS44595 (CAS 139520-84-8)



Prochloraz BTS40348 (CAS 67747-01-7)



Prothioconazole-desthio

(CAS

120983-64-4)

Table S10. Comparison between data-independent (DIA) and vs data-dependent (DDA) acquisitions based on sediment and biofilm quantification. Results are expressed in ng/g dry weight (dw)

	Climbazol		Cyproconazol		Difenconazol		Epiconazole		Fenbuconazole		Flusilazol		Imazalil		Ketoconazole		Metconazole		Myclobutanil		Penconazol		Pro. BTS44595		Propiconazol		Proth.-desethio		Tebuconazol		Triflumizole				
	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA					
SED1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
SED2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.01	0.03					
SED3	0.14	0.14	-	-	-	-	0.06	0.07	-	-	-	-	-	-	-	-	-	-	-	-	-	0.28	0.06	-	-	-	-	-	-						
SED4	0.04	0.05	-	-	-	-	-	0.16	0.15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.09	0.08						
SED5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.33	0.22	-	-	-	-	-	-						
SED6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.43	0.39	-	-					
SED7	0.13	0.12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.26	0.17	-	-	-	-	-	-	-						
SED8	0.06	0.06	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.18	0.04	-	-					
SED9	0.14	0.12	-	-	0.24	0.19	0.01	0.08	-	-	-	-	-	-	-	-	-	-	-	-	-	0.90	0.63	0.14	0.09	0.80	0.50	-	-						
SED10	0.09	0.09	-	-	-	0.19	0.20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.90	0.61	0.10	0.07	0.65	0.47	-	-						
SED11	0.49	0.49	-	-	3.47	3.21	0.04	0.31	-	-	0.67	0.68	-	-	-	-	0.10	0.09	-	-	0.20	0.20	-	-	3.90	2.45	0.53	0.57	1.50	4.10	-				
SED12	-	-	-	-	0.24	0.23	0.04	0.42	-	-	-	-	-	-	-	-	0.05	0.05	0.18	0.12	-	-	0.12	0.08	-	-	0.33	0.33	0.61	0.48	-	-			
SED13	-	-	0.09	0.16	2.05	2.12	0.19	1.97	-	-	2.75	3.04	-	-	-	-	0.25	0.25	-	-	-	-	0.14	0.12	1.59	1.05	0.67	0.75	3.36	4.63	-	-			
SED14	-	-	-	-	0.80	0.82	-	-	-	-	1.07	1.13	-	-	-	-	-	-	-	-	0.29	0.30	-	-	-	-	-	-	-	1.00	1.02				
SED15	-	-	-	-	9.17	9.54	0.45	0.44	-	-	0.18	0.18	-	-	-	-	-	-	0.25	0.13	0.38	0.38	0.13	0.12	-	-	0.08	0.05	-	-	-	-			
SED16	-	-	-	-	0.96	1.00	0.20	0.20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.53	0.53	0.23	0.25	-	-				
SED17	-	-	0.06	0.10	6.72	6.67	1.53	1.57	-	-	2.55	2.84	-	-	-	-	0.16	0.16	-	-	-	-	0.19	0.17	1.21	0.82	1.39	1.52	2.06	1.92	-	-			
SED18	-	-	-	-	-	2.50	2.40	0.15	0.20	-	-	-	-	-	-	-	-	0.10	0.07	0.24	0.24	0.04	0.03	-	-	-	-	0.17	0.10	-	-	-	-		
SED19	0.12	0.11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.28	0.16	-	-	0.16	0.17	-	-	-	-			
SED20	0.26	0.25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.72	0.49	-	-	0.23	0.46	-	-	-	-			
SED21	0.15	0.14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.44	0.29	-	-	0.18	0.30	-	-	-	-			
SED22	0.07	0.04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.79	0.53	-	-	-	-	-	-	-	-			
SED23	0.17	0.15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.38	4.13	-	-	0.13	0.23	-	-	-	-			
SED24	-	-	-	-	-	0.15	0.17	-	-	0.32	0.31	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.11	0.10	-	-	-	-				
SED25	-	-	-	-	-	0.62	0.54	-	-	1.09	1.14	-	-	0.14	0.10	-	-	-	-	-	0.15	0.16	-	-	-	-	0.15	0.32	-	-	-	-			
SED26	0.17	0.17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.45	0.33	-	-	0.09	0.49	-	-	-	-			
SED27	0.18	0.19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.45	0.45	-	-	0.22	0.31	-	-	-	-			
SED28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.10	0.16	-	-	-	-			
SED29	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
SED30	0.05	0.06	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.37	0.22	-	-	-	-	-	-	-	-			
SED31	0.07	0.07	-	-	-	0.28	0.27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.31	0.19	-	-	-	-	-	-	-	-				
SED32	0.11	0.08	0.09	0.17	0.74	0.66	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4.10	2.70	-	-	0.25	0.31	-	-	-	-				
SED33	0.09	0.05	0.07	0.15	1.15	1.05	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.63	0.61	-	-	6.41	4.07	-	-	0.26	0.33	-	-		
SED34	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.21	0.04	-	-	1.45	0.88	-	-	-	-	-	-		
SED35	0.19	0.18	-	-	1.70	1.33	-	-	-	-	-	-	-	-	-	1.26	0.54	0.74	0.77	-	-	-	-	0.37	0.37	-	-	2.99	2.03	-	-	0.25	0.54	-	-

-, n.d. or < LOQ . In particular, prochloraz BTS40348 was detected in two sediments but was < LOQ. Thus, it was not included in this table.

Table S10 continued.

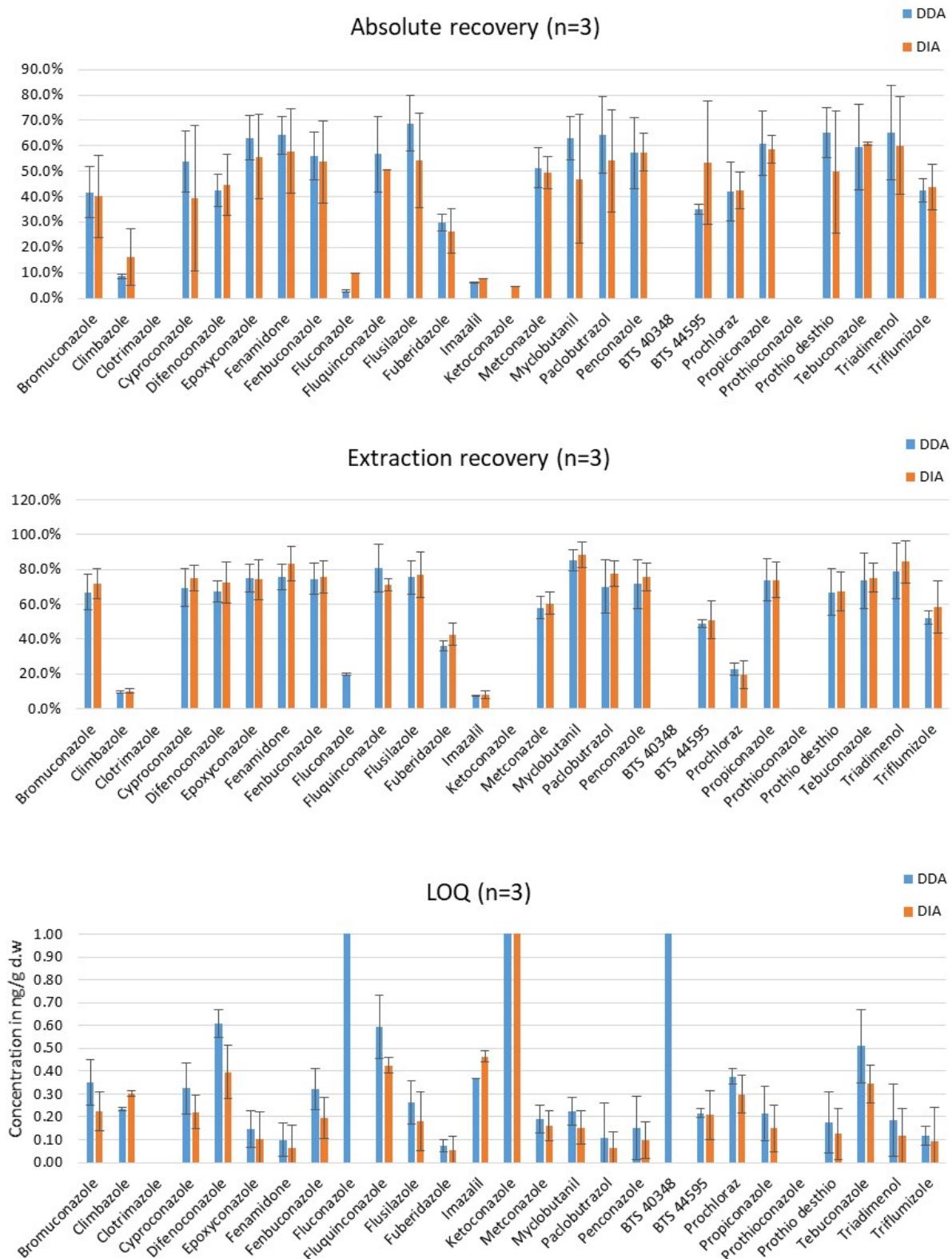
	Climbazol		Epoxiconazole		Flusilazole		Fuberidazole		Ketoconazole		Metconazole		Propiconazole		Tebuconazole	
	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA	DIA	DDA
BioF1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF2	50.3	73.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF3	-	-	-	-	22.1	14.8	3.2	< LOQ	-	-	-	-	-	-	-	-
BioF4	4.8	8.4	-	-	13.9	11.8	-	-	-	-	-	-	-	-	-	-
BioF5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF6	3.4	5.8	-	-	-	-	-	-	-	-	-	4.0	3.0	-	-	-
BioF7	5.9	12.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF12	8.9	4.6	-	-	-	-	-	-	-	-	7.9	4.3	-	-	12.7	8.5
BioF13	3.1	4.0	-	-	-	-	-	-	-	-	-	-	-	-	6.5	4.6
BioF14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.8	4.1
BioF15	3.3	2.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF16	3.5	3.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF17	4.2	5.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF18	6.7	6.9	-	-	-	-	-	-	-	-	-	-	-	-	1.5	2.3
BioF19	43.6	48.5	2.6	3.1	-	-	-	-	204.4	197.5	-	-	-	-	-	-
BioF20	0.0	5.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BioF21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-, n.d. or < LOQ

Overall, comparison between DIA and DDA did not show notable difference in the detection frequency (with existing characteristic fragments for confirmation of identity) and detected level (based on area of molecular ion in full scan) in sediment or biofilms ([Table S10](#)). The absolute and extraction recoveries and LOQs were similar between DIA and DDA acquisition although some of the chemicals presented higher LOQ values in DIA (i.e. 2 to 3 times) than in DDA ([Figure S3](#)). This could, however, be an artifact associated with the sample reinjection. In addition to possible changing ion suppression/enhancement at the source level, the samples and their extract could change a bit during their storage at -20°C between the two injections.

Section 4. Occurrence of antifungal azoles in Swiss aquatic ecosystems

A)



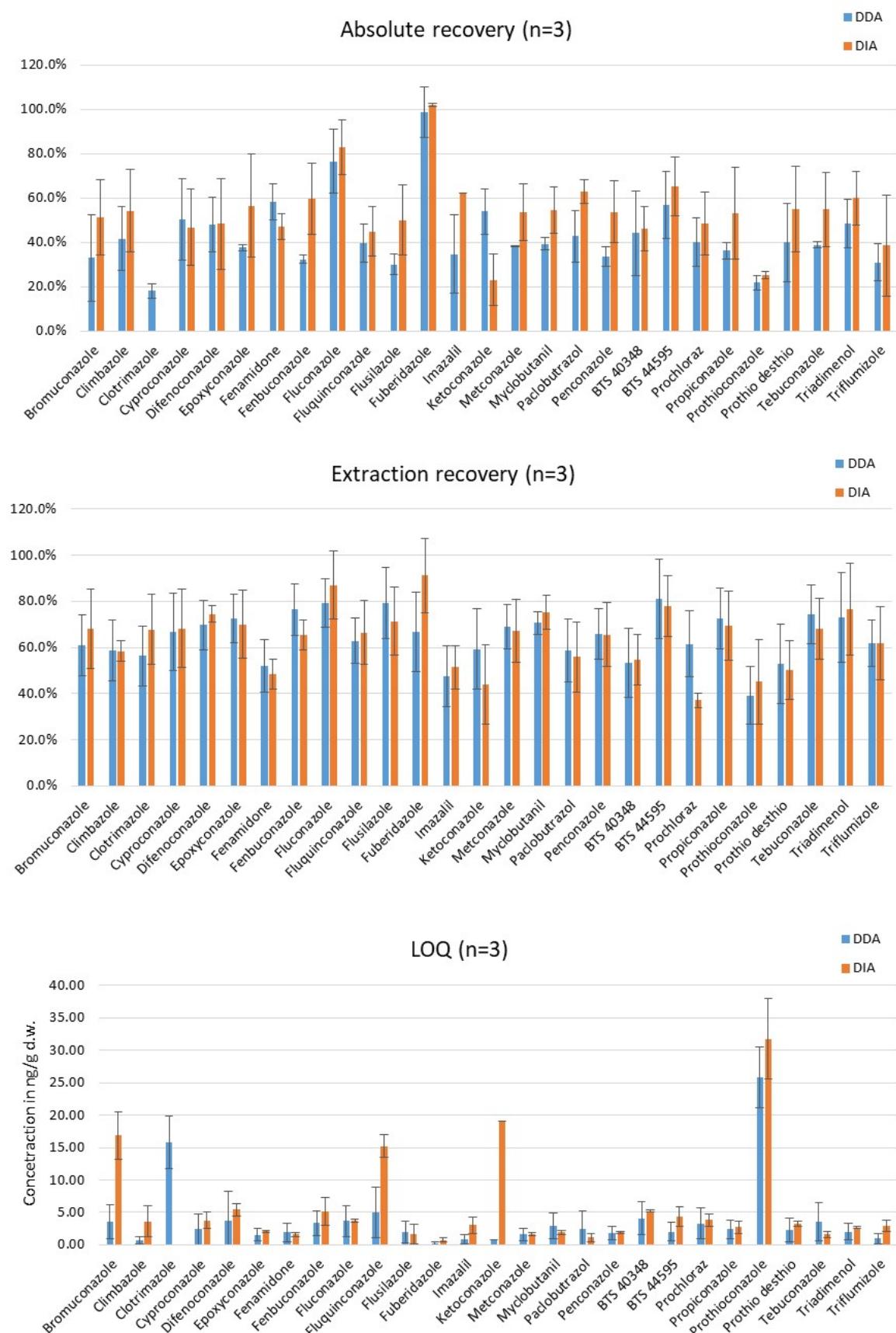
B

Figure S3. Data-independent (DIA) vs data-dependent (DDA) acquisition in (A) sediment and (B) biofilms

Table S11. List of antifungal azoles investigated in the present study. The check marks indicate whether the compounds were retrospectively detected in the samples and/or included in the final list for data dependent acquisition in new samples to validate the DIA.

Use	Compounds	Class	LogKow ^a	BioT Half-life ^a	Log BAF ^a	Use (Kg) ^b	Detected	Final list ^c
Pesticides	Imazalil	Imidazole	4.1	4.57	2.71	10-100	V	V
	Oxpoconazole		4.93	9.28	3.51	?		
	Prochloraz		4.13	70.8	3.29	10000-100000	V	V
	Triflumizole		1.5	3.08	0.55	100-1000	V	V
	Azaconazole	Triazole	2.73	1.82	1.35	Forbiden		V
	Bitertanol		4.07	8.26	3.03	?		V
	Bromuconazole		3.54	4.52	2.23	?		V
	Cyproconazole		3.25	2.9	1.9	10000-100000	V	V
	Difenconazole		5.2	21.2	3.31	10000-100000	V	V
	Diniconazole		3.92	16.3	3.26	?		
	Epiconazole		3.47	5	2.41	10000-100000	V	V
	Etaconazole		3.64	3.91	2.03	?		
	Fenamidone		3.45	0.33	1.97	10000-100000	V	V
	Fenbuconazole		4.23	3.23	2.2	100-1000	V	V
	Fluquinconazole		3.73	10.6	2.25	1000-100000		V
	Flusilazole		4.89	55.4	2.9	10000-100000	V	V
	Flutriafol		2.52	6.35	1.33	?		
	Fuberidazole		2.37	0.551	1.61	?	V	V
	Furconazole		3.84	14.4	2.83	?		
	Hexaconazole		3.66	8.24	2.83	Forbiden		
	Imibenconazole		5.64	40.8	4.23	?		
	Ipcnazole		4.65	7.17	3.04	?		
	Ipfen trifluconazole		6.24	137	6.21	?		
	Mefentrifluconazole		4.56	42.5	3.77	?		
	Metconazole		4.19	4.58	2.56	1000-10000	V	V
	Myclobutanil		3.5	5.35	1.95	1000-10000	V	V
	Paclobutrazol		3.36	2.5	2.16	10000-100000	V	V
	Penconazole		4.67	15.3	3.55	1000-10000	V	V
	Propiconazole		4.13	6.2	2.64	10000-100000	V	V
	Prothioconazole		3.09	0.25	1.75	10000-100000		V
	Prothiocronazole-desthi		3.05	1.96	2.02	?	V	V
	Quinconazole		3.53	14.2	2.54	?		
	Simeconazole		2.99	7.63	2	?		
	Tebuconazole		3.89	5.13	2.64	10000-100000	V	V
	Tetraconazole		4.25	8.69	2.58			
	Triadimefon		2.94	2.68	1.8	?		
	Triadimenol		2.95	2.79	2.06	1000-10000	V	V
	Triticonazole		4.11	5.48	2.28	10-100		
	Uniconazole		3.28	9.92	2.65	?		
Pharmaceuticals	Bifonazole	Imidazole	5.71	1.5	2.76	100-1000		
	Butoconazole		7.41	211	6.8	?		
	Climbazole		3.76	4.78	2.67	?	V	V
	Clotrimazole		6.26	41.8	5.59	1000-10000		V
	Econazole		5.61	22.4	4.56	10-100		
	Fenticonazole		7.26	39.2	5.9	10-100		
	Isoconazole		6.25	37.3	5.5	10-100		
	Itraconazole		6.16	0.197	1.89	100-1000		
	Ketoconazole		4.45	0.991	2.55	?	V	V
	Luliconazole		3.61	2.39	2.48	100-1000		
	Micronazole		6.25	37.3	5.5	100-1000		
	Omoconazole		6.09	247	6.26	?		
	Oxiconazole		6.45	122	6.32	?		
	Sertaconazole		6.6	10.1	4.5	10-100		
	Sulconazole		6.46	39.3	5.68	?		
	Tioconazole		5.43	6.58	3.53	?		
	Albaconazole	Triazole	2.36	2	1.38	?		
	Efinaconazole		2.7	0.57	1.63	?		
	Fluconazole		0.25	1.64	0.09	100-1000	V	V
	Posaconazole		4.77	0.0495	1.34	10-100		
	Ravuconazole		3.74	3.73	2.63	?		
	Voriconazole		4.11	5.48	2.28	10-100		

^aValues predicted from EPI suite v1.4. with BioT Half-life, the whole body primary biotransformation rate estimate for fish ; BAF, the bioaccumulation factor at the highest level

^bfrom <https://www.blw.admin.ch>

^cFinal inclusion list for data dependent acquisition in new samples (i.e. sediment and biofilms)

? means that the actual use is unknown

Table S12. Predicted environmental concentrations (PEC) from the European Food Safety Authority (EFSA) dossiers. Values are expressed as the median of the PEC calculated from different scenarios of the FOCUS fate model.

	Surface water ($\mu\text{g/L}$)	Sediment (ng/g d.w.)
Bromuconazole	n.f.	n.f.
Climbazole	n.f.	n.f.
Clotrimazole	n.f.	n.f.
Cyproconazole	5.2	15.6
Difenconazole	1.4	3.7
Epoxyconazole	0.7	1.3
Fenamidone	13.2	45.6
Fenbucoconazole	2.6	68.6
Fluconazole	n.f.	n.f.
Flusilazole	n.f.	n.f.
Fuberidazole	0.7	4.3
Imazalil	0.45	21.5
Ketoconazole	n.f.	n.f.
Metconazole	1.2	79.3
Myclobutanil	0.47	0.78
Paclobutrazole	1.2	2.2
Penconazole	2.75	57.5
Prochloraz	8.1	125.3
Propiconazole	0.7	4.8
Prothio-desethio	1.2	3.2
Tebuconazole	0.8	2.5
Triadimenol	3.5	5.2
Triflumizole	0.06	0

n.f. not found

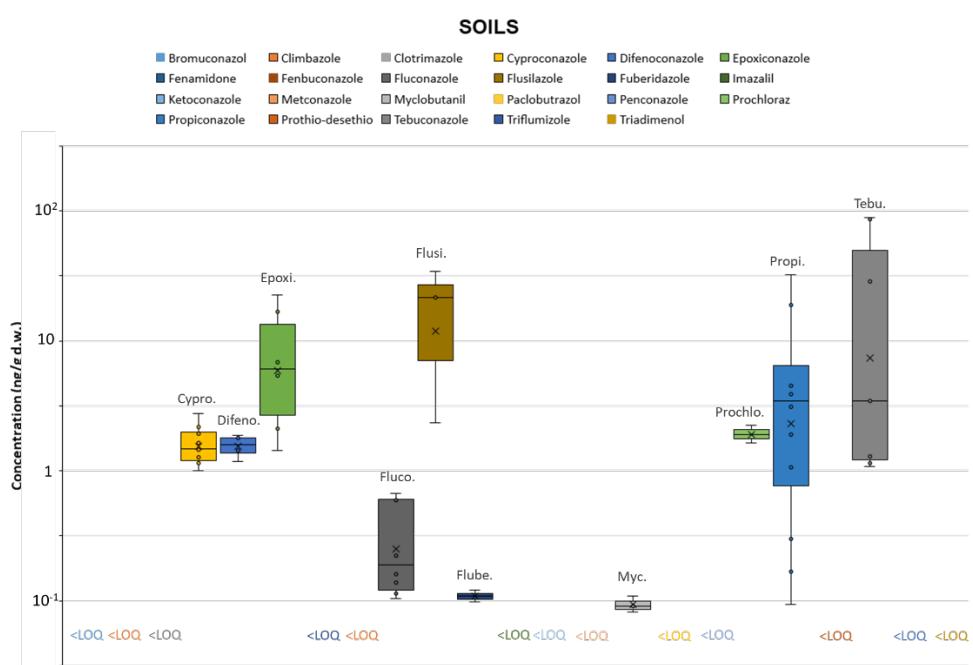


Figure S4. Level of antifungal azoles in soils. Results are expressed in ng/g_{dry} weight of soil. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

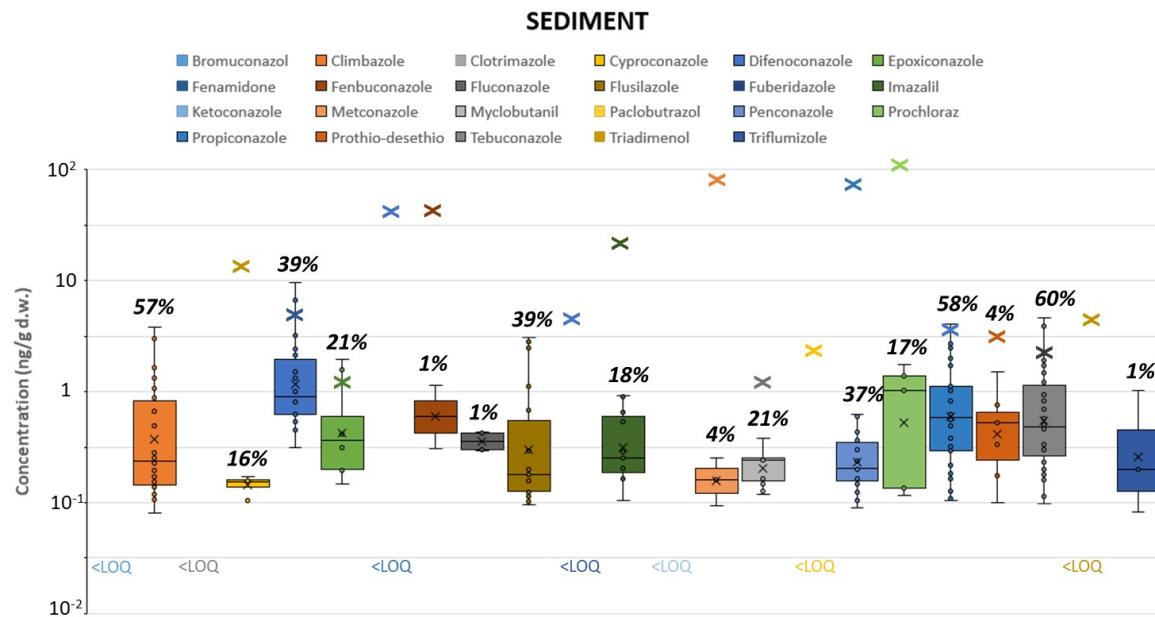


Figure S5. Level of antifungal azoles in sediments. Results are expressed in ng/g_{dry} weight sediment. Colored crosses are the PEC values from the EFSA calculated as the mean of FOCUS modeled values. Percentage values are the detection frequency of the compounds. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

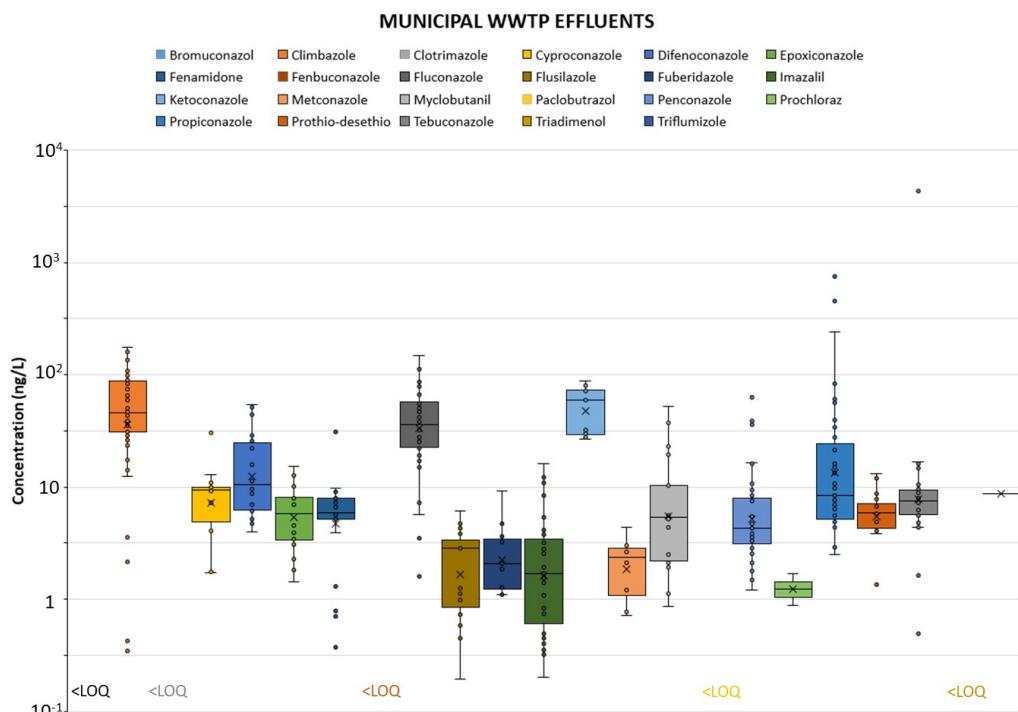


Figure S6. Level of antifungal azoles in municipal effluents. Results are expressed in ng/L of water. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

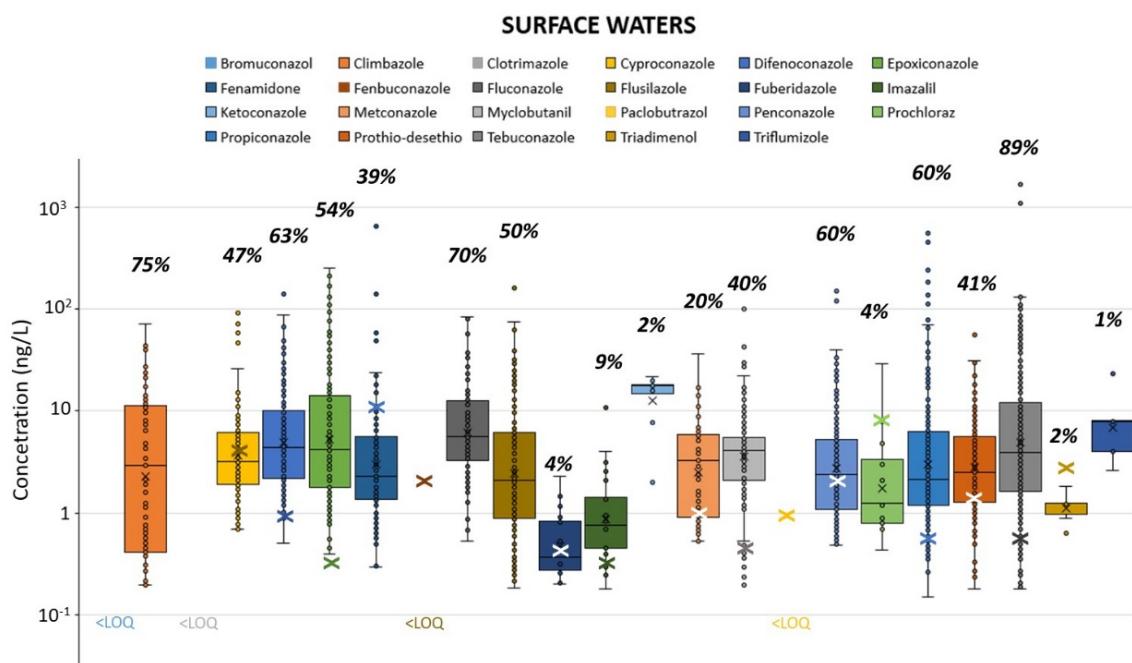


Figure S7. Level of antifungal azoles in surface waters. Results are expressed in ng per liter of water. Colored crosses are the PEC values from the EFSA calculated as the mean of FOCUS modeled values. Percentage values are the detection frequency of the compounds. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

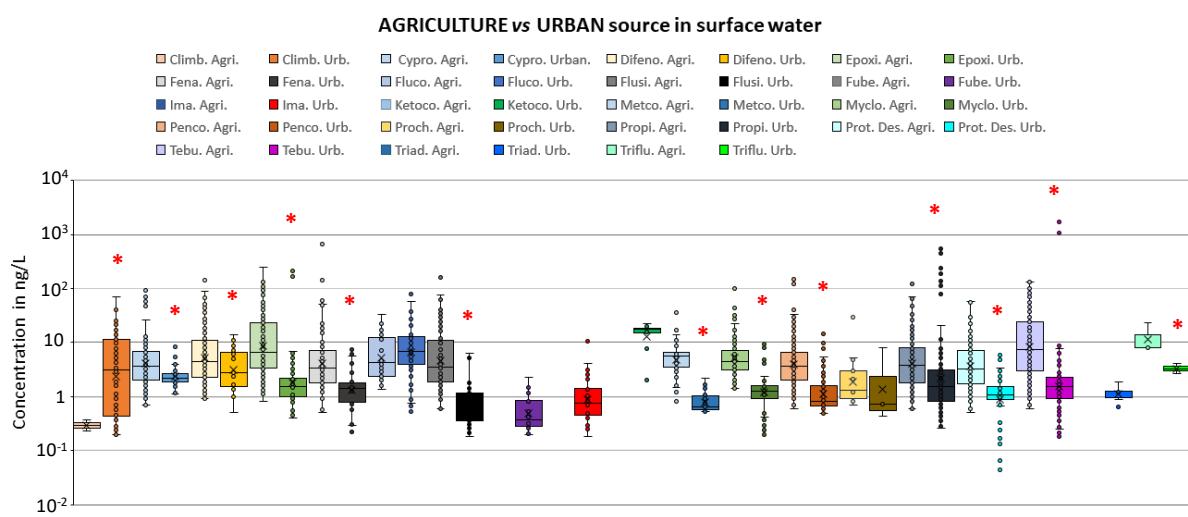
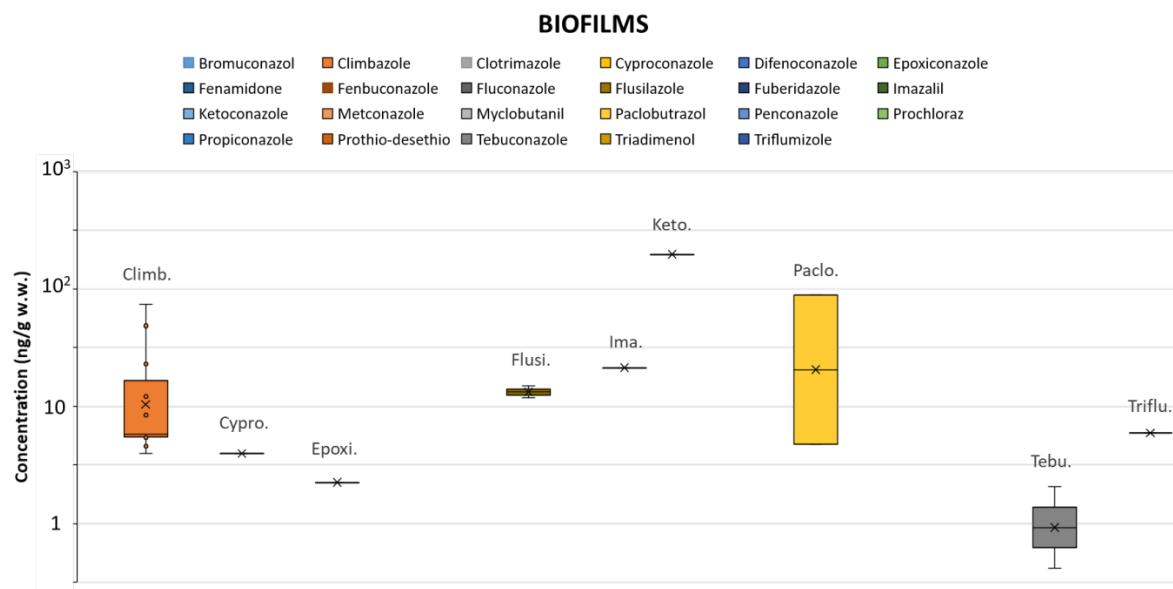
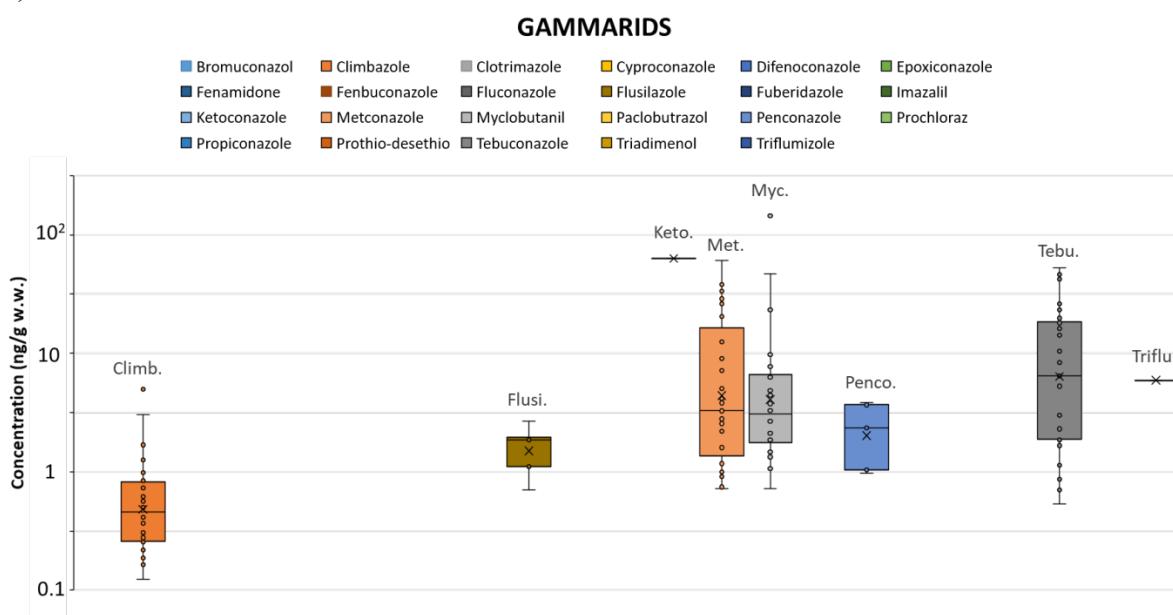


Figure S8. Comparison of level of antifungal azoles in surface waters under agricultural or urban pressure. Results are expressed in ng per liter of water. *, significant statistical difference from student t.test ($p<0.01$) between agriculture and urban conditions. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

A)



B)



C)



D)

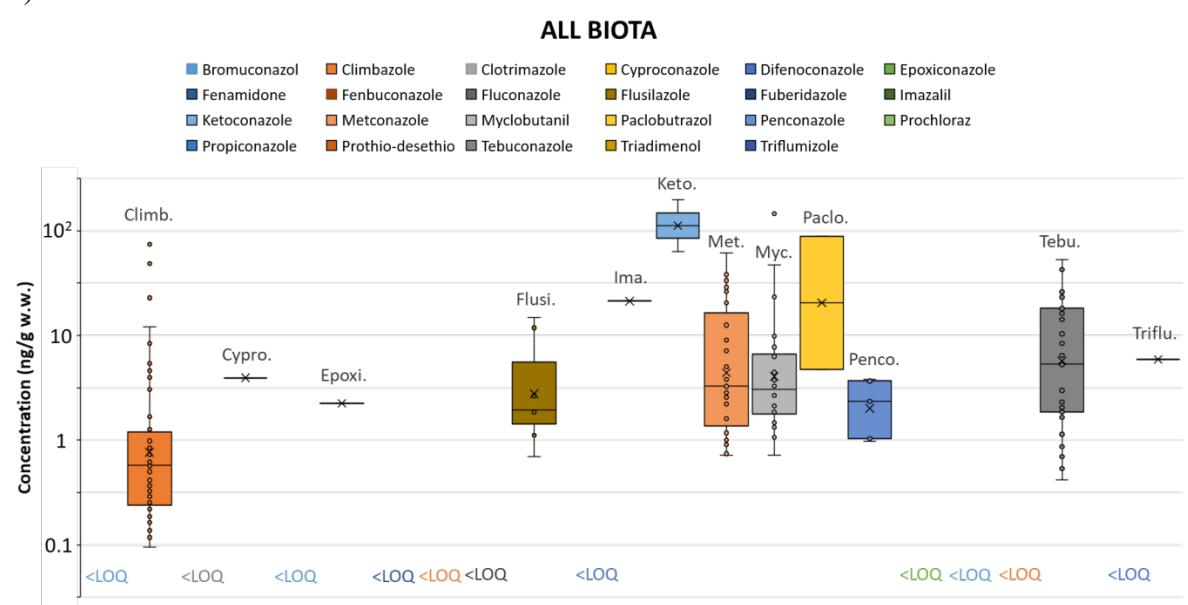


Figure S9. Level of antifungal azoles in biofilms (A), gammarids (B), fish (C) and all biota (D). Results are expressed in ng/g wet weight. Concentration axis is in log scale. Colored <LOQ refer to investigated chemical investigated but below the LOQ.

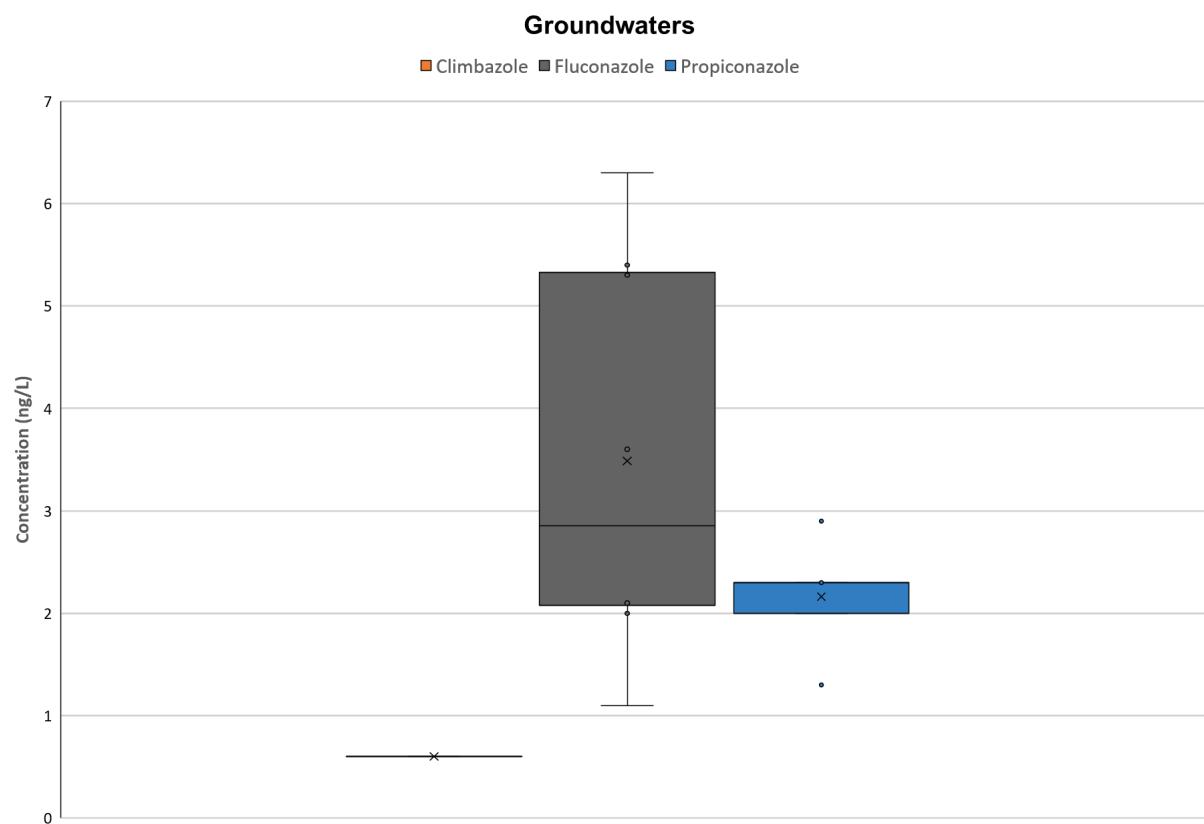


Figure S10. Level of antifungal azoles in groundwaters. Results are expressed in ng/L. Concentration axis is in log scale.

Only three azoles were detected in this compartment

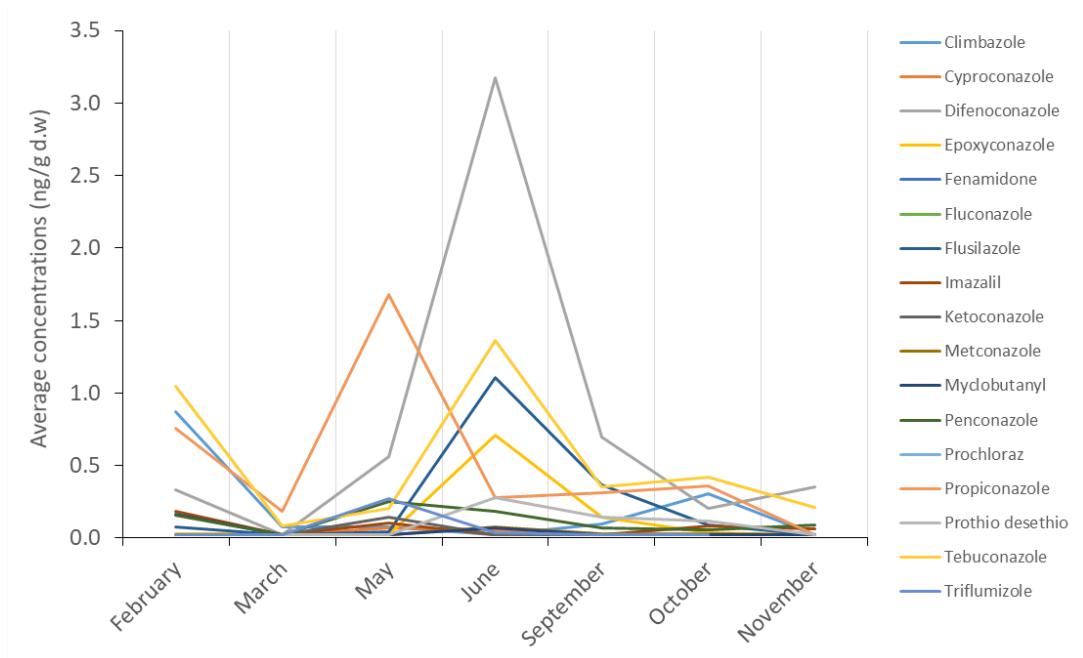


Figure S11. Seasonal trends of azoles in surface waters. Results are expressed as median concentration for all surface waters.

Section 5. Partitioning modelling and BAF calculation

Fugacity model

In the present study, we compared the actual concentration of antifungal azoles to the predicted ones by the fugacity model. To this end, we used the freely available software from the University of Trent.

(<https://www.trentu.ca/academic/aminss/envmodel/models/models.html>).

To model the distribution of antifungal azoles, we used the EQC – standard environment parameters of the software with slight modification at the lipid fraction (i.e. 0.027 is the average lipid content in gammarids, 0.06 for biofilms and 0.05 for fish) (Table S13).

Table S13. Environmental parameters used to implement the fugacity model level I

Compartments	Volume (m ³)	Density (kg/m ³)	Organic carbon (g/g)	Lipid fraction (g/g)
Air	1.e14	1.19	-	-
Aerosol	2.e3	2000	-	-
Water	2.e11	1000	-	-
Suspended particles	1.e6	1500	0.2	-
Fish	2.e5	1000	-	0.027
Soil	9.e9	2400	0.02	-
Sediment	1.e8	2400	0.04	-

In addition, we used the physico-chemical properties of the chemicals provided in the Pesticides Properties Database (PPDB), <https://sitem.herts.ac.uk/aeru/ppdb/>; Pubchem, <https://pubchem.ncbi.nlm.nih.gov/>; or Chemspider <http://www.chemspider.com/> websites) or modelled from EPI suite (i.e. pharmaceuticals) and the total used amount in Switzerland provided by the Federal office of Agriculture (<https://www.blw.admin.ch/blw/en/home.html>) (Table S14).

As emission amount, we use the total use per year in Switzerland as reported in the **table S4**

Table S14. Concentration of antifungal azoles in the pore water calculated from the equilibrium partitioning model. Results are expressed in ng/L.

		Climb	Cyprocon	Epoxicon	Flusilazol	Propiconol	Tebucon	Difenocon	Metcon	Myclobutanil	Pencon	Triflumizole	BTS44595	Prothiodesethio	Fenbucone	Imazalil	Ketocon
	foc																
SED1	0.021					14.1											
SED2	0.028					1.0											
SED3	0.0044	7.1		14.1	0.0												
SED4	0.02165	0.5		6.3	1.8							2.7					
SED5	0.006					33.1	30.3										
SED6	0.016																
SED7	0.0018	14.6				85.8	63.2										
SED8	0.0003	45.6															
SED9	0.05	0.2				3.9											
SED10	0.06	0.3				3.2		0.6			0.4						
SED11	0.04	0.5	13.3		1.0	70.3	8.8	2.4			5.6						
SED12	0.03	0.4	12.1		2.2	109.4	9.7	4.0			8.1						
SED13	0.07					12.1					0.3						
SED14	0.02	2.1				100.8	29.2	9.3			9.0			1.5	6.1	13.4	
SED15	0.0076	3.5		10.3	8.7	76.3	66.7	3.2					#DIV/0!				
SED16	0.0078	2.5			5.7	72.5	60.9	3.4					#DIV/0!				
SED17	0.0415	2.6		7.1	9.8	54.4	99.6	10.0	2.0		2.2		#DIV/0!	#DIV/0!			
SED18	0.042	0.6				3.6	4.1										
SED19	0.045	0.7				6.0	6.8										
SED20	0.015	0.6				32.4											
SED21	0.091	0.4				3.3	5.4										
SED22	0.038																
SED23	0.0105			36.9	3.9		45.7	2.8		21.9			#DIV/0!	#DIV/0!			
SED24	0.0442		9.8	41.6	41.4	21.9	105.6	6.2	5.1		0.5		#DIV/0!	#DIV/0!			
SED25	0.0431				15.7		3.9	2.5			3.1	17.3					
SED26	0.0213			19.2	5.0		8.2	57.9		11.4	8.1		#DIV/0!				
SED27	0.029			6.3	1.5		8.7	4.5					#DIV/0!	#DIV/0!			
SED28	0.0397		7.3	36.9	43.0	19.0	48.8	21.7	3.6				#DIV/0!	#DIV/0!			
SED29	0.0386				38.9		18.3	2.7	0.0		7.0	3.8					
SED30	0.0168			11.0	4.1		6.0	18.4	0.0	8.6	6.5		#DIV/0!				
	Koc	4517	364	1073	1664	1086	992	7730	1116	517	2205	1373			4425	4753	3103

Calculations were based on the following equation $Cipw = Cised / Koc \times foc$ with $Cipw$ is the concentration of the compound i in the pore water, $Cised$ the concentration in the sediment, Koc the partitionning coefficient of the compound and foc the fraction of organic carbon in the sediment.

Table S15. Physico-chemical properties of investigated antifungal azoles

Compounds	Class	Molecular mass (g/mol)	Vapor Pressure (Pa) ^a	Water solubility (g/m3) ^a	Melting point (°C) ^a	LogKow ^b	BioT 1/2 life (d) ^b	Log BAF ^b	Persistence (d) ^b	Soil DT50 (d) ^c	Water- Sediment DT50 (d) ^c	Water DT50 (d) ^c	Use (Kg) ^d
Imazalil		297.18	1.6E-04	184	51.5	4.1	4.57	2.71	113.8	76.3	117.0	7.8	100.0
Prochloraz	Imidazole	376.7	1.5E-04	26.5	48.3	4.13	70.8	3.29	225.8	120.0	359.0	2.0	100000.0
Triflumizole		345.75	1.9E-04	10.5	63	1.5	3.08	0.55	420.8	13.0	81.3	2.7	1000.0
Azaconazole		300.14	5.3E-07	300	112.6	2.73	1.82	1.35	108.3	-	-	-	Forbiden
Bitertanol		347.42	1.4E-09	3.8	118	4.07	8.26	3.03	78.8	23.0	39.2	27.0	10000 ^e
Bromuconazole		377.06	4.0E-06	48.3	84	3.54	4.52	2.23	120.8	190.0	275.0	1.7	10000 ^e
Cyproconazole		291.78	2.6E-05	93	106.5	3.09	2.9	1.9	116.3	142.0	1000.0	-	100000
Difenoconazole		406.26	3.3E-08	15	82.5	5.2	21.2	3.31	343.3	130.0	1053.0	3.0	100000
Epoxiconazole		329.76	1.0E-05	7.1	136.7	3.47	5	2.41	371.3	354.0	119.8	65.8	100000
Fenamidone		311.4	3.4E-07	7.8	136.8	3.45	0.33	1.97	87.5	6.9	97.0	24.0	100000
Fenbuconazole		336.82	3.4E-07	2.47	126.5	4.23	3.23	2.2	128.3	60.0	3.4	-	1000.0
Fluquinconazole		376.17	6.4E-06	1.15	191	3.73	10.6	2.25	326.3	350.0	13.7	3.5	100000
Flusilazole		315.39	3.9E-05	41.9	53.2	4.89	55.4	2.9	295.8	300.0	365.0	1.0	100000
Fuberidazole	Triazoles	184.19	9.0E-07	71	292	2.37	0.551	1.61	32.6	6.0	15.1	0.6	10000 ^e
Metconazole		319.83	2.1E-08	30.4	104.2	3.85	4.58	2.56	118.3	142.2	465.0	8.0	10000
Myclobutanil		288.78	2.0E-04	132	70.9	3.5	5.35	1.95	78.3	560.0	626.0	12.0	10000
Paclobutrazol		293.8	1.9E-06	22.9	164	3.36	2.5	2.16	116.3	112.0	787.0	164.0	100000
Penconazole		284.18	3.7E-04	73	60.3	4.67	15.3	3.55	117.5	117.0	853.0	2.0	10000
Propiconazole		342.22	5.6E-05	150	87.1	4.13	6.2	2.64	115.8	71.8	561.0	6.0	100000
Prothioconazole		344.26	7.4E-06	22.5	140.3	3.09	0.25	1.75	199.2	14.1	-	-	100000
Prothio.-destho		312.194	1.1E-06	25.97	164.73	3.05	1.96	2.02	310.8	-	-	-	10000 ^e
Tebuconazole		307.822	1.7E-06	36	105	3.89	5.13	2.64	118.3	63.0	365.0	242.6	100000
Triadimenol		295.76	5.0E-07	72	132.5	2.95	2.79	2.06	104.2	250.0	91.0	53.0	10000
Triticonazole		317.81	1.0E-06	9.3	137	4.11	5.48	2.28	107.1	237.0	392.0	158.0	100
Climbazole		292.77	9.6E-05	8.281	153.07	3.76	4.78	2.67	108.3	300.0	-	-	10000^e
Clotrimazole	Imidazoles	344.842	5.0E-06	3.7	155	6.26	41.8	5.59	202.5	-	-	-	10000
Ketoconazole		531.431	8.5E-12	0.0866	146	4.45	0.991	2.55	365.8	-	-	-	10000^e
Fluconazole	Triazoles	306.277	2.1E-06	1	138	0.25	1.64	0.09	337.1	-	-	-	1000

^a, From PPDB, Chemspider or PubChem websites ; ^b, calculated from EPISuite1.4 ; ^c, from PPDB; ^d, values from the federal office for Agriculture (FOAG); ^e, actual values unknown, mean value of the usage class was used instead

In blue and bold are the chemicals at least detected in three compartments and so use for the partitioning modeling (see below)

In Green, less persistent; in Yellow, Moderately persistent; in Orange: persistent; In Red, very persistent [EU Guidance. (9188/VI/97 rev. 8.)]

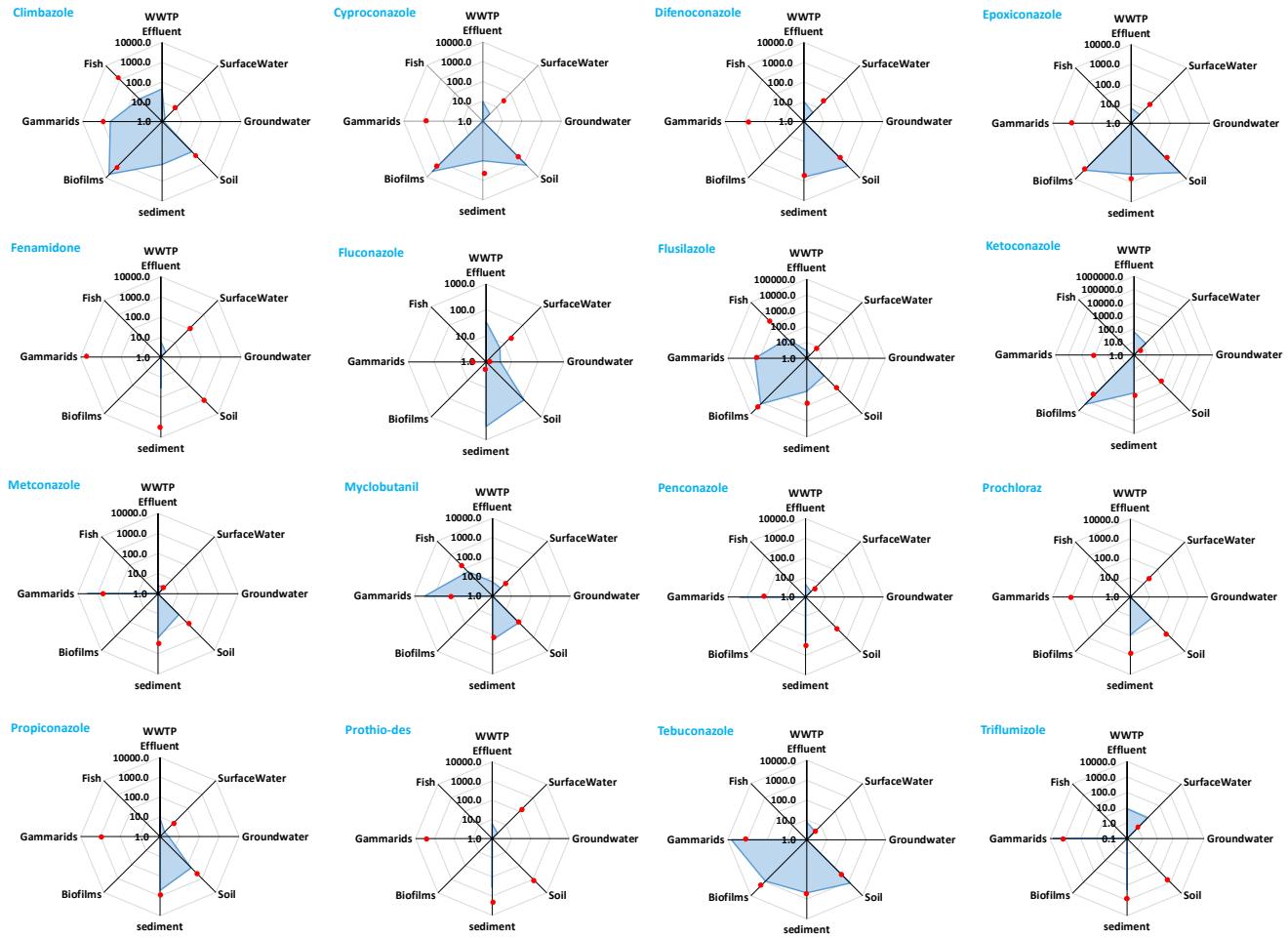


Figure S12. Comparison between actual and predicted partitioning of detected antifungal azoles between environmental compartments. Results are expressed in ng/L (WWTP, surface water or groundwater) or in ng/kg d.w (sediment, soil) and ng/kg w.w (biota). Red dots represent the values predicted by the fugacity model level I. Only chemicals detected in at least 3 compartments were used for the calculation.

Table S16. Log bioaccumulation factor (BAF) from detected azoles in gammarids and fish: literature vs predicted (EPI suite & Fugacity) vs apparent field values. Results are expressed in L/kg lipid weight with lipid content of 2.7% in gammarids and 5% in fish.

	Gammarids				Fish			
	Munz et al. 2018	EPI suite	Fugacity	Field	Literature	EPI suite	Fugacity	Field
Climbazole	2.8	4.11	3.76	3.45	-	3.97	3.76	3.69
Flusilazole	-	4.14	3.87	4.58	-	3.80	3.83	4.28
Metconazole	-	4.08	3.85	4.12				
Myclobutanil	-	3.34	2.89	3.68	-	3.26	2.89	3.82
Penconazole	3.4	5.05	3.72	4.97	-	-	-	-
Tebuconazole	3.1	4.07	3.70	4.06	-	-	-	-

Section 6. Environmental Risk Assessment of antifungal azoles

To assess the environmental risk related to the occurrence of antifungal azoles, we used the quality standards (QS) provided in the literature (INERIS, Ecotox Center (Switzerland),

Moschet et al. 2014). For those without QS values, we calculated them as described in the Technical Guidance Document (TGD) [9].

For water, since we did not have enough ecotoxicity data, we used the assessment factor (AF) method for chronic exposure based on the most sensitive species by using the following equation.

$$QS_{fw, eco} = \frac{NOEC \text{ min}}{AF}$$

To this end, we used the NOEC (No Observable Effect Concentration) values provided by the literature (INERIS) and the AF values defined as following: 10 for chemicals with results from at least three species representing three trophic levels. 50 for chemicals, with two trophic level results; 100 for chemicals with one long-term result. Values of NOEC, AF and calculated QS and those from the literature are provided in the **table S15**. The lowest QS values were used as $QS_{fw, eco}$ for further calculation

Table S17. Parameters for calculation of environmental quality standards in fresh surface water

Chemicals	NOEC algae & plants	NOEC invertebrates	NOEC vertebrates	AF	Calculated QS_{fw}	INERIS QS_{fw}	Moschet al. 2014 QS_{fw} ug/L	Lowest $QS_{fw, eco}$ $\mu\text{g/L}$
	$\mu\text{g/L}$	$\mu\text{g/L}$	$\mu\text{g/L}$		$\mu\text{g/L}$	$\mu\text{g/L}$		
Climbazole	n.a.	n.a.	n.a.	-	-	-	-	-
Clotrimazole	n.a.	n.a.	n.a.	-	-	-	-	-
Cyproconazole	6	19	125	10	0.6	0.6	18.9	0.6
Difenoconazole	8.6	5.6	7.6	10	0.56	0.56	0.76	0.56
Epoxyconazole	1.8	630	10	10	0.18	0.2	0.19	0.18
Fenamidone	900	9.5	70	10	0.95	-	1.25	1
Fenbuconazole	290	78	23	10	2.3	2	-	2.0
Fluconazole	n.a.	n.a.	n.a.	-	-	-	-	-
Flusilazole	n.a.	n.a.	n.a.	-	-	-	1	1
Fuberidazole	n.a.	120	n.a.	100	1.2	-	-	1.2
Imazalil	457	25	225	10	2.5	2.5	-	2.5
Ketoconazole	n.a.	n.a.	n.a.	-	-	-	-	-
Metconazole	n.a.	160	2.91	50	0.0582	-	-	0.06
Myclobutanil	n.a.	1000	200	50	4	-	55	4
Paclbutrazole	n.a.	320	3300	50	6.4	-	-	6.4
Penconazole	96	60	320	10	6	6	-	6
Prochloraz	n.a.	22.2	24.9	50	0.444	-	-	0.4
Propiconazole	16	205	68	10	1.6	1.6	1.8	1.6
Prothio-desthio	73	100	3340	10	7.3	-	-	7.3
Tebuconazole	34.2	10	6.25	10	0.625	1	1.2	0.6
Triadimenol	n.a.	100	3130	50	2	-	-	2
Triflumizole	n.a.	180	44	50	0.88	-	-	0.88

AF, Assessment factor ; n.a. not available ; - cannot be calculated ; fw, freshwater

For sediment, we use the Equilibrium Partitioning (EqP) method to calculate the $QS_{sed, EqP}$. This method is usually employed if no reliable sediment toxicity data are available to estimate the QS. Thus, the $QS_{sed, EqP}$ was calculated with the following equation (EC, 2011):

$$QS_{sed, EqP, ww} \left[\frac{\mu\text{g}}{\text{kg}} \right] = \frac{K_{sed-water}}{RHO_{sed}} * QS_{fw, eco} \left[\frac{\mu\text{g}}{\text{L}} \right] * 1000$$

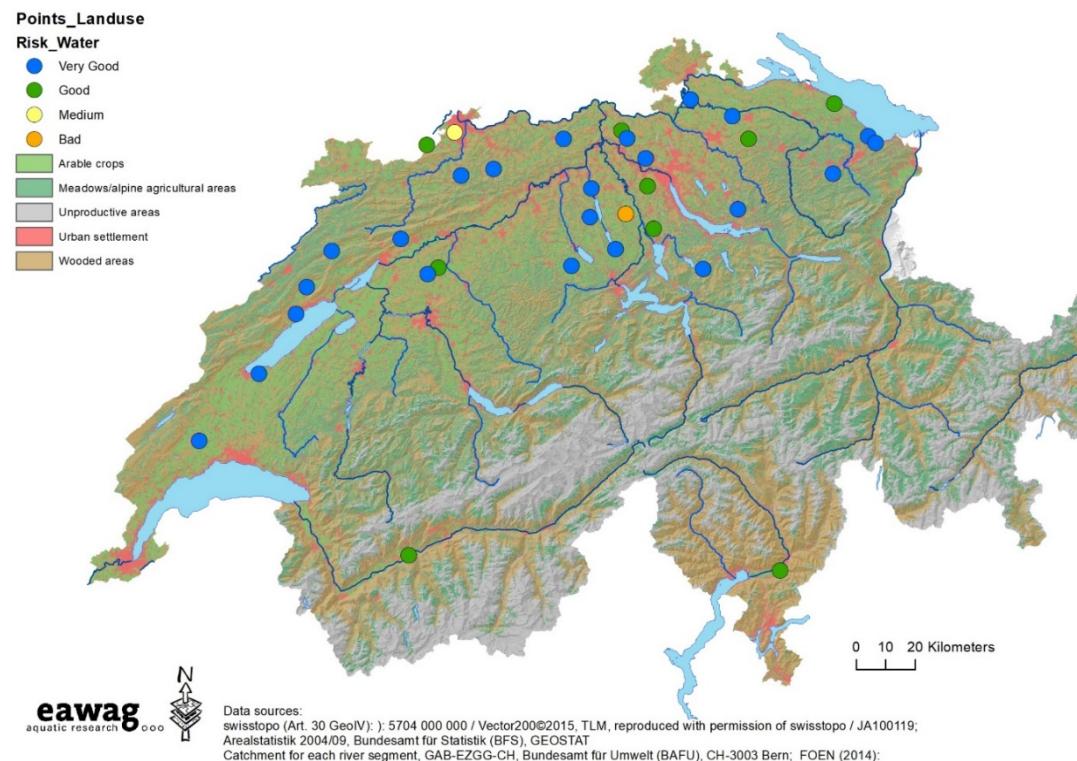
In this study, we used the selected AA-QS_{sw} and default values of Foc_{sed} (0.05), Fair_{sed} (0), Fwater_{sed} (0.8), RHO_{solid} (2500), RHO_{sed} (1300), Fsolid_{sed} (0.2) and Koc from the literature (INERIS). All the values and resulting calculations are presented in the **table S16**.

Table S18. Parameters for calculation of quality standards in sediment

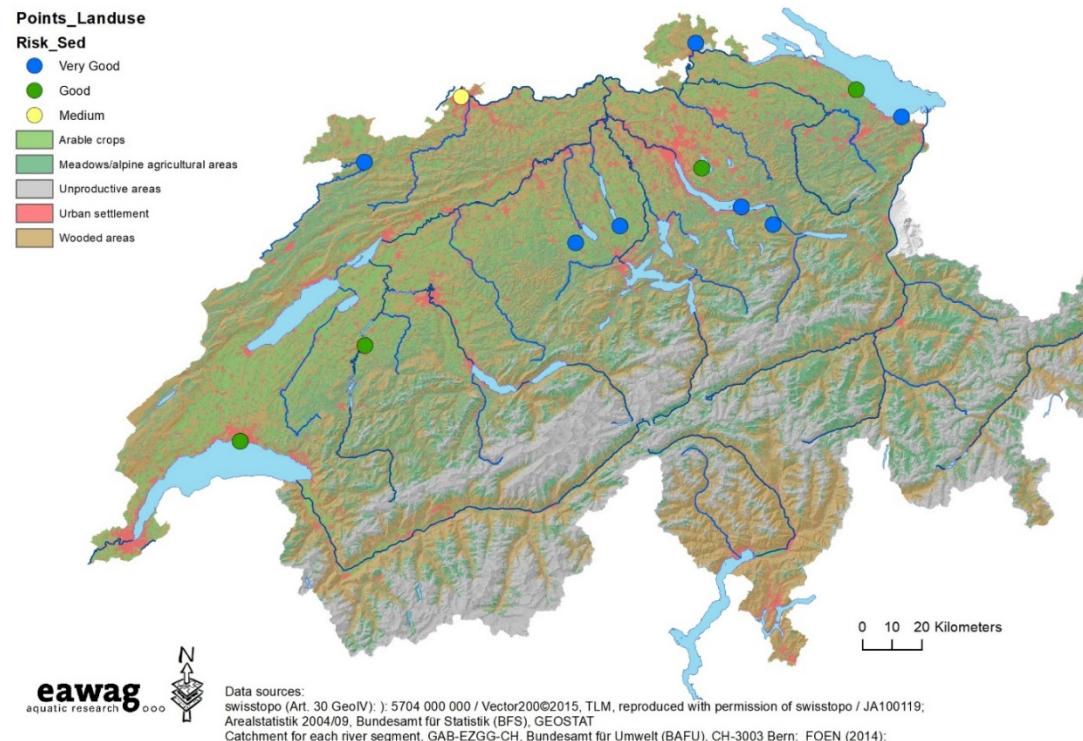
	AA-QS _{fw}	Koc	Foc	Kp _{sed}	Ksed-water	Fair _{sed}	Fwater _{sed}	Fsolid _{sed}	QS sed, EqP, ww	Rho solid	Rho sed	Fsolid sed	Conv	INERIS QS _{sed}	Selected AA-QS _{sed} , ng/g d.w.
	μg/L	ng/g w.w											ug/kg d.w.	ng/g d.w.	
Climbazole	n.c.	-	-	-	-	-	-	-	-	-	-	-	-	-	n.a.
Clotrimazole	n.c.	-	-	-	-	-	-	-	-	-	-	-	-	-	n.a.
Cyproconazole	0.6	364	0.05	18.2	9.9	0	0.8	0.2	4.6	2500	1300	0.2	2.6	10	11.9
Difenoconazole	0.56	7730	0.05	386.5	194.1	0	0.8	0.2	83.6	2500	1300	0.2	2.6	500	217.3
Epoxyconazole	0.18	1073	0.05	53.7	27.6	0	0.8	0.2	3.8	2500	1300	0.2	2.6	3	3.0
Fenamidone	1	388	0.05	19.4	10.5	0	0.8	0.2	8.1	2500	1300	0.2	2.6	n.a.	21.0
Fenbucoconazole	2	4425	0.05	221.3	111.4	0	0.8	0.2	171.4	2500	1300	0.2	2.6	80	80.0
Fluconazole	n.c.	-	-	-	-	-	-	-	-	-	-	-	-	-	n.a.
Flusilazole	1	1664	0.05	83.2	42.4	0	0.8	0.2	32.6	2500	1300	0.2	2.6	n.a.	84.8
Fuberidazole	1.2	605	0.05	30.3	15.9	0	0.8	0.2	14.7	2500	1300	0.2	2.6	n.a.	38.2
Imazalil	2.5	4753	0.05	237.7	119.6	0	0.8	0.2	230.0	2500	1300	0.2	2.6	275	275.0
Ketoconazole	n.c.	-	-	-	-	-	-	-	-	-	-	-	-	-	n.a.
Metconazole	0.06	1116	0.05	55.8	28.7	0	0.8	0.2	1.3	2500	1300	0.2	2.6	n.a.	3.4
Myclobutanil	4	517	0.05	25.9	13.7	0	0.8	0.2	42.2	2500	1300	0.2	2.6	n.a.	109.8
Paclobutrazole	6.4	400	0.05	20.0	10.8	0	0.8	0.2	53.2	2500	1300	0.2	2.6	n.a.	138.2
Penconazole	6	2205	0.05	110.3	55.9	0	0.8	0.2	258.1	2500	1300	0.2	2.6	250	250.0
Prochloraz	0.4	1440	0.05	72.0	36.8	0	0.8	0.2	11.3	2500	1300	0.2	2.6	n.a.	29.4
Propiconazole	1.6	1086	0.05	54.3	28.0	0	0.8	0.2	34.4	2500	1300	0.2	2.6	250	89.4
Prothio-desthio	7.3	0.05	0.0	0.8	0	0.8	0.2	4.5	2500	1300	0.2	2.6	n.a.	11.7	
Tebuconazole	0.6	992	0.05	49.6	25.6	0	0.8	0.2	11.8	2500	1300	0.2	2.6	51	30.7
Triadimenol	2	750	0.05	37.5	19.6	0	0.8	0.2	30.1	2500	1300	0.2	2.6	n.a.	78.2
Triflumizole	0.88	1373	0.05	68.7	35.1	0	0.8	0.2	23.8	2500	1300	0.2	2.6	n.a.	61.8

AA, annual average; n.a. not available ; n.c. not calculated; w.w. wet weight; d.w. dry weight

A)



B)



C)

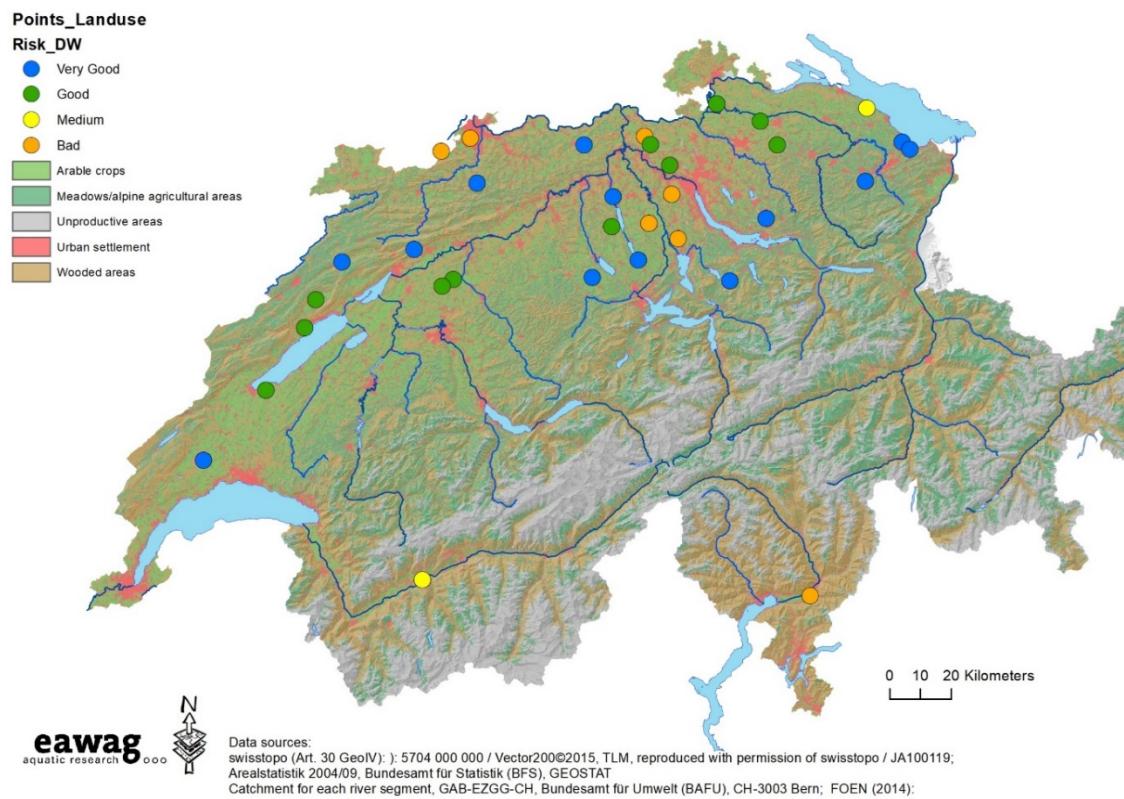


Figure S13. Risk Maps in surface water (A), sediment (B) and surface water used for drinking water (C). The risk presented here is the highest RQ among all the samples from a same site.

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