

## Electronic Supplementary Information

### **Determination of contaminants of emerging concern in raw pig manure as a whole. Difference with the analysis of solid and liquid phases separately.**

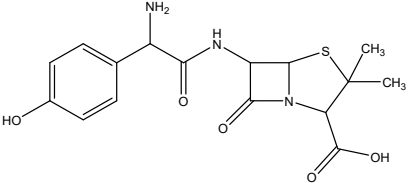
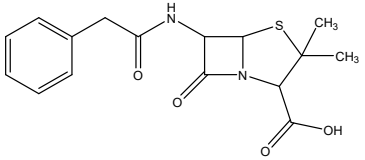
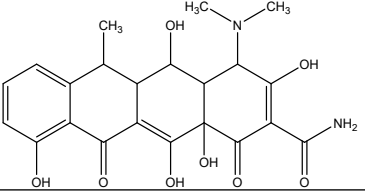
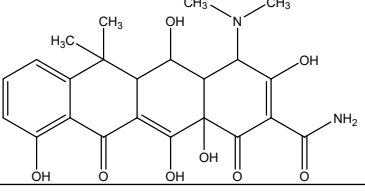
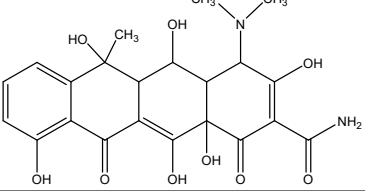
Cristina Portela-Monge<sup>a,b</sup>, Silvia Bolado<sup>b,c</sup>, Rebeca López-Serna<sup>a,b</sup>, Juan José Jiménez<sup>\*a,b</sup>

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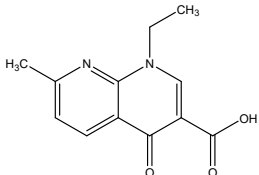
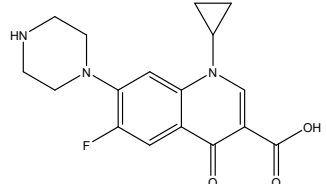
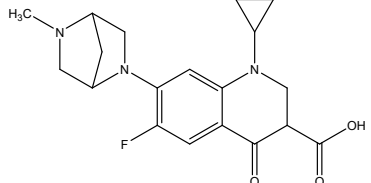
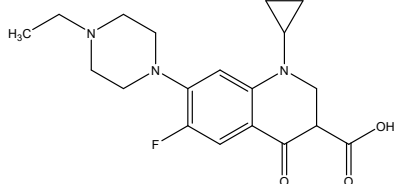
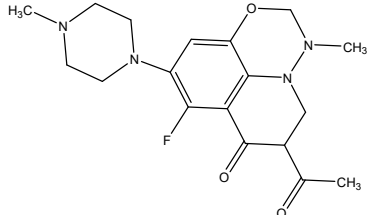
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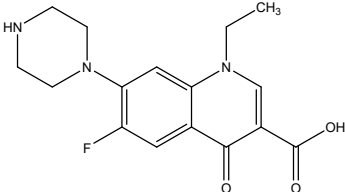
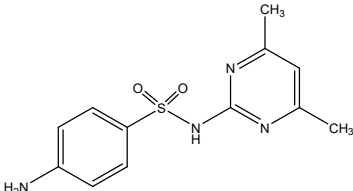
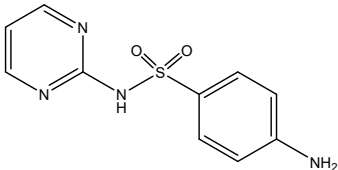
Supplementary data 1: List of target analytes, abbreviations, and their physicochemical properties (Source: Scifinder).

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Antibiotic	β-lactams	Amoxicillin (AMO)	365.4	C <sub>16</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub> S		Most Acidic: 2.44 Most Basic: 7.14	0.883
		Penicillin G (PEN)	334.39	C <sub>16</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub> S		Most Acidic: -1.32 Most Basic: 2.45	1.918
	Tetracyclines	Doxycycline (DOX)	444.43	C <sub>22</sub> H <sub>24</sub> N <sub>2</sub> O <sub>8</sub>		Most Acidic: 4.50 Most Basic: 10.84	1.777
		Oxytetracycline (OTC)	460.43	C <sub>22</sub> H <sub>24</sub> N <sub>2</sub> O <sub>9</sub>		Most Acidic: 4.50 Most Basic: 10.80	0.479
		Tetracycline (TTC)	444.43	C <sub>22</sub> H <sub>24</sub> N <sub>2</sub> O <sub>8</sub>		Most Acidic: 4.50 Most Basic: 11.02	0.617

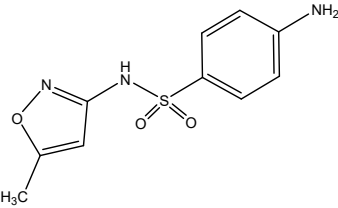
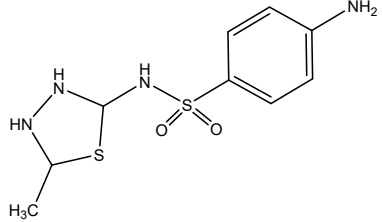
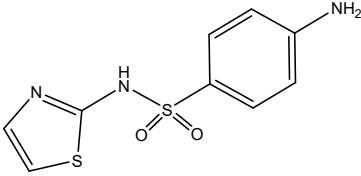
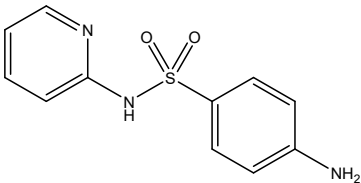
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C		
Antibiotic	Quinolones	Nalidixic acid (AND)	232.24	C <sub>12</sub> H <sub>22</sub> N <sub>2</sub> O <sub>3</sub>		Most Acidic: 3.45 Most Basic: 6.12	0.025		
		<b>Fluoroquinolones (quinolone subfamily):</b>							
		Ciprofloxacin (CIP)	331.34	C <sub>17</sub> H <sub>18</sub> FN <sub>3</sub> O <sub>3</sub>		Most Acidic: 6.43 Most Basic: 8.68	1.625		
		Danofloxacin (DAN)	357.38	C <sub>19</sub> H <sub>20</sub> FN <sub>3</sub> O <sub>3</sub>		Most Acidic: 6.43 Most Basic: 9.00	1.811		
		Enrofloxacin (ENR)	359.39	C <sub>19</sub> H <sub>22</sub> FN <sub>3</sub> O <sub>3</sub>		Most Acidic: 6.43 Most Basic: 7.76	2.306		
		Marbofloxacin (MAR)	362.36	C <sub>17</sub> H <sub>19</sub> FN <sub>4</sub> O <sub>4</sub>		Most Acidic: 6.02 Most Basic: 7.34	-0.641		

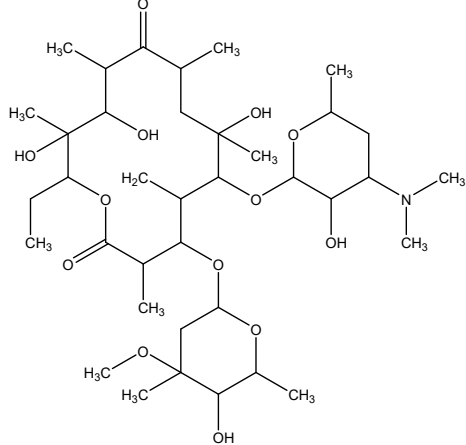
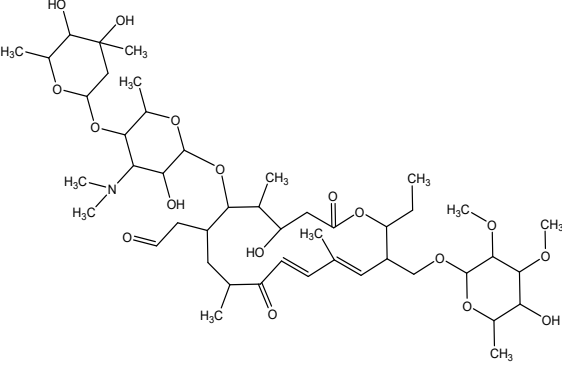
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Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Antibiotic	Quinolones	Norflloxacin (NOR)	319.33	C <sub>16</sub> H <sub>18</sub> FN <sub>3</sub> O <sub>3</sub>		Most Acidic: 0.16 Most Basic: 8.68	1.744
	Sulfonamides	Sulfadimidine (SDD)	278.33	C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S		Most Acidic: 1.69 Most Basic: 7.89	0.296
		Sulfadiazine (SDZ)	250.28	C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S		Most Acidic: 1.00 Most Basic: 6.81	-0.074

Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Antibiotic	Sulfonamides	Sulfamethoxazole (SMX)	253.28	C <sub>10</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub> S		Most Acidic: 1.39 Most Basic: 5.81	0.659
		Sulfamethizole (SMZ)	270.33	C <sub>9</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub>		Most Acidic: 2.07 Most Basic: 5.51	0.52
		Sulfathiazole (STZ)	255.32	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S <sub>2</sub>		Most Acidic: 2.19 Most Basic: 7.24	0.05
		Sulfapyridine (SPD)	249.29	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S		Most Acidic: 2.13 Most Basic: 8.54	0.469

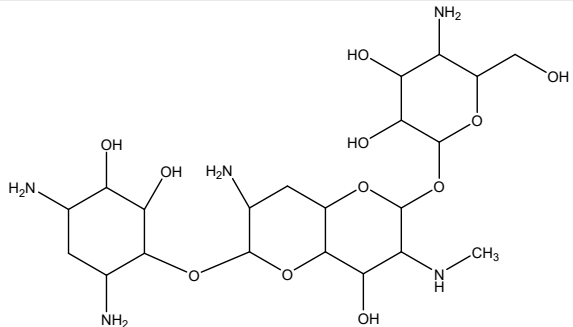
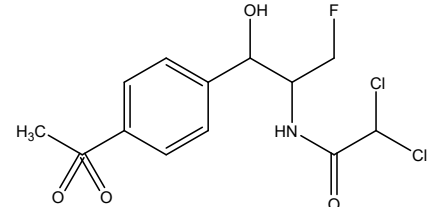
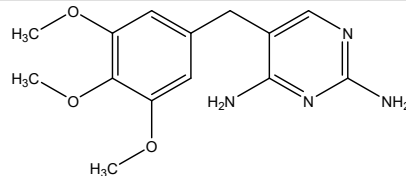
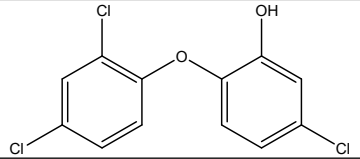
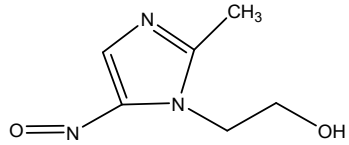
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Antibiotic	Macrolides	Erythromycin (ERY)	733.93	C <sub>37</sub> H <sub>67</sub> NO <sub>13</sub>		Most Acidic: 8.16 Most Basic: 13.09	1.909
		Tylosin (TYL)	916.1	C <sub>46</sub> H <sub>77</sub> NO <sub>17</sub>		Most Acidic: 7.39 Most Basic: 13.06	0.628

Supplementary data 1, continued.

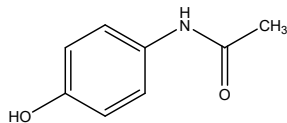
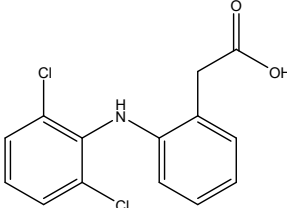
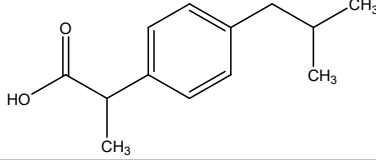
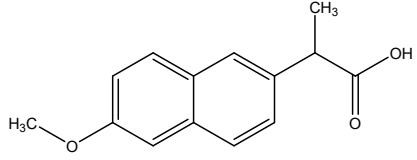
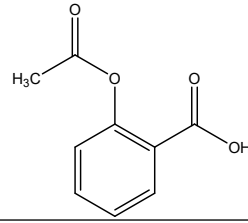
Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Antibiotic	Macrolides	Clarithromycin (CTM)	747.95	C <sub>38</sub> H <sub>69</sub> NO <sub>13</sub>		Most Acidic: 8.16 Most Basic: 13.08	2.805
	Pleuromutilins	Tiamulin (TIA)	493.74	C <sub>28</sub> H <sub>47</sub> NO <sub>4</sub> S		Most Acidic: 9.74 Most Basic: 14.65	4.38

Supplementary data 1, continued.

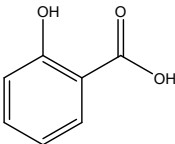
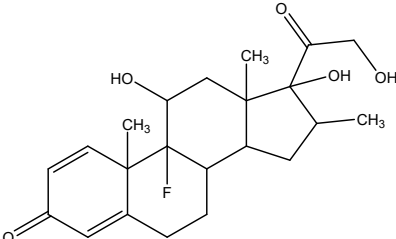
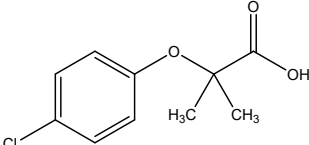
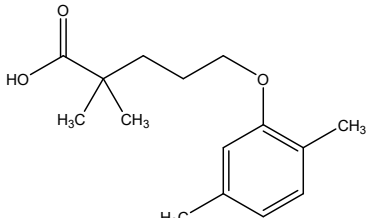
Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> p at 25°C
Antibiotic	Aminoglycosides	Apramycin (APR)	539.58	C <sub>21</sub> H <sub>41</sub> N <sub>5</sub> O <sub>11</sub>		Most Acidic: 9.48 Most Basic: 12.91	-3.427
	Phenicols	Florphenicol (FLO)	358.21	C <sub>12</sub> H <sub>14</sub> Cl <sub>2</sub> FNO <sub>4</sub> S		Most Acidic: 1.79 Most Basic: 10.73	1.175
	Diamino-pyrimidines	Trimethoprim (TMP)	290.32	C <sub>14</sub> H <sub>18</sub> N <sub>4</sub> O <sub>3</sub>		Most Acidic: 7.04 ±0.10	0.594
	Antimicrobials/ Antiprotozoals	Triclosan (TCS)		289.54	C <sub>12</sub> H <sub>7</sub> Cl <sub>3</sub> O <sub>2</sub>		Most Acidic: 7.80
Metronidazole (MTN)			171.15	C <sub>6</sub> H <sub>9</sub> N <sub>3</sub> O <sub>3</sub>		Most Acidic: 2.58 Most Basic: 14.44	-0.135



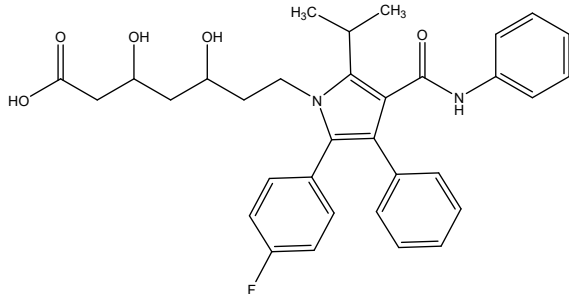
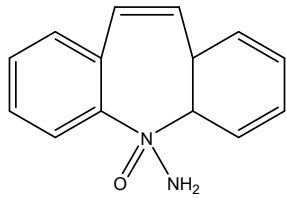
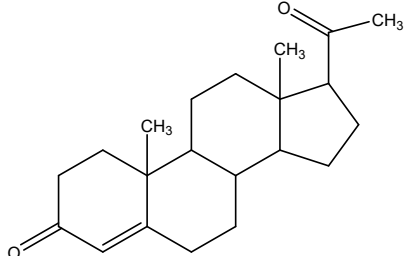
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> p at 25°C		
Analgesics/ Anti-inflammatories	Analgesics	Acetaminophen (AAF)	151.16	C <sub>8</sub> H <sub>9</sub> NO <sub>2</sub>		Most Acidic: 1.72 Most Basic: 9.86	0.475		
	NSAIDs (Nonsteroidal anti-inflammatory drug)	Diclofenac (DCF)	296.15	C <sub>14</sub> H <sub>11</sub> Cl <sub>2</sub> NO <sub>2</sub>		Most Acidic: -2.26 Most Basic: 4.18	4.548		
		Ibuprofen (IBP)	206.28	C <sub>13</sub> H <sub>18</sub> O <sub>2</sub>		Most Acidic: 4.41	3.502		
		Naproxen (NPX)	230.26	C <sub>14</sub> H <sub>14</sub> O <sub>3</sub>		Most Acidic: 4.84	2.876		
		<b>Salicylates (NSAID subfamily):</b>							
		Acetylsalicylic acid (AAS)	180.16	C <sub>9</sub> H <sub>8</sub> O <sub>4</sub>		Most Acidic: 3.48	1.399		

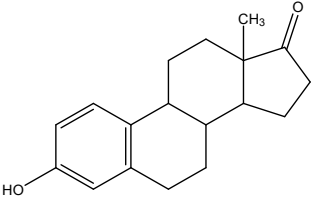
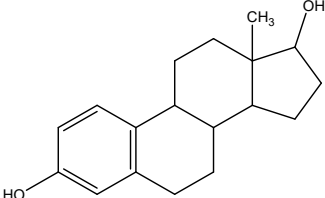
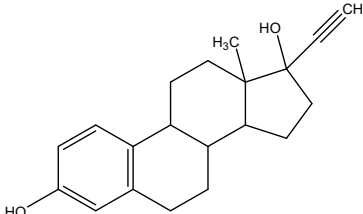
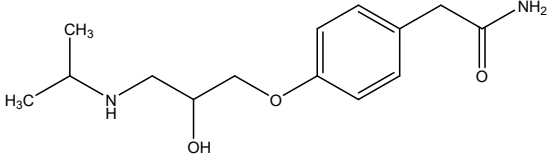
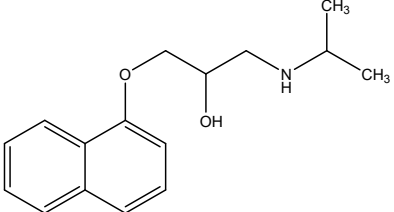
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> p at 25°C
Analgesics/ Anti-inflammatories	NSAIDs (Nonsteroidal anti-inflammatory drug)	Salicylic acid (ASC)	138.12	C <sub>7</sub> H <sub>6</sub> O <sub>3</sub>		Most Acidic: 3.01	2.011
	Corticoesteroid	Dexamethasone (DEX)	392.46	C <sub>22</sub> H <sub>29</sub> FO <sub>5</sub>		Most Acidic: 12.13	2.033
Lipid regulators	Active substance of fibrates	Clofibric acid (ACF)	214.65	C <sub>10</sub> H <sub>11</sub> ClO <sub>3</sub>		Most Acidic: 3.18	2.425
	Fibrates	Gemfibrozil (GEM)	250.33	C <sub>15</sub> H <sub>22</sub> O <sub>3</sub>		Most Acidic: 4.75	4.302

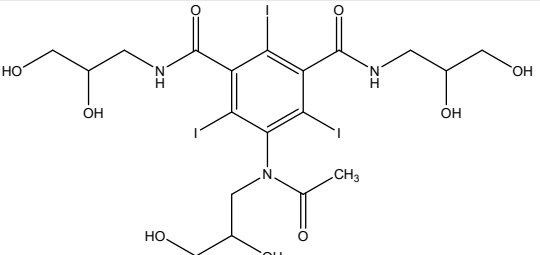
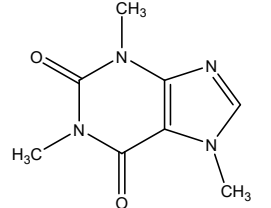
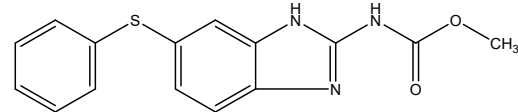
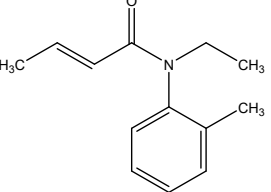
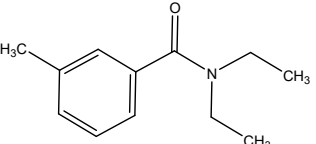
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Lipid regulators	Statins	Atorvastatin (ATV)	558.64	C <sub>33</sub> H <sub>35</sub> FN <sub>2</sub> O <sub>5</sub>		Most Acidic: 0.38 Most Basic: 4.29	3.846
Psychiatric drugs / anticonvulsants		Carbamazepine (CBM)	236.27	C <sub>15</sub> H <sub>12</sub> N <sub>2</sub> O		Most Acidic: -0.49 Most Basic: 13.94	1.895
Hormones	Natural hormones	Progesterone (PGT)	341.46	C <sub>21</sub> H <sub>30</sub> O <sub>2</sub>			3.827

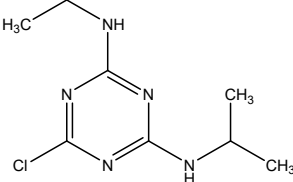
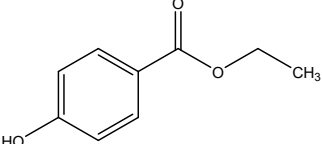
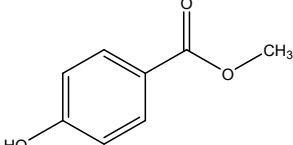
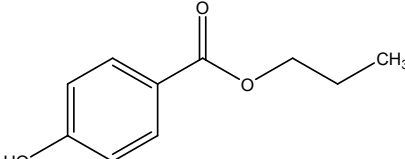
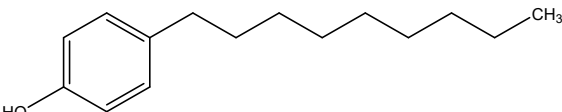
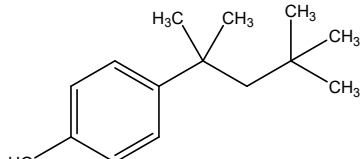
Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Hormones	Natural hormones	Estrone (E1)	270.37	C <sub>18</sub> H <sub>22</sub> O <sub>2</sub>		Most Acidic: 10.25	3.624
		17-β-estradiol (E2)	272.38	C <sub>18</sub> H <sub>24</sub> O <sub>2</sub>		Most Acidic: 10.27	4.146
	Synthetic hormones	17-α-ethinylestradiol (EE2)	296.4	C <sub>20</sub> H <sub>24</sub> O <sub>2</sub>		Most Acidic: 10.24	4.106
β-blockers	Cardiovascular drugs	Atenolol (ATN)	266.34	C <sub>14</sub> H <sub>22</sub> N <sub>2</sub> O <sub>3</sub>		Most Acidic: 9.43 Most Basic: 13.88	0.335
		Propranolol (PPN)	259.34	C <sub>16</sub> H <sub>21</sub> NO <sub>2</sub>		Most Acidic: 9.50 Most Basic: 13.84	2.9

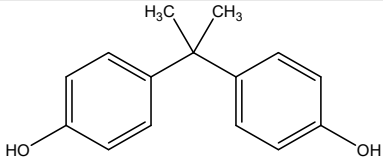
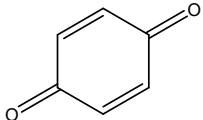
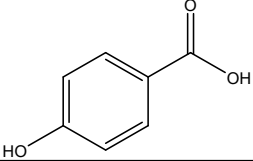
## Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> p at 25°C
Radiological contrast agent		Iohexol (IOH)	821.14	C <sub>19</sub> H <sub>26</sub> I <sub>3</sub> N <sub>3</sub> O <sub>9</sub>		Most Acidic: -2.72 Most Basic: 11.35	-2.921
Stimulants		Caffeine (CAF)	194.19	C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub>		Most Basic: 0.52	-0.628
Anti-parasitics	Benzimidazoles	Fenbendazole (FEN)	299.35	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S		Most Acidic: 5.25 Most Basic: 10.80	2.364
		Crotamiton (CRT)	203.28	C <sub>13</sub> H <sub>17</sub> NO		Most Basic: 1.14	2.464
Insect repellent		N,N-diethyl-meta-toluamide (DEET)	191.27	C <sub>12</sub> H <sub>17</sub> NO		Most Basic: -1.37	2.419

Supplementary data 1, continued.

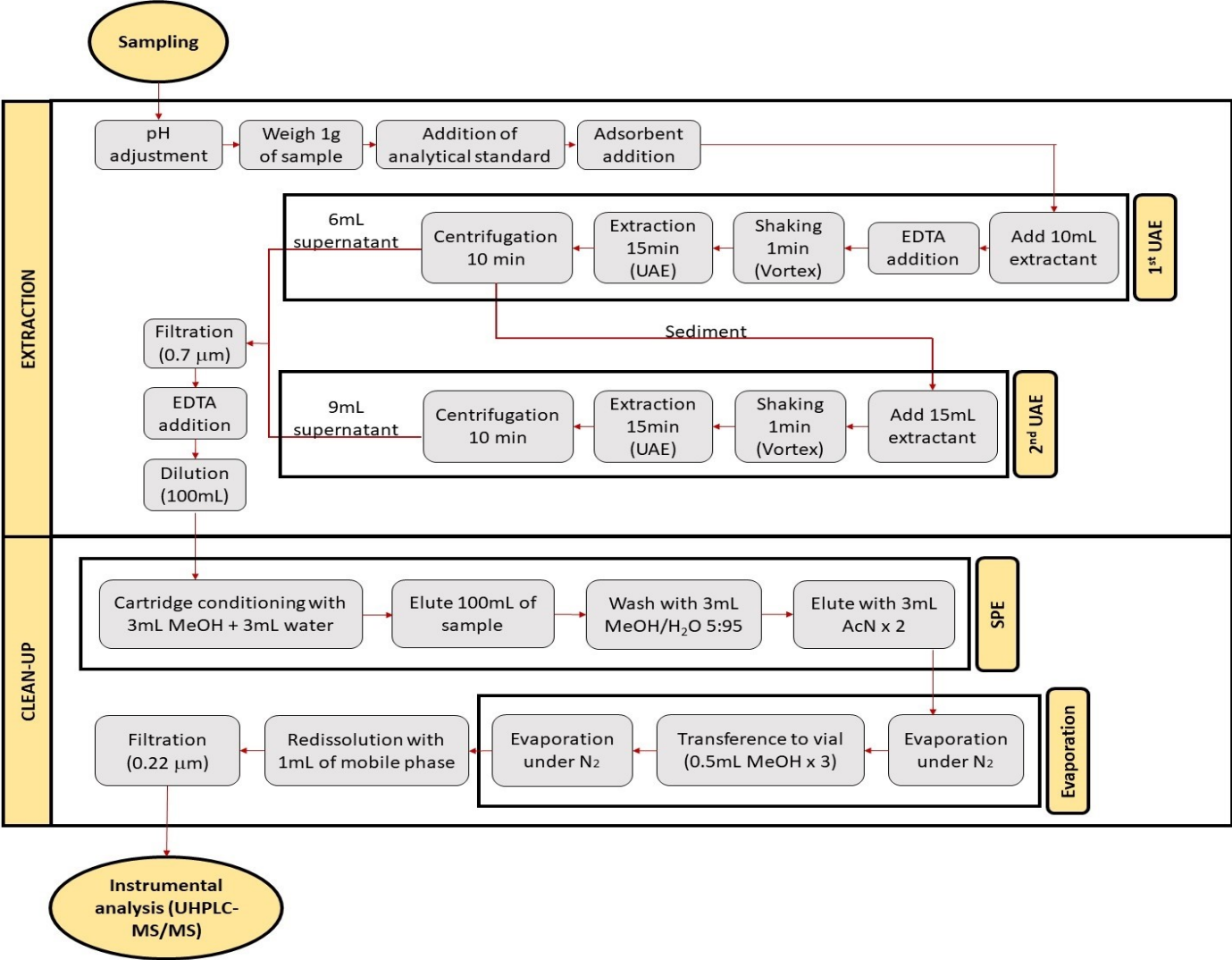
Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Herbicide		Atrazine (ATZ)	215.68	C <sub>8</sub> H <sub>14</sub> ClN <sub>5</sub>		Most Basic: 2.27	2.636
Preservatives	Parabens	Ethylparaben (EPR)	166.17	C <sub>9</sub> H <sub>10</sub> O <sub>3</sub>		Most Acidic: 8.31	2.391
		Methylparaben (MPR)	152.15	C <sub>8</sub> H <sub>8</sub> O <sub>3</sub>		Most Acidic: 8.31	1.882
		Propylparaben (PPR)	180.2	C <sub>10</sub> H <sub>12</sub> O <sub>3</sub>		Most Acidic: 8.23	2.901
Surfactants	Alkylphenols	4-nonylphenol (NNF)	220.35	C <sub>15</sub> H <sub>24</sub> O		Most Acidic: 10.15	6.142
		4-tert-octylphenol (TOP)	206.32	C <sub>14</sub> H <sub>22</sub> O		Most Acidic: 10.15	5.18

Supplementary data 1, continued.

Therapeutic class	Therapeutic subclass	Analytes	MW <sup>1</sup> (amu)	Molecular formula	Structure	pKa <sup>2</sup> at 25°C	log <sup>3</sup> P at 25°C
Plasticizers		Bisphenol A (BPA)	228.29	C <sub>15</sub> H <sub>16</sub> O <sub>2</sub>		Most Acidic: 10.29	3.641
Other compounds	p-quinones	1,4-Benzoquinone (BZQ)	108.09	C <sub>6</sub> H <sub>4</sub> O <sub>2</sub>			0.394
		4-hydroxybenzoic acid (AHB)	138.12	C <sub>7</sub> H <sub>6</sub> O <sub>3</sub>		Most Acidic: 4.57	1.401

<sup>1</sup>MW: Molecular Weight; <sup>2</sup>Ka: Acidity constant; <sup>3</sup>P: Partition coefficient

Supplementary data 2: Sample preparation process scheme.





**Supplementary data 3: SRMs and mass spectrometry instrumental conditions for the target analytes. Declustering potential (DP), collision energy (CE), and collision cell exit potential (CXP). The entrance potential (EP) voltage for initial ion collimation has hold at 10V and the observation time for each transition is 7 ms.**

RT (min)	Analytes	Q1 (m/z)	Q3 (m/z)	DP (volts)	CE (volts)	CXP (volts)
0.52	<b>ATN 1</b>	267.1	145.1	11	33	24
	ATN 2	267.1	190.3	11	29	4
0.54	<b>AMO 1</b>	365.9	348.9	26	13	28
	AMO 2	365.9	114.0	26	29	12
0.72	<b>MTN 1</b>	172.0	128.0	41	21	6
	MTN 2	172.0	82.0	41	35	14
0.72	<b>IOH 1</b>	821.8	804.0	126	33	26
	IOH 2	821.8	602.8	126	43	46
0.83	<b>AAF 1</b>	152.0	110.0	61	23	16
	AAF 2	152.0	108.9	61	55	14
1.05	<b>SDZ 1</b>	251.0	155.9	71	23	20
	SDZ 2	251.0	108.0	71	31	12
1.35	<b>STZ 1</b>	256.0	155.9	96	21	8
	STZ 2	256.0	108.1	96	33	12
1.42	<b>SPD 1</b>	250.1	156.1	61	23	10
	SPD 2	250.1	108.1	61	35	12
1.64	<b>TMP 1</b>	291.0	230.1	51	33	18
	TMP 2	291.0	261.1	51	35	16
2.22	<b>MAR 1</b>	362.9	320.1	66	23	24
	MAR 2	362.9	326.7	66	25	24
2.73	<b>TTC 1</b>	445.0	410.0	51	27	32
	TTC 2	445.0	427.1	51	19	32
2.90	<b>OTC 1</b>	461.0	426.1	151	27	30
	OTC 2	461.0	442.9	151	19	32
3.03	<b>SMZ 1</b>	270.9	156.0	31	21	10
	SMZ 2	270.9	108.1	31	35	12
3.04	<b>APR 1</b>	271.0	156.0	50	20	19
	APR 2	271.0	180.0	50	40	19
3.06	<b>CAF 1</b>	195.0	137.9	71	27	18
	CAF 2	195.0	110.0	71	31	16
3.19	<b>SDD 1</b>	279.0	186.0	86	25	22
	SDD 2	279.0	124.1	86	33	6
3.31	<b>NOR 1</b>	320.1	276.2	96	27	18
	NOR 2	320.1	233.1	96	37	16
3.55	<b>CIP 1</b>	332.0	313.9	31	29	38
	CIP 2	332.0	231.1	31	57	16

Supplementary data 3, continued.

RT (min)	Analytes	Q1 (m/z)	Q3 (m/z)	DP (volts)	CE (volts)	CXP (volts)
3.66	<b>SMX 1</b>	254.0	156.0	66	23	24
	SMX 2	254.0	108.0	66	33	16
3.68	<b>FLO 1</b>	357.8	339.9	66	13	24
	FLO 2	357.8	241.0	66	25	14
3.73	<b>DAN 1</b>	358.0	340.1	86	33	24
	DAN 2	358.0	314.1	86	27	38
3.73	<b>ENR 1</b>	360.0	316.0	91	29	38
	ENR 2	360.0	341.9	91	33	38
3.94	<b>AHB 1</b>	136.8	92.8	-5	-16	-15
	AHB 2	136.8	64.9	-5	-40	-13
3.96	<b>ASC 1</b>	136.9	93.0	-40	-22	-15
	ASC 2	136.9	94.7	-40	-38	-33
4.06	<b>MPR 1</b>	153.0	120.9	66	21	14
	MPR 2	153.0	108.9	66	15	30
4.09	<b>PPN 1</b>	260.1	183.1	66	25	12
	PPN 2	260.1	116.1	66	25	8
4.11	<b>DOX 1</b>	445.0	427.9	111	27	34
	DOX 2	445.0	410.1	111	37	36
4.13	<b>PEN 1</b>	334.9	160.0	111	23	18
	PEN 2	334.9	176.0	111	19	16
4.19	<b>BPA 1</b>	227.0	227.1	-60	-14	-15
	BPA 2	227.0	211.1	-60	-26	-13
4.37	<b>TIA 1</b>	494.1	192.2	51	29	10
	TIA 2	494.1	119.0	51	59	12
4.43	<b>ERY 1</b>	734.2	576.1	46	25	36
	ERY 2	734.2	157.8	46	37	22
4.46	<b>TYL 1</b>	916.2	772.3	156	43	36
	TYL 2	916.2	174.1	156	51	10
4.47	<b>EPR 1</b>	165.0	136.9	-35	-20	-11
	EPR 2	165.0	136.0	-35	-20	-13
4.51	<b>AND 1</b>	233.1	187.1	21	37	18
	AND 2	233.1	159.0	21	45	18
4.57	<b>CTM 1</b>	748.3	590.2	96	25	40
	CTM 2	748.3	157.9	96	41	26
4.59	<b>CBM 1</b>	237.0	194.2	66	29	12
	CBM 2	237.0	193.2	66	47	6
4.68	<b>ATZ 1</b>	216.0	173.9	71	25	22
	ATZ 2	216.0	103.9	71	41	16
4.70	<b>DEET 1</b>	192.1	119.3	56	23	10
	DEET 2	192.1	90.9	56	41	10

Supplementary data 3, continued.

RT (min)	Analytes	Q1 (m/z)	Q3 (m/z)	DP (volts)	CE (volts)	CXP (volts)
4.71	PPR 1	178.9	137.1	-60	-20	-13
	PPR 2	178.9	136.1	-60	-24	-7
4.75	DEX 1	392.9	355.1	41	19	20
	DEX 2	392.9	147.0	41	39	10
4.81	ACF 1	212.9	127.1	-35	-24	-15
	ACF 2	212.9	85.0	-35	-14	-9
4.83	FEN 1	300.0	268.1	96	29	22
	FEN 2	300.0	159.0	96	49	10
4.84	NPX 1	231.1	185.1	56	21	12
	NPX 2	231.1	170.0	56	37	10
4.86	CRT 1	204.1	69.0	61	35	12
	CRT 2	204.1	136.0	61	27	14
4.90	E1 1	271.1	253.3	101	19	10
	E1 2	271.1	133.1	101	35	12
4.90	E2 1	273.0	255.0	46	17	14
	E2 2	273.1	107.0	61	41	14
4.93	EE2 1	297.1	107.0	81	33	12
	EE2 2	297.1	77.1	71	79	10
4.95	TOP 1	205.0	205.1	-200	-14	-19
	TOP 2	205.0	148.0	-200	-26	-7
5.04	ATV 1	559.2	440.2	26	33	38
	ATV 2	559.2	250.1	26	59	18
5.09	DCF 1	293.9	250.0	-10	-18	-7
	DCF 2	293.9	214.1	-10	-28	-9
5.10	IBP 1	205.0	159.1	-35	-10	-15
	IBP 2	205.0	160.9	-35	-12	-21
5.13	PGT 1	315.1	109.0	141	31	10
	PGT 2	315.1	297.2	141	23	28
5.13	BZQ 1	109.0	80.9	121	19	4
	BZQ 2	109.0	53.3	121	29	12
5.22	GEM 1	249.0	121.0	-5	-30	-7
	GEM 2	249.0	127.0	-85	-14	-5
5.24	TCS 1	286.8	286.9	-90	-6	-17
	TCS 2	286.8	141.8	-90	-48	-15
5.62	NNF 1	219.1	132.9	-65	-42	-7
	NNF 2	219.1	117.0	-65	-80	-13
5.66	AAS 1	181.1	160.9	71	17	14
	AAS 2	181.1	125.1	71	19	16



Supplementary data 4: Preliminary experiments to select the most suitable adsorbent according to the highest mean value of peak areas (n=7). Sample preparation conditions are those described in section 2.3, modifying only the type of adsorbent; spiking with 1000 ng g<sup>-1</sup> of each CEC.

Analytes	p-value*	Mean value of peak areas **		
		ODS	Alumina	Alumina + ODS
PEN	0.0023	1579650	<u>2614833</u>	1010950
OTC	0.0012	<u>9368500</u>	5133167	2160550
DOX	0.025	<u>79936667</u>	<u>66115000</u>	53893333
TTC	0.021	<u>6169000</u>	<u>5013167</u>	4073333
MAR	0.00026	<u>12992667</u>	<u>10731333</u>	4969000
ENR	<0.0001	13819833	<u>28428333</u>	6588000
DAN	<0.0001	<u>24601667</u>	<u>19815000</u>	8262833
SDZ	<0.0001	<u>20950000</u>	16571667	7832833
STZ	<0.0001	<u>76271667</u>	<u>64583333</u>	31960000
SMZ	<0.0001	<u>77346667</u>	<u>65641667</u>	29150000
SDD	0.0011	<u>108893333</u>	<u>104366667</u>	63071667
SMX	<0.0001	<u>73266667</u>	56526667	37323333
TYL	<0.0001	644330	<u>25213333</u>	674383
TIA	<0.0001	11716667	<u>253616667</u>	15633167
APR	<0.0001	<u>17690000</u>	<u>20066667</u>	6214500
TMP	<0.0001	105841667	<u>227133333</u>	76101667
FLO	<0.0001	4685167	<u>5382667</u>	3872333
FEN	<0.0001	9363667	<u>61566667</u>	12395500
DEX	<0.0001	987733	<u>13883333</u>	954317
PGT	<0.0001	622033	<u>17616667</u>	847283
AMO	N.D.			
MPR	0.65	6857000	8155000	7203333
AAF	<0.0001	<u>16420000</u>	12336667	6132833
CBM	<0.0001	298783333	<u>558283333</u>	290683333
PPN	<0.0001	1786767	<u>85060000</u>	2625083
SPD	N.D.			
MTN	<0.0001	<u>22173333</u>	<u>19681667</u>	6227000
AND	N.D.			
NPX	0.68	41400000	38228333	37266667
CTM	<0.0001	4125833	<u>192250000</u>	7223333
ERY	<0.0001	146530	<u>6504333</u>	226628
AAS	0.0020	<u>591517</u>	<u>515683</u>	211493
NOR	<0.0001	<u>4478667</u>	<u>3246833</u>	1401633

Supplementary data 4, continued.

Analytes	p-value*	Mean value of peak areas **		
		ODS	Alumina	Alumina + ODS
BZQ		N.D.		
ATV	<0.0001	4320333	<u>16396667</u>	6805333
ATN	0.00011	<u>4645667</u>	<u>4711667</u>	927833
CAF	<0.0001	<u>125805000</u>	<u>130178333</u>	39703333
ATZ	<0.0001	236883333	<u>49316667</u>	240650000
IOH	<0.0001	<u>519333</u>	<u>621817</u>	255150
DEET	<0.0001	154116667	<u>447433333</u>	153300000
CIP	0.0034	<u>17561667</u>	<u>14670000</u>	8229000
E2		N.D.		
EE2	0.033	<u>3542500</u>	2625167	2967667
CRT	<0.0001	26690000	<u>271433333</u>	33895000
E1	<0.0001	2283667	<u>13670000</u>	2327000
EPR	0.0030	2312667	<u>3504500</u>	2189333
PPR	<0.0001	1262667	<u>3080333</u>	1254900
DCF	0.0029	1967667	<u>2807500</u>	1778333
IBP	0.49	278167	249667	244517
ASC	<0.0001	<u>43305000</u>	33733333	19360000
ACF	0.17	28141667	26138333	22606667
BPA		N.D.		
TCS		N.D.		
TOP		N.D.		
NNF		N.D.		
AHB	<0.0001	<u>51883333</u>	41675000	23108333
GEM	<0.0001	2606667	<u>9461833</u>	2789833

\*p<0.05 : there is significant difference after an ANOVA, the mean values are different.

\*\* In bold and underlined: most suitable adsorbents based on the highest responses obtained.

N.D.: Not detected.

**Supplementary data 5: Experimental design to screen the effect of 4 sample preparation factors, 1000 ng g<sup>-1</sup> of each CEC.**

<b>Experiment</b>	<b>%Methanol</b>	<b>pH</b>	<b>Amount of alumina (g)</b>	<b>%EDTA</b>
1	10	3	0.1	0
2	20	8	0.1	0
3	20	8	0.3	0.4
4	15	5.5	0.2	0.2
5	10	3	0.3	0.4
6	15	5.5	0.2	0.2
7	10	8	0.3	0
8	10	8	0.1	0.4
9	15	5.5	0.2	0.2
10	20	3	0.1	0.4
11	20	3	0.3	0
12	10	3	0.1	0
13	20	8	0.1	0
14	20	8	0.3	0.4
15	15	5.5	0.2	0.2
16	10	3	0.3	0.4
17	15	5.5	0.2	0.2
18	10	8	0.3	0
19	10	8	0.1	0.4
20	15	5.5	0.2	0.2
21	20	3	0.1	0.4
22	20	3	0.3	0

**Supplementary data 6: R<sup>2</sup> statistics and p-values of the sample preparation factors after carrying out the experimental design.**

	R <sup>2</sup> (%)	Factors				Interactions		
		A: %Methanol	B: pH	C: alumina amount (g)	D: %EDTA	AB+CD	AC+BD	AD+BC
PEN	68	--	0.0007 (-)	--	--	--	--	--
OTC	73	--	--	--	0.0001 (+)	--	--	--
DOX	71	--	--	--	0.0002 (+)	--	--	--
TTC	67	--	--	--	0.0004 (+)	--	--	--
MAR	66	--	--	0.0059 (-)	--	--	0.0055 (-)	--
ENR	73	--	0.0011 (-)	0.025 (-)	--	--	0.012 (-)	--
DAN	78	--	0.0001 (-)	0.014 (-)	--	--	--	--
SDZ	32	--	--	--	--	--	--	--
STZ	34	--	--	--	--	--	--	--
SMZ	44	--	--	--	--	--	--	--
SDD	64	--	--	--	--	--	--	0.042 (-)
SMX	84	--	--	0.044 (+)	0.018 (+)	--	0.033 (-)	0.037 (-)
TYL	22	--	--	--	--	--	--	--
TIA	46	--	--	--	--	--	--	--
APR	31	--	--	--	--	--	--	--
TMP	56	--	--	--	--	--	--	--
FLO	56	--	0.0070 (-)	--	--	--	--	--
FEN	60	--	--	--	--	--	0.026 (-)	--
DEX	76	--	--	0.025 (+)	--	--	--	0.040 (-)
PGT	61	--	0.015 (-)	--	--	--	--	--
MPR	55	--	0.0079 (+)	--	--	--	--	--
AAF	61	--	--	--	--	--	--	--
CBM	36	--	--	--	--	--	--	--
PPN	71	--	0.0001 (-)	--	--	--	--	--
MTN	75	--	0.0033 (+)	--	--	--	--	--
NPX	81	--	0.014 (-)	0.018 (+)	--	--	--	0.0079 (-)
CTM	67	--	--	--	--	--	0.036 (-)	--
ERY	78	--	0.015 (-)	--	--	--	0.043 (-)	--
AAS	30	--	--	--	--	--	--	--
NOR	77	--	0.0002 (-)	0.011 (-)	--	--	--	--
ATV	72	--	0.0015 (+)	--	0.035 (+)	--	0.018 (-)	--



**Supplementary data 6, continued.**

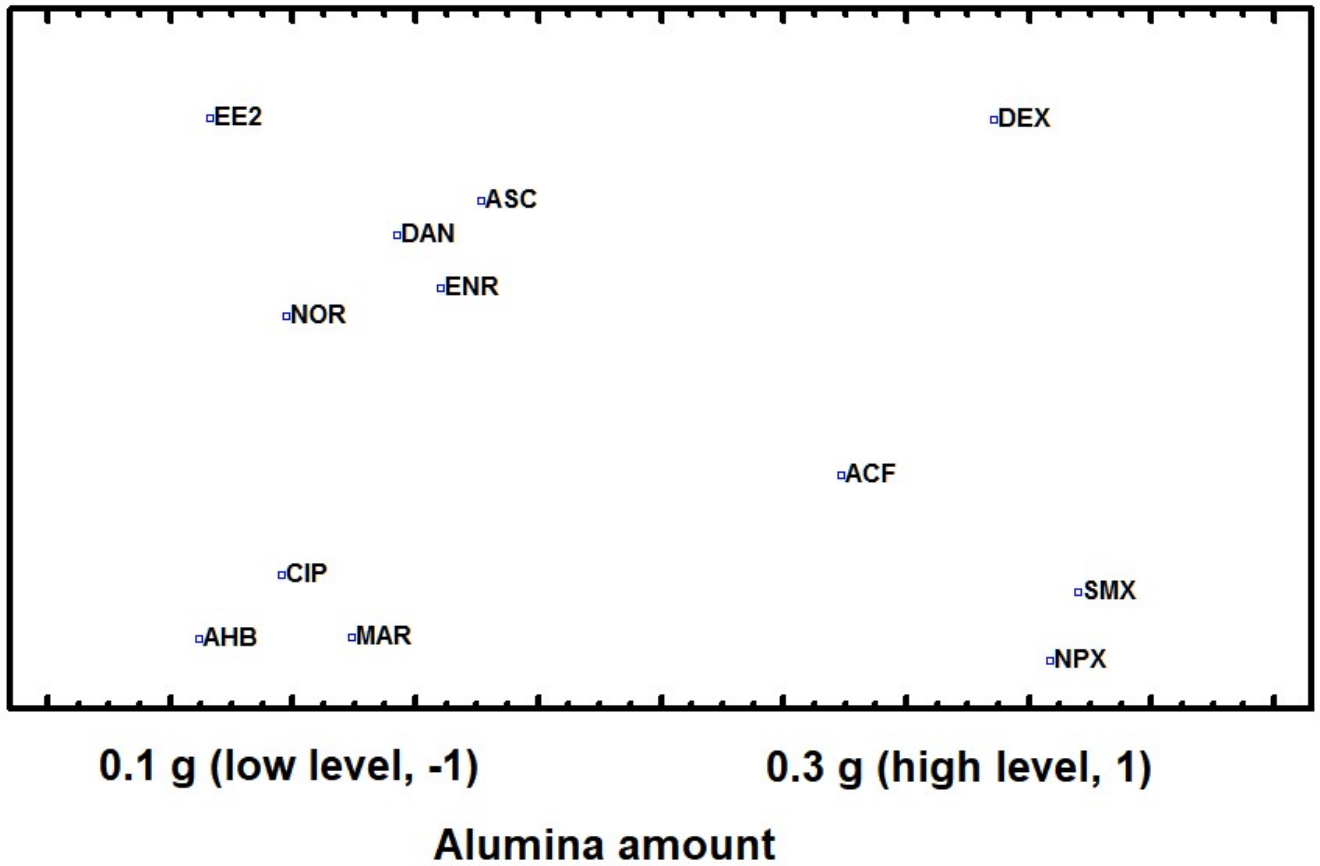
Analytes	R <sup>2</sup> (%)	Factors				Interactions		
		A: %MeOH	B: pH	C: Al <sub>2</sub> O <sub>3</sub> amount (g)	D: %EDTA	AB+CD	AC+BD	AD+BC
<b>ATN</b>	88	--	<0.0001(+)	--	--	--	--	--
<b>CAF</b>	58	--	0.017 (+)	--	--	--	--	--
<b>ATZ</b>	20	--	--	--	--	--	--	--
<b>IOH</b>	62	0.044 (-)	--	--	--	--	--	--
<b>DEET</b>	77	--	0.040 (+)	--	--	--	--	--
<b>CIP</b>	75	--	0.0005 (-)	0.013 (-)	--	--	--	--
<b>EE2</b>	64	--	0.0052 (+)	0.028 (-)	--	--	--	--
<b>CRT</b>	71	--	--	--	--	--	--	--
<b>E1</b>	63	--	--	--	--	--	--	0.044 (-)
<b>EPR</b>	51	--	--	--	--	--	--	--
<b>PPR</b>	33	--	--	--	--	--	--	--
<b>DCF</b>	44	--	--	--	--	--	--	--
<b>IBP</b>	70	--	--	--	--	--	--	--
<b>ASC</b>	85	--	<0.0001 (-)	0.016 (-)	0.041 (+)	--	--	0.020 (+)
<b>ACF</b>	82	--	0.023 (-)	0.0023 (+)	--	--	--	0.024 (-)
<b>AHB</b>	86	--	<0.0001 (-)	0.011 (-)	0.033 (+)	--	0.042 (-)	0.015 (+)
<b>GEM</b>	74	--	0.026 (+)	--	--	--	0.011 (-)	--

--: no significant effect (p value > 0.05)

(+): Positive effect

(-): Negative effect

Supplementary data 7: Diagram of dispersion showing the CECs whose optimum extraction pH is 3, and distribution according to their optimum alumina amount.



**Supplementary data 8: CECs and concentrations found in the RM sample used to validate the method after a standard addition calibration.**

<b>Compound</b>	<b>Concentration (ng g<sup>-1</sup>)</b>
<b>PEN</b>	--
<b>OTC</b>	21
<b>DOX</b>	1969
<b>TTC</b>	--
<b>MAR</b>	128
<b>ENR</b>	125
<b>DAN</b>	47
<b>SDZ</b>	16
<b>STZ</b>	--
<b>SMZ</b>	--
<b>SDD</b>	--
<b>SMX</b>	--
<b>TYL</b>	--
<b>TIA</b>	84
<b>APR</b>	--
<b>TMP</b>	310
<b>FLO</b>	365
<b>FEN</b>	43
<b>DEX</b>	50
<b>PGT</b>	--
<b>MPR</b>	72
<b>AAF</b>	100
<b>CBM</b>	15
<b>PPN</b>	204

<b>Compound</b>	<b>Concentration (ng g<sup>-1</sup>)</b>
<b>MTN</b>	--
<b>NPX</b>	104
<b>CTM</b>	--
<b>ERY</b>	--
<b>AAS</b>	--
<b>NOR</b>	--
<b>ATV</b>	--
<b>ATN</b>	--
<b>CAF</b>	41
<b>ATZ</b>	--
<b>IOH</b>	--
<b>DEET</b>	75
<b>CIP</b>	--
<b>EE2</b>	3869
<b>CRT</b>	--
<b>E1</b>	--
<b>EPR</b>	--
<b>PPR</b>	--
<b>DCF</b>	42
<b>IBP</b>	--
<b>ASC</b>	--
<b>ACF</b>	183
<b>AHB</b>	15906
<b>GEM</b>	--

-- : not detected

**Supplementary data 9: Validation parameters. Intermediate calibration levels; taking into account the total concentrations in raw manure sample: sum of the own and spiked concentrations. Each calibration standard was injected once.**

Compound	R <sup>2</sup>	Linear range (ng g <sup>-1</sup> )	Additional calibration levels (ng g <sup>-1</sup> )							
Penicillin G	0.986	7-5137	85	173	331	696	1696	3443		
Oxytetracycline	0.978	29-4891	94	177	327	672	1619	3277		
Doxycycline	0.994	1977-6776	1985	2049	2132	2278	2605	3554	5191	
Tetracycline	0.966	8-5127	17	85	173	330	694	1691	3435	
Marbofloxacin	0.970	137-7791	244	419	826	1938	3886	5773		
Enrofloxacin	0.996	135-7945	205	385	800	1935	3922	5848		
Danofloxacin	0.997	57-5770	66	142	240	416	822	1934	3882	
Sulfadiazine	0.989	25-7757	35	112	211	388	799	1923	3891	5797
Sulfathiazole	0.988	9-7663	19	95	193	368	775	1888	2835	5722
Sulfamethizole	0.958	9-7663	19	95	193	368	775	1888	2835	5722
Sulfadimidine	0.972	10-7819	19	97	197	376	791	1926	3913	5839
Sulfomethoxazole	0.999	9-7663	19	95	193	368	775	1888	2835	5722
Tylosin	0.954	8-6651	16	82	168	320	673	1639	3329	4967
Tiamulin	0.960	92-1612	100	161	241	382	711			
Apramycin	0.963	9-5547	18	92	187	357	751	1829	3717	
Trimethoprim	0.986	319-8051	328	405	505	682	1092	2216	4183	6091
Florphenicol	0.995	374-8170	384	461	561	740	1154	2287	4271	6193
Fenbendazole	0.973	52-5765	61	137	236	411	818	1930	3877	
Dexamethasone	0.981	60-7713	69	145	243	419	825	1937	3885	5772

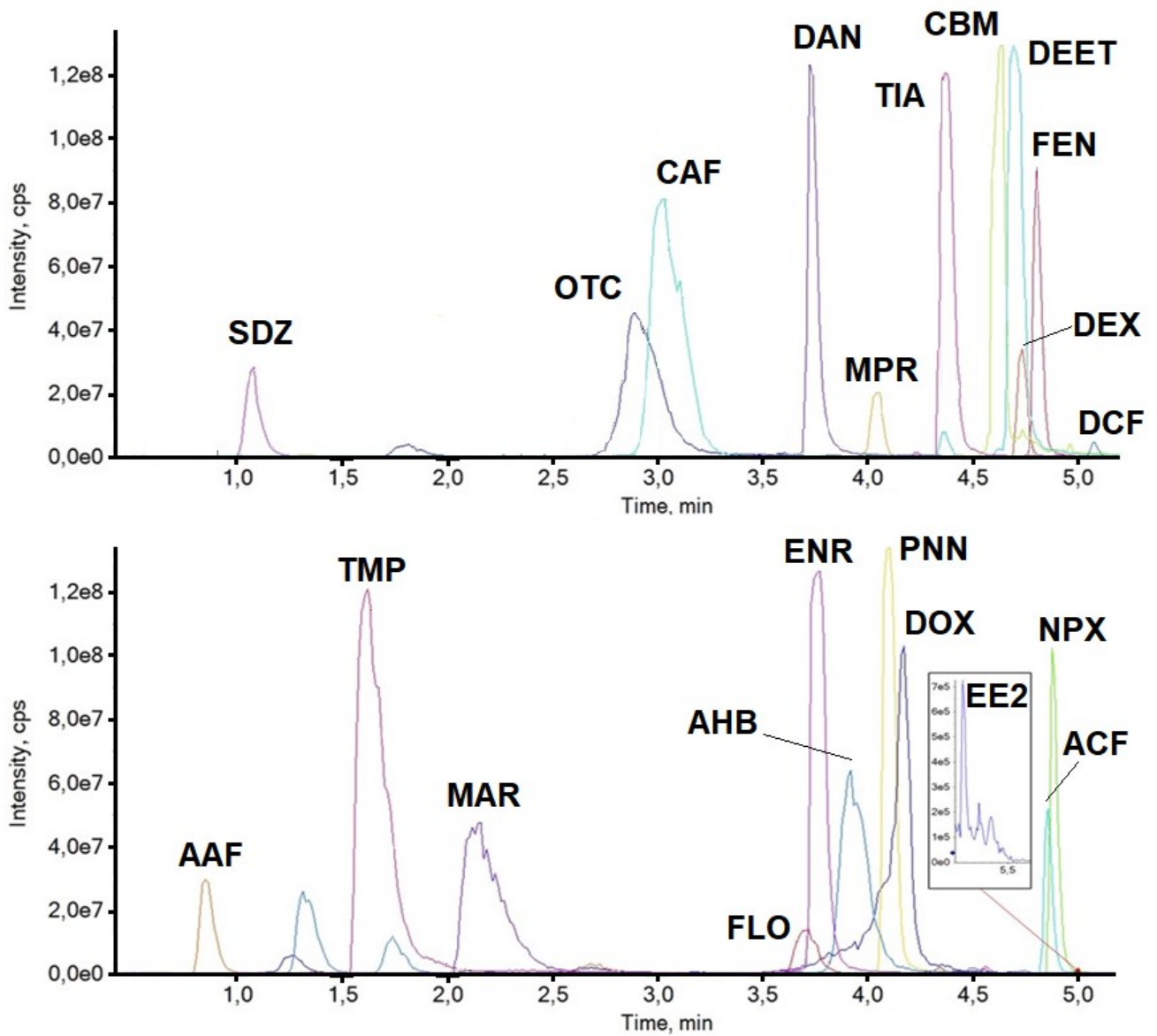
**Supplementary data 9, continued.**

Compound	R <sup>2</sup>	Linear range (ng g <sup>-1</sup> )	Additional calibration levels (ng g <sup>-1</sup> )							
			19	96	195	372	783	1907	3874	
Progesterone	0.978	10-5781	19	96	195	372	783	1907	3874	
Methylparaben	0.995	81-7891	91	168	269	448	863	1998	3985	5911
Acetaminophen	0.998	109-7841	119	195	295	472	883	2006	3973	5881
Carbamazepine	0.983	24-390	34	111	211					
Propranolol	0.994	213-7060	221	289	377	534	898	1893	3635	5323
Metronidazole	0.997	10-7741	19	96	195	372	783	1907	3874	5781
Naproxen	0.995	113-7923	123	200	301	479	895	2030	4017	5943
Clarithromycin	0.967	10-1905	19	95	195	372	782			
Erythromycin	0.998	9-7663	19	95	193	368	775	1888	2835	5722
Acetylsalicylic acid	0.946	1907-7741	3874	5781						
Norfloxacin	0.974	9-7663	19	95	193	368	775	1888	2835	5722
Atorvastatin	0.946	4-3612	9	45	91	174	365	890	1808	2697
Atenolol	0.996	9-7663	19	95	193	368	775	1888	2835	5722
Caffeine	0.989	51-7743	60	136	235	412	820	1938	3896	5793
Atrazine	0.979	10-1918	19	96	196	374	788			
Iohexol	0.997	9-7624	19	94	192	366	771	1878	3816	5693
DEET	0.976	84-1963	103	202	377	784				
Ciprofloxacin	0.992	10-7780	19	96	196	374	787	1916	3894	5810

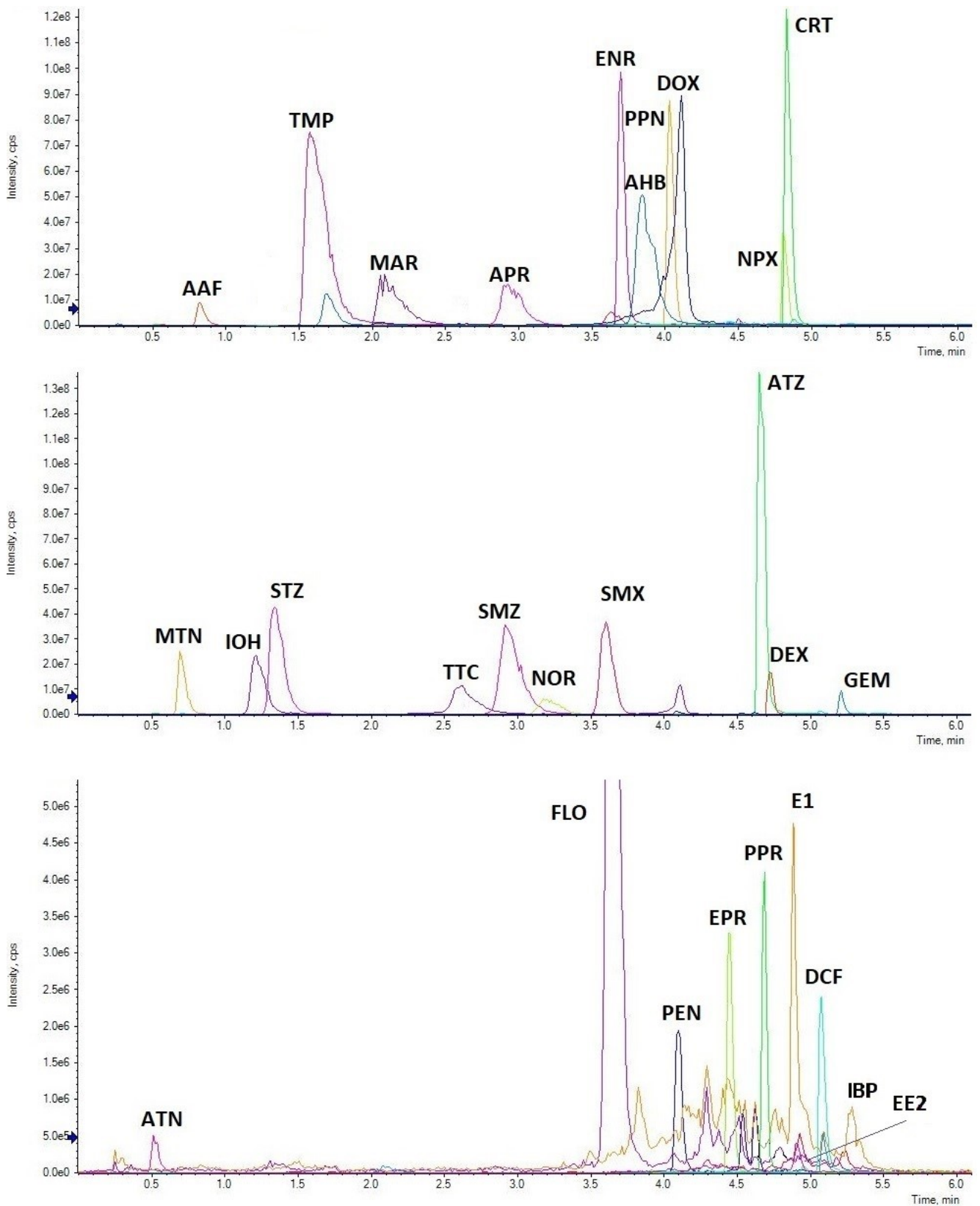
Supplementary data 9, continued.

Compound	R <sup>2</sup>	Linear range (ng g <sup>-1</sup> )	Additional calibration levels (ng g <sup>-1</sup> )							
17- $\alpha$ -ethinylestradiol	0.992	7704-11532	8745	9591	10126					
Crotamiton	0.998	9-365	19	94	191					
Estrone	0.939	195-7741	372	783	1907	3875	5781			
Ethylparaben	0.986	10-7819	19	97	197	376	791	1926	3913	5839
Propylparaben	0.994	10-7819	19	97	197	376	791	1926	3913	5839
Diclofenac	0.991	51-7321	60	132	225	392	778	1835	3685	5478
Ibuprofen	0.991	193-7663	368	775	1887	3835	5722			
Salicylic acid	0.908	1907-7741	3874	5781						
Clofibric acid	0.988	192-7768	202	277	374	547	950	2051	3979	5847
4-hydroxibenzoic acid	0.976	16001-23647	16100	162778	16668	17812	19780	21686		
Gemfibrozil	0.998	9-7663	19	95	193	368	775	1888	2835	5722

**Supplementary data 10: Superposition of extracted ion chromatograms. Most intense transitions for the CECs found in the raw manure sample used to validate the analytical method, spiked at 8000 ng g<sup>-1</sup>.**

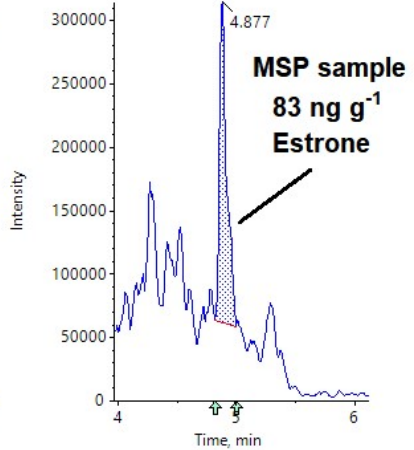
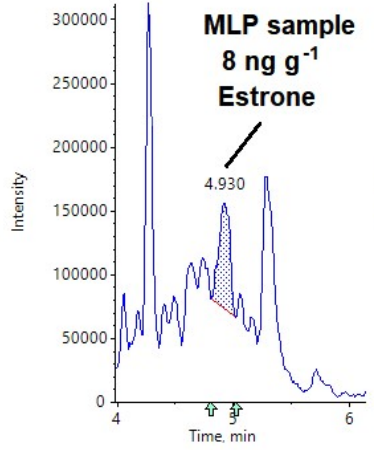
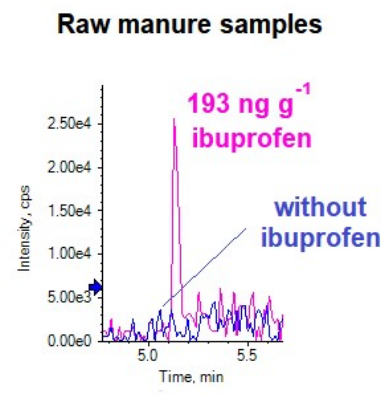
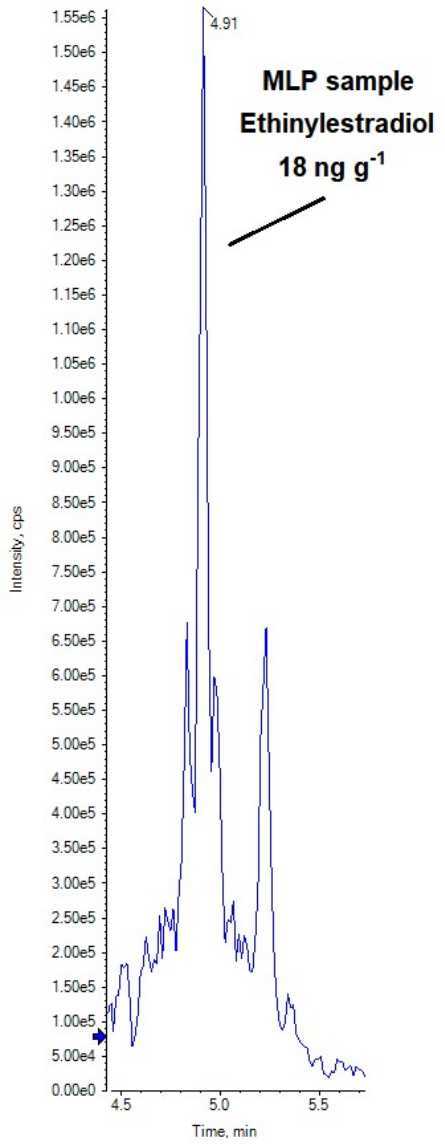


**Supplementary data 11: Superposition of extracted ion chromatograms. Most intense transitions for some CECs of a centrifuged raw manure sample, spiked at 1000 ng g<sup>-1</sup>.**





**Supplementary data 12: Extracted ion chromatograms for some compounds in low concentration.**



**Supplementary data 13: CECs and concentrations found in the analysis of two RM samples (uncentrifuged and centrifuged RM), and in the solid phase (MSP) and liquid phase (MLP) of each RM sample. Assays in duplicate.**

Compound	Uncentrifuged manure						Centrifuged manure					
	MSP 1 (ng g <sup>-1</sup> )	MSP 2 (ng g <sup>-1</sup> )	MLP 1 (ng g <sup>-1</sup> )	MLP 2 (ng g <sup>-1</sup> )	RM 1 (ng g <sup>-1</sup> )	RM 2 (ng g <sup>-1</sup> )	MSP 1 (ng g <sup>-1</sup> )	MSP 2 (ng g <sup>-1</sup> )	MLP 1 (ng g <sup>-1</sup> )	MLP 2 (ng g <sup>-1</sup> )	RM 1 (ng g <sup>-1</sup> )	RM 2 (ng g <sup>-1</sup> )
OTC	20	37	28	18	21	35	93	117	5	4	31	11
DOX	75	75	34	18	748	1434	313	470	3	16	1996	1942
MAR	121	181	70	85	188	124	434	487	32	24	130	126
ENR	34	28	2	0.1	20	27	22	23	0.8	0.7	43	9
DAN	118	71	1	1	47	119	14	43	0.5	0.6	91	58
SDZ	10	28	11	12	65	82	24	9	14	14	89	9
TIA	-- (<0.03)	5.7	0.2	0.5	112	2	13	13	0.4	0.3	48	48
TMP	3	10	1	0.8	24	36	8	7	0.1	0.1	40	29
FLO	61	42	9	14	82	72	-- (<0.1)	-- (<0.1)	-- (<0.3)	-- (<0.3)	-- (<3)	-- (<3)
PGT	95	60	74	66	44	31	-- (<0.2)	-- (<0.2)	17	4	-- (<0.3)	-- (<0.3)
MPR	2	14	-- (<0.19)	-- (<0.19)	51	107	7	9	0.6	0.6	23	17
AAF	19	39	5	9	70	62	-- (<1)	-- (<1)	-- (<0.15)	-- (<0.15)	-- (<2)	-- (<2)
CBM	-- (<1)	4.7	0.5	0.3	13	5	6	5	0.3	0.4	17	-- (<0.05)
PPN	24	27	2	3	31	23	52	57	1	1	22	40
NPX	99	83	34	4	72	72	-- (<2)	-- (<2)	-- (<0.5)	-- (<0.5)	-- (<3)	-- (<3)
CTM	9	0.2	0.7	-- (<0.1)	31	38	-- (<0.1)	-- (<0.1)	0.6	0.4	0.3	0.4
AAS	-- (<41)	384	54	-- (<0.3)	>7741	>7741	-- (<41)	-- (<41)	-- (<0.3)	-- (<0.3)	-- (<193)	-- (<193)
ATV	-- (<2.4)	-- (<2.4)	-- (<0.05)	-- (<0.05)	-- (<0.1)	-- (<0.1)	-- (<2.4)	4	-- (<0.05)	0.5	-- (<0.1)	-- (<0.1)

Supplementary data 13, continued.

Compound	Uncentrifuged manure						Centrifuged manure					
	MSP 1 (ng g <sup>-1</sup> )	MSP 2 (ng g <sup>-1</sup> )	MLP 1 (ng g <sup>-1</sup> )	MLP 2 (ng g <sup>-1</sup> )	RM 1 (ng g <sup>-1</sup> )	RM 2 (ng g <sup>-1</sup> )	MSP 1 (ng g <sup>-1</sup> )	MSP 2 (ng g <sup>-1</sup> )	MLP 1 (ng g <sup>-1</sup> )	MLP 2 (ng g <sup>-1</sup> )	RM 1 (ng g <sup>-1</sup> )	RM 2 (ng g <sup>-1</sup> )
CAF	4	3	3	1	6	15	7	7	1	1	0.9	2
DEET	2	6	0.7	0.9	4	4	-- (<1)	-- (<1)	0.7	1	5	7
CIP	10	-- (<1.3)	0.4	0.3	-- (<0.4)	24	37	64	1	0.6	13	6
EE2	197	1191	319	102	1974	1932	241	342	53	18	1625	2086
CRT	6	2	0.8	0.6	17	86	0.4	7	0.3	0.2	13	45
E1	83	137	24	21	<764	<764	146	297	8	11	<764	<764
ASC	721	518	3	12	56382	22767	517	704	22	28	14905	16305
ACF	5	5	4	0.2	14	26	-- (<0.8)	-- (<0.8)	-- (<0.12)	-- (<0.12)	-- (<1)	-- (<1)
AHB	718	666	5	10	>23647	17.742	591	335	12	25	15586	16226

--: not found. Detection limit is shown in parentheses.

Supplementary data 14: Percentage of removal of CECs in the farm centrifugation against the coefficient of partition of the CEC. The ionization state, according to  $pK_a$ , is shown with a number: without electric charge, 0; with positive charge, +1, with negative charge, -1; unknown state,  $\pm$ .

