

A review of Non-targeted screening approaches to monitoring groundwater

By

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## List of Acronyms

CWA	Clean Water Act
EPA	Environmental Protection Agency
GC-MS	Gas Chromatography Mass Spectrometry
GC-TOF-MS	Gas Chromatography Time-of-Flight Mass Spectrometry
LC-MS	Liquid Chromatography Mass Spectrometry
LC-TOF-MS	Liquid Chromatography Time-of-Flight Mass Spectrometry
NGWA	National Groundwater Association
NTA	Non-targeted Analysis
POCIS	Polar Organic Chemical Integrative Sampler
SPE	Solid Phase Extraction
SSA	Suspect Screening Analysis
TSA	Targeted Screening Analysis

## **Abstract**

BAKER, AURORA. A review of non-targeted screening approaches to monitoring groundwater.

(Under the direction of Dr. Elizabeth Nichols and Dr. Melanie Hedgespeth.)

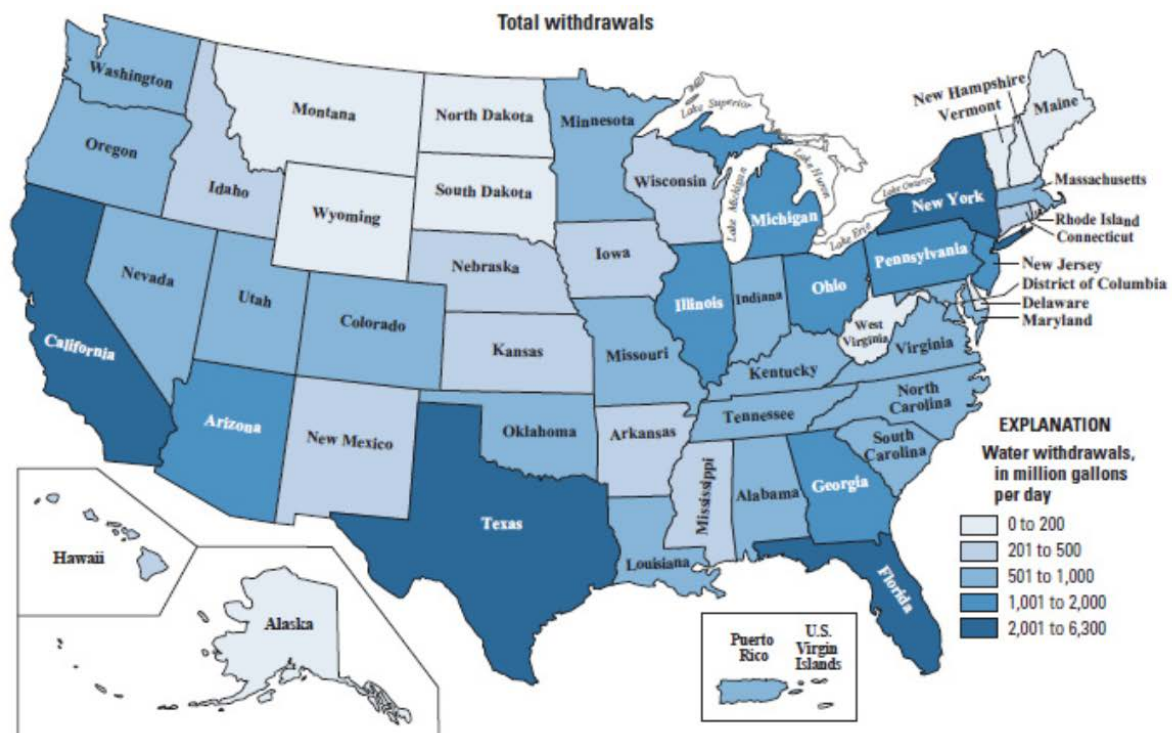
Monitoring groundwater for non-regulated contaminants has proven to be an experimental area for researchers. Currently, no standard approach has been identified for monitoring groundwater for non-regulated contaminants. Given the discharged items, such as pharmaceuticals and other waste products that have entered groundwater by ways of storage tanks of gasoline or other chemicals, septic systems, uncontrolled hazardous wastes, landfills, atmospheric contaminants and road salts (TGF, 2017). There has been concern that the non-regulated contamination would lead to adverse health effects on the human, animal and plant populations. The purpose of this review is to summarize the current knowledge of non-targeted screening methods available for analyzing groundwater and to identify relevant data gaps from existing studies. Many studies have been conducted globally using non-targeted screening approaches. Several studies were able to reach low detection limits. A limiting factor for many of the studies was the availability of analytical reference standards for identification of some of the compounds that were previously undetected. Most of the studies took grab samples and then followed with solid phase extraction, which limited them to a snapshot of the actual contamination instead of providing an extended period. The use of non-targeted screening (NTA) for monitoring groundwater seems to have potential due to the low detections levels reached in the studies. Current efforts of various research labs gave insight into what non-targeted screening involves and what actions needed to occur for a standard non-targeted analysis method.

## **ACKNOWLEDGEMENTS**

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## **1.0 Introduction**

In the United States, groundwater aquifers supply about 37 percent of the drinking water for the county and city water departments (USGS, 2017). In **Figure 1.**, the total amount of public withdrawals of surface water and groundwater in the year 2010 are shown by the millions of gallons used in each state per day. In North Carolina, between 501 and 1,060 million gallons were withdrawn each day. In the data compiled for the “2000 compilation of water use”, there were a reported 66 aquifers in the United States that were purposed for public, industrial and agricultural uses (Reilly et al., 2008). Of these aquifers only 20 were used for approximately 90% of the groundwater water uses in 2000 (Reilly et al., 2008).

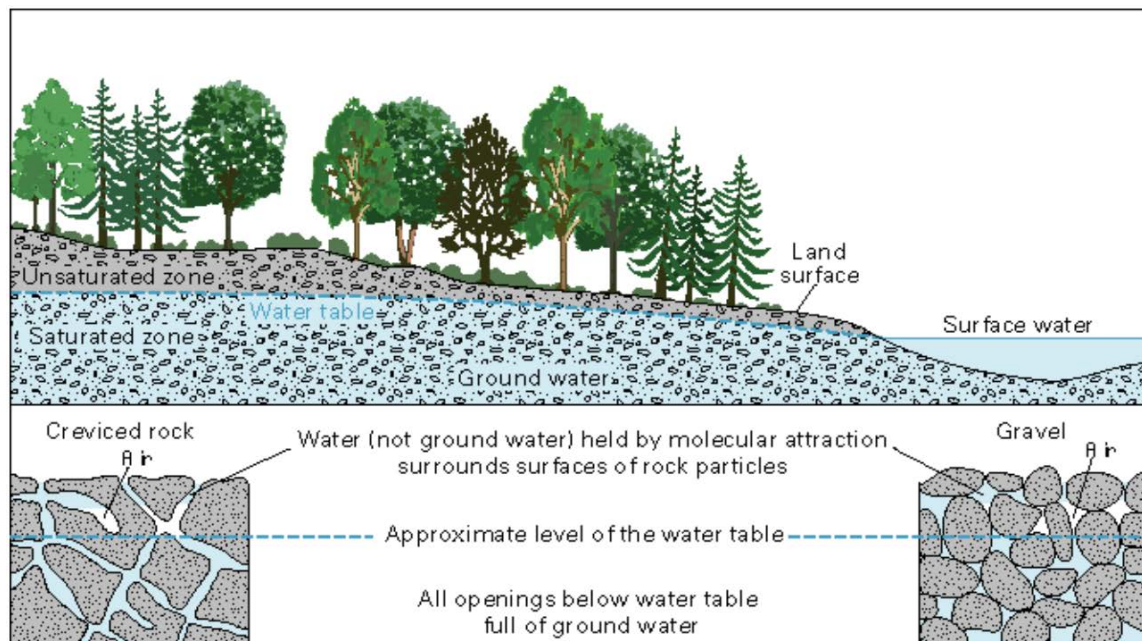


**Figure 1.** Total public surface water and groundwater withdrawals in 2010. (USGS, 2017).

Aquifers can be confined or unconfined. A confined aquifer, also known as an artesian aquifer, occurs when the porous rock layers in the earth tilt so there is less

porous rock above and below the porous layer causing pressure (USGS, 2018). An unconfined aquifer occurs when the water is not under pressure by porous rock layers but rather by atmospheric pressure (NGWA, 2012) In **Figure 2**, the groundwater is in the porous rock layer which is also known as the saturated zone. In the figure, there is a distinct separation between the rocks allowing the water between them to build up.

There are differences between a confined and unconfined aquifer. In **Figure 3**, one of the major differences is that the unconfined aquifer is located above the impermeable layer. The water from the unconfined aquifer can be drawn out through the water table well and surface water outlets. The confined aquifer is shown to be below the impermeable layer and is only accessible through the artesian wells that penetrate through that impermeable layer.

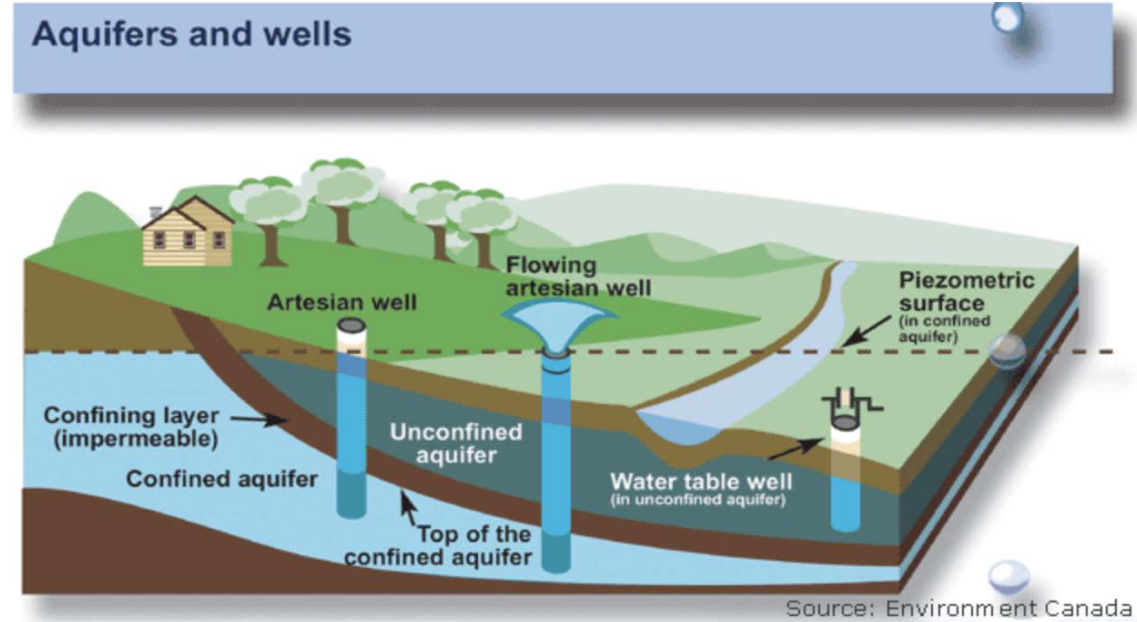


**Figure 2** - Displays the difference between the unsaturated zone and the saturated zone where the groundwater is located (USGS, 2018).



In an unconfined aquifer or a confined aquifer, the sources of water come from precipitation that has soaked into the ground. For an unconfined aquifer, the sources of water can come from precipitation, surface water bodies, such as a lake, stream or spring (NGWA, 2012), and human activities such as irrigation. Aquifers become contaminated by the infiltration of contaminants in water applied to land by application of solids, such as contaminated soil or biosolids, and by materials spilled or burned in the subsurface. Some of the very common contaminants that are often found include: pesticides, pharmaceuticals and personal care products (PPCPs). The U.S. EPA reported that from 2008 to 2012 the United States alone accounted for 16 - 18% of pesticide expenditures (US EPA, 2017). In 2012 alone, the United States was responsible for 21% herbicides, 14% insecticides and 10% fungicides expenditures that occurred (US EPA., 2017). Furthermore, the U.S. Department of Agriculture reported that 50 million Americans drink groundwater that possibly contains pesticides (Alavanjah., 2009). In 2015, the U.S. Department of Commerce (2016), reported that India ranked in the top 5 sources of pharmaceutical imports and the Netherlands ranked in the top 5 for export destinations of pharmaceuticals. Additionally, it was reported that the United States had \$333 billion in pharmaceutical sales (U.S. Department of Commerce, 2016). While Poland did not make any list for the top 5 it was considered the 22nd country out of 25 on the list for pharmaceutical exports (U.S. Department of

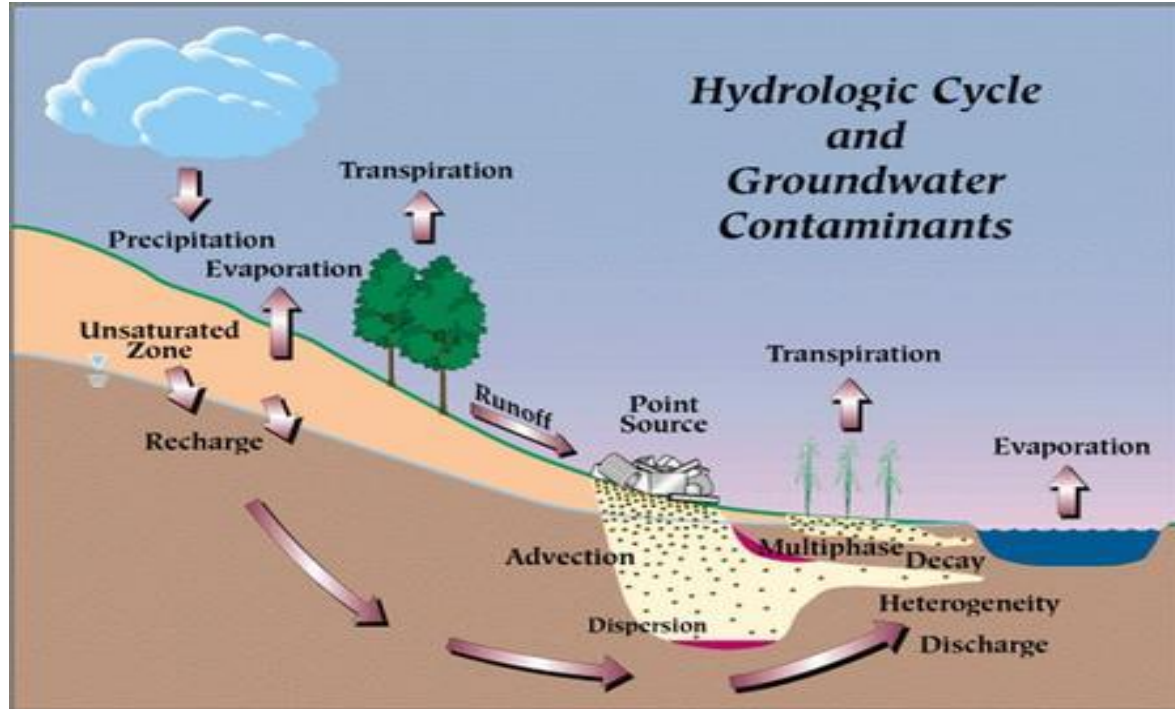
Commerce, 2016).



**Figure 3** - Displays the difference between confined and unconfined aquifers (USGS, 2018).

In **Figure 4**, the precipitation causes the runoff to push the contaminants out from the point source, which can include but are not limited to industrial plants, agricultural farms, animal farms, landfills, urban spots, vehicles and hazardous waste dump sites, into the ground where they undergo advection and then are dispersed into the areas of the confined and unconfined aquifers. Once the contaminants have reached the aquifers they undergo decay or take on new characterization before being released into the atmosphere by transpiration and/or evaporation. After being absorbed into the atmosphere the contaminants are re-released by precipitation back into the unsaturated zone of the ground to undergo the cycle again. The constant cycling of contaminants aids in their accumulation in the porous and permeable soils make monitoring of

aquifers a necessity.



**Figure 4** - Displays the steps of the hydrologic cycle and where groundwater contaminants would enter the cycle (Lane, 2016).

Groundwater monitoring currently occurs by using aquifers. Those aquifers are most often sampled using some type of grab sample. A grab sample is an immediate sample of media, such as, soil or surface water, from one location and at one point in time. The grab sample would then be sent for analysis, such as solid phase extraction (SPE). There are typically four steps to a SPE. First, the sample cartridge is conditioned with a solvent to wet the sorbent followed by a loading solution that contains the analyte being slowly filtered through the solid phase. Then the analyte and any unwanted materials are retained on the sorbent by adsorption. Lastly, the sorbet is washed using a pure solvent or mixture of solvents that differ from the polarity of the analyte to remove the unwanted materials before being left with the target analyte. This process is then

followed by some type of mass spectrometry. The mass spectrometer allows for electron or chemical ionization in positive or negative ion mode. The instrument can detect and record the relative masses in abundances of ions sorting them based on their mass to charge ratios, which aids in their identification. Additional measurements are taken in conjunction with the grab sample which include: temperature, dissolved oxygen, specific electrical conductance, pH, reduction-oxidation potential, alkalinity and acid neutralization capacity and turbidity (USGS, 2011). The additional measurements are important as they help to understand the presence or persistence and concentration of the organic contaminants in the media.

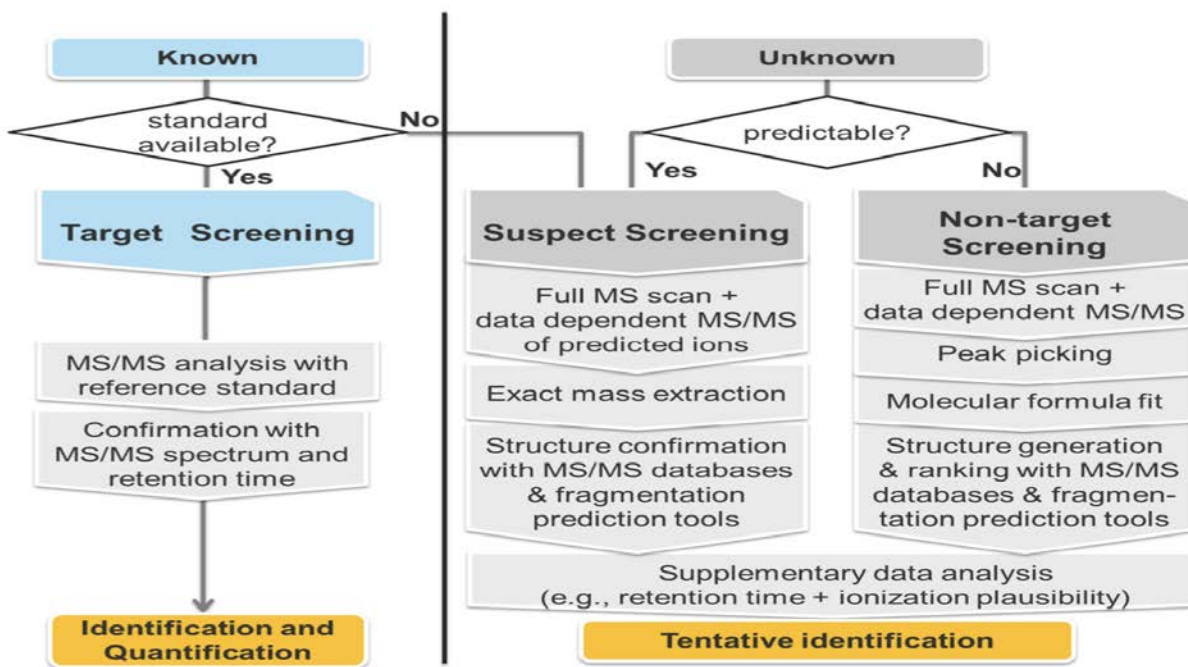
Another type of sampling that can be used for monitoring groundwater but is used less often is passive sampling. Passive sampling of groundwater can occur through the use of a Polar Organic Chemical Integrative Sampler (POCIS), which is specifically used for monitoring polar organic contaminants by adsorption. This sampler can be placed inside an aquifer for an extended period. The sampler works by having the contaminants diffuse into the sorbent, which is the membrane layer of the sampler. The POCIS sample can then undergo SPE or chromatography, before the ions are separated by some form of mass spectrometry, similarly to a grab sample.

The Environmental Protection Agency (EPA) has published several approved analytical methods based on the regulations in the Clean Water Act (CWA) for regulated contaminants. These approved analytical methods cover the following topics: chemical, microbiological, whole effluent toxicity, radiochemical and pharmaceutical. However, there is less regulation and methodology when it comes to monitoring organic contaminants. According to the EPA, there are currently 1,000s to 10,000s of non-

regulated organic contaminants that stem from “dust, soil, food, air, water, products, plants, animals” and humans (Sobus, 2016). With a lack of regulation and standard methodology, many independent parties have conducted their own research on the topic of monitoring organics. These studies have heavily contributed to our knowledge of methodology that could be used to monitor organic contaminants. The different methodologies that have been explored for monitoring organic contaminants are targeted, suspect and non-targeted screening.

Targeted screening analysis (TSA) is often utilized when there are specific contaminants, such as, acetone, arsenic, iron and cyanide, that are being screened (NCDEQ, 2013). Of those hundreds of chemicals being screened their chemical structures are easily found within chemical databases, such as the Distributed Structure-Searchable Toxicity (DSSTox) Database Network, Toxicity Forecaster (ToxCast) or another public database and they are expected to be found in the water samples (Sobus, 2016). Suspect screening analysis (SSA) is utilized when there is a greater amount of chemicals of interest to be identified that included some that are known and some that are unknown. For SSA there could be hundreds of listed chemicals of interest that you are aware could be in the sample but you are not specifically looking for them or expecting them to be in the sample. The third method of analysis, as shown in **Figure 5**, is non-targeted screening analysis (NTA). For NTA, there are no known chemicals and no chemicals of interest. Thus, you are screening a sample with the knowledge that thousands of chemicals could be detected but you have no listed chemicals that you specifically set out to find.

In these screening approaches mass spectrometers and chromatograms are commonly relied upon. In NTA, samples go through an extraction phase to obtain analytes. The analytes then go through an identification process which may include cross references of databases with known elements. Once parts of the analyte are identified the similarities between components of the analytes structure would be matched to known chemicals and grouped. In the end there would be a group of identified chemical features and non-identifiable features. Although some of the chemical features would remain non-identifiable; however, they could still be used to fingerprint groundwater since the features can be matched to list of some current chemicals.



**Figure 5.** Displays the workflow process of targeted, suspect and non-targeted screening (Bletsou et al., 2015).

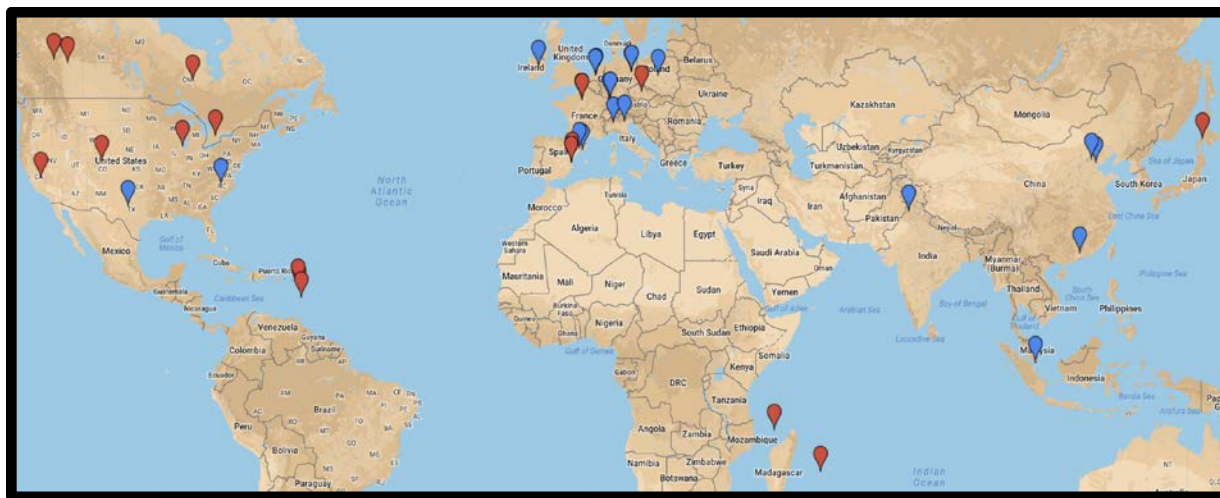
## 2.0 Methods

In order to summarize current knowledge of NTA methods for groundwater, as well as, identify relevant data gaps, identify the process of NTA, and the next steps in NTA research in monitoring groundwater, the following process was implemented. First, a search of all available literature was completed using the following databases: ScienceDirect, SciVerse ScienceDirect, Web of Science, PubMed, and Analytical Chemistry (ACS Publications). The terms of groundwater and non-targeted screening were searched for in each database. Additionally, the time period selected only brought up the articles that were published during the early 2000s until the current year, 2017. As a result of the time period and search terms over 2,403 scholarly journal articles came up in the databases. From the thorough list of available articles, a set of 50 articles that were good candidates for the review's overall objectives were selected. Details from each of the 50 articles were compiled into a synthesis matrix. The synthesis matrix included information, such as, study location, study duration, study variables, sample types, analytical instruments, software applications, limitations, analysis methodology, identifiable features, chemicals screened, chemicals identified, the number of unidentifiable features, study objectives, conclusions and next steps for each source. Next, a table was created only detailing the chemicals that were screened for each study in conjunction with the instruments used and software in the analysis of those screened chemicals. After each source had been added to the matrix, the list of sources that focused on the targeted, suspect and non-targeted methodology were selected and the irrelevant articles were removed. This process left approximately 30 articles to be analyzed in the review. Of these articles, the chemicals that had been

screened were organized by chemical class and analysis method. The limits of detection and recovery percentages were then added to the synthesis matrix to determine which analysis method was most effective.

### 3.0 Results

NTA studies for groundwater have occurred in several locations throughout the United States, as well as, in other countries including Canada, Italy, Germany, Ireland, France, India, Poland, Spain, China, Singapore, Czech Republic and Japan. The majority of studies were conducted in the United States (17%) and in Northwestern Europe (45%). The specific locations within the countries are displayed by **Figure 6**.



**Figure 6.** Displays the sampling sites locations from the sources. The sites in “blue” represent the studies that used Liquid Chromatography Mass Spectrometry (LC-MS) and Gas Chromatography Mass Spectrometry (GC-MS) for analysis. Sites in “red” represent the studies that used Liquid Chromatography Time-of-Flight Mass Spectrometry (LC-TOF-MS) and/or Gas Chromatography Time-of-Flight Mass Spectrometry (GC-TOF-MS) for analysis.

The studies that were conducted took place beginning in the year 2002 and ending in 2015. The sampling that occurred on most of the studies were from



groundwater aquifers. Although there were some samples taken from surface water, drinking water and wastewater. The samples on most of the studies used a grab sampling and SPE technique as opposed to a passive sampler, such as, POCIS. The sampling periods ranged from yearly and monthly periods. The sampling periods that occurred on some of the studies were not specified. The use of amber glass bottles for the samples was consistent across more than 40% of the studies. All of the studies used some form of mass spectrometry to perform their analysis of their groundwater samples, as well as, surface water, wastewater and drinking water. Common software that was utilized on many of the studies was MassLynx, Xcalibur, Sigmaplot, MassHunter and Analyst. Additional software that was utilized less on the studies included: TargetLynx, TurboMass, Hystar, MSXcelerator, Shimadzu, MS Workstation 8, Agilent qualitative and MEDUSA. The instrumentation used for the studies varied among the analysis methods; however, 17% of the studies used the Waters Acquity LC system for LC-MS analysis. A few studies followed an USEPA method however most did not follow specified methods. In Zemo et al., 2017 the USEPA methods that were utilized included 3630C for silica gel cleanup; 8015B for nonhalogenated organics using GC/FID; and 8270C for semi volatile organic compounds by GC-MS. In Chen et al., 2017 the USEPA method of 521 regarding determining Nitrosamines by the use of SPE and GC-MS was utilized.

### **3.1 LC vs GC vs TOF**

There were 15 studies that used LC for analytical separation while only 7 studies used GC. Out of the 20 total studies that used LC-MS or GC-MS, only one study used

both (Preiss et al., 2012). In evaluating the results of both methods, there did not appear to be a significant distinction between the results (Preiss et al., 2012). In the aqueous samples, that were evaluated using both methods, they appeared to have low concentration levels of compounds making any attempt to distinguish structures futile (Preiss et al., 2012). In Table 1, the pesticides, pharmaceuticals and personal care products (PPCPs) identified by LC and GC/MS are listed.

**Table 1.** Pesticides & PPCPs identified by LC & GC/MS

Chemical Classes	Chemicals
Herbicides	Bentazone; 2,4-D, Bromoxynil, Dicamba, Triclopyr, and Mecoprop; Glyphosate; Clofibric acid
Fungicides	Ethylenebisdithiocarbamates - Ethylenethiourea, Prophylenebisdithiocarbamate -Propylenethiourea
	Phenoxy acid pesticides (2,4-D, MCPA, 2,4,5-T, 2,4-DB, MCPB, 2,4,5-TB, cloprop, dichlorprop, fenoprop and mecoprop), Halogenated aliphatic acid pesticides (flupropanate, MCA, TCA and dalapon), Aromatic acidic pesticides (dicamba, 2,3,6-TBA, clopyralid, quinclorac and quinmerac)  150 Pesticide metabolites
PPCPs	Phenazone, Propylphenazone, N, N-diethyl-methylbenzamide, Ranitidine, Atenolol, Paracetamol, Xylometazoline, Ofloxacin, Ciprofloxacin, Ornidazole, Fluconazole, Repaglinide, Losartan, Omeprazole, Piroxicam, Ketoconazole, Olmesartan, Telmisartan, Clopidogrel, Imepenem, Ampicillin, Naphazoline, Metoprolol, Celiprolol, Antazoline, Mebeverine, Erythromycin, Eprosartan, Pioglitazone, Cetrizine, meloxicam, Valsartan, Diclofenac, Ranitidine, Doripenem, Amoxicillin, Amlodipine, Fluoxetine, Lornoxicam, Rosuvastatin, Atorvastatin, Pitavastatin, Fenofibrate, Loratidine, Caffeine, Carbamazepine 10,11-epoxide, Metoprolol, N-acetylaminoantipyrine, oxazepam,

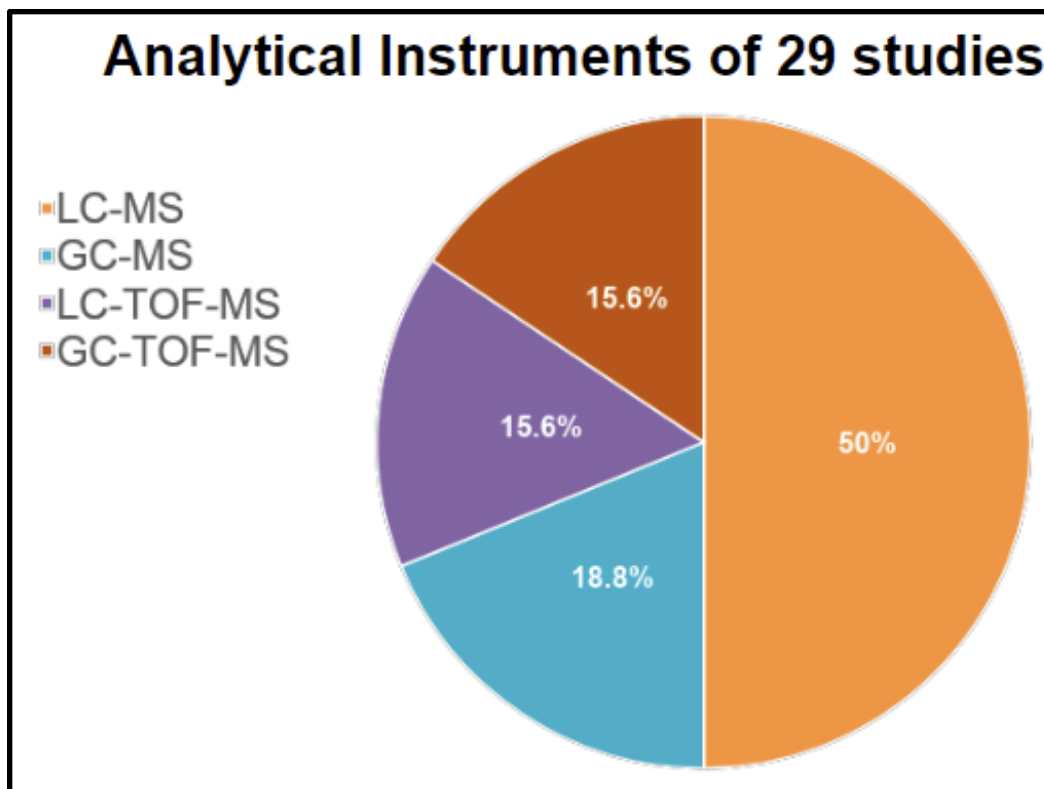
	phenazone, propyphenazone, tramadol, Methylparaben, Ethylparaben, Propylparaben, Butylparaben, Benzophenone, 3-(4-methylbenzylidene)camphor, N,N-diethyltoluamide, 17-a ethynyl estradiol, 17-b estradiol, Estrone, Estriol, Progesterone, Testosterone, Sulfamethoxazole, lincomycin, Sulfamethazine, Tylosin, Trimethoprim, Triclosan, Erythromycin, Naproxen, Ibuprofen, Salicylic acid, Gemfibrozil, Meprobamate, Fluoxetine, Diltiazem, Paroxetine, Valsartan, Atenolol, Diphenhydramine, Triamterene Caffeine, Paraxanthine, N,N-diethyl-meta-toluamide, Cotinine, Acetaminophen, Ketoprofen, Fenoprofen, Propyphenazone, Gemfibrozil, Diclofenac, Indomethacin, Salicylic acid, Crotonamiton, Trimethoprim, Diatrizoic acid, Diethyltoluamide, Bisphenol A
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There were a total of 9 studies that used TOF analysis. For the studies that used TOF analysis only 2 explored both LC-TOF and GC-TOF analysis. Of those studies only one was able to make a distinction between the results of the two methods (Hernández et al., 2015). From the distinction, it was determined that the GC-TOF analysis allowed for greater detection limits and more specificity (Hernández et al., 2015). In Table 2, the pesticides and pharmaceuticals and personal care products (PPCPs) identified by LC and GC-TOF/MS are listed. In **Figure 7** the studies have been broken down percentage-wise to show that a majority of the studies that took place over the 13-year period of 2002 to 2015 focused on the use of LC-MS to analyze their groundwater samples. Through the use of LC-MS both volatile and non-volatile molecules can be analyzed, whereas, GC-MS would only allow the analysis of volatile and semi volatile molecules.

**Table 2.** Pesticides & PPCPs identified by LC & GC-TOF/MS

Chemical Classes	Chemicals
------------------	-----------

Herbicides	Prometon, Deisopropylprometon, Hydroxyprometon, Hydroxyatrazine, Deethylatrazine, Propazine, Simazine, Cyanazine acid, Deisopropylatrazine, Tebutam, Benfluraline, Sebuthylazine, Terbutylazine, Metsulfuronmethyl, Chlorotoluron, Diflufenican, Atrazine, Simazine
Fungicides	Azoxystrobine, Difeconazole, Metalaxyl, Thiabendazol, Fenarimol, Carbendazim, Propiconazole, Imazalil
Insecticides	Carbosulfan, Diazinon
	Pirimicarb, 2-Aminobenzimidazole, Naphthalene, Acenaphthylene, Acenaphthene, Pentachlorobenzene, 4-t-Octylphenol, Fluorene, Chlorpropham, Trifluralin, Alpha-HCH, Simazine, 4-n-Octylphenol, Hexachlorobenzene-13C6, Hexachlorobenzene, Terbutylazine-D5, Terbutylazine, Beta-HCH, Propyzamide, Lindane, Phenanthrene, Anthracene, 4-N-Nonylphenol, Metribuzin, Endosulfan ether, Alachlor, PCB, Metolachlor, Chlorpyrifos, Aldrin, Pendimethalin, Chlorfenvinphos, Isodrin, Fluoranthene, Pyrene, Endosulfan I, p,p'-DDE-D8, p,p'-DDE, Dieldrin, Endrin, PCB, BDE, p,p'-DDD, Endosulfan II, PCB, p,p'-DDT, Pentachlorophenol, Diuron, Carbendazim, Azoxystrobine, Metazachlor, Piperonyl butoxide, Phoxime, Fenarimol, Triadimenol
PPCPs	Amitriptyline, Dosulepin, Chlorprothixene, Butamirate, Dosulepin carbinol, Melitracene carbinol, Valsartan, Irbesartan, Venlafaxine, Carbamazepine, Tonalide, Octocrylene, Clindamicyn, Lincomycin, Ofloxacin, 4-aminoantipyrine-N-formyl and 4-aminoantipyrine-N-acetyl, Caffeine, Carbamazepine, Ibuprofen, Progesterone, Acetaminophen, Diclofenac, 4-androstenedione, Ofloxacin, Testosterone, Drospirenone, Bezafibrate, Norethindrone, Estrone, Sulfamethoxazole, Levonorgestrel, Ethinylestradiol, Trimethoprim, Atenolol, Norfloxacin, Sulfamethazine, 17-beta-Estradiol, Ciprofloxacin, Metronidazole, Bisphenol A, Thiepinon, 2-Isopropenyl-benzophenone, 2-Chloroprothioxanten-9-one



**Figure 7.** Percentages of studies that used GC, LC and TOF to analyze groundwater.

### 3.2 Study Objectives

The studies that began in the early 2000s were focused mainly on finding the rate of occurrence of specific chemicals, while the studies that took place later in the decade shifted towards a focus on developing and validating study methods. Most of the studies aimed to develop new procedures all together or to improve on existing procedures through the use of LC, GC and TOF/MS.

**Table 3** - Studies focused on development and validation of GC, LC and TOF methods.

Study Reference	Location	Analysis Type	Sample Type	Chemicals Screened
Planas et al., 2015	Barcelona & Catalonia,	GC - MS	Groundwater & Tap Water	MX & BMXs

	Spain			
Kapelewska et al., 2016	Northeastern Poland	GC - MS	Groundwater	PCPs & Hormones
Ripollés et al., 2012	Barcelona/Valencia, Spain	LC - MS	Groundwater	ETU & PTU
Xue et al., 2015	Tianjin/ Beijing, China	LC - MS	Groundwater	Antibiotics
Sjerps et al., 2016	Netherlands & Europe	LC - MS	Groundwater & Drinking water	Not specified
Sanchis et al., 2012	Catalonia, Spain	LC - MS	Groundwater	Glyphosate
McManus et al., 2014	Ireland	LC - MS	Groundwater	Herbicides
Cherta et al., 2012	Castellón, Spain	GC - MS	Groundwater & Surface water	Herbicides & PAHs
Lava et al., 2013	Vicenza Province, Italy	GC - MS	Groundwater	Benzotrifluoride derivative compounds
Soulier et al., 2016	Waters/ Guyancourt, France	LC-TOF-MS	Groundwater	Not specified
Hernández et al., 2015	Valencia, Spain	LC-TOF-MS & GC-TOF-MS	Groundwater, Surface water & Wastewater	Pharmaceuticals
Brunswick et al., 2015	Alberta, Canada	LC-TOF-MS	Groundwater, Surface water & Wastewater	Total Naphthenic acids
Kresinová et al., 2016	Czech Republic	LC-TOF-MS	Groundwater	Psychopharmaceuticals

Another significant focus for several studies was testing the methods of LC/GC/TOF-MS for water quality and screening for diverse types of chemicals and

products. All of the studies that focused on water quality had some type of groundwater sample that was tested. A few studies included samples from surface water and wastewater sources as well. In addition to focusing on water quality, a handful of studies set out to determine the occurrence of those compounds in the samples through the use of LC/GS/TOF-MS (Jindal et al., 2015; Wolf et al., 2012).

**Table 4** - Studies focused on water quality and chemical fate/behavior.

<b>Study Reference</b>	<b>Location</b>	<b>Analysis Type</b>	<b>Sample Type</b>	<b>Chemicals Screened</b>
McEachran et al., 2016	North Carolina, USA	LC - MS	Groundwater, Surface water & Wastewater	Pharmaceuticals & Steroid hormones
Ter Laak et al., 2012	Nieuwegein, Netherlands	LC - MS	Groundwater	Industrial chemicals and products
Jindal et al., 2015	Nagar/ Punjab, India	LC - MS	Groundwater	Drug residues of 40 medicinal classes
Wolf et al., 2012	Rastatt, Germany	LC - MS	Groundwater	Pharmaceuticals & Artificial sweeteners
Reemtsma et al., 2013	Karlsruhe, Germany	LC - MS	Groundwater & Surface water	Pesticides
Castiglioni et al., 2015	Milan, Italy	LC - MS	Groundwater, Wastewater & Drinking water	Perfluorinated compounds
Kirishima et al., 2017	Hokkaido, Japan	TOF	Groundwater	Actinide & Fission products
Zemo et al., 2017	California, USA	GC-TOF-MS	Groundwater	Petroleum Biodegradation Metabolite Plumes

The identification of specific chemicals after sample extraction from various groundwater sources was the next objective of several studies. For studies with this

purpose, up to 66 analytes, which included artificial sweeteners, such as sucralose and pesticides, such as atrazine were targeted for detection and identification in the groundwater, surface water, drinking water and wastewater samples (Han Tran et al., 2013; Vulliet et al., 2014).

**Table 5** - Studies focused on detection and identification of specific chemicals

<b>Study Reference</b>	<b>Location</b>	<b>Analysis Type</b>	<b>Sample Type</b>	<b>Chemicals Screened</b>
Chen et al., 2017	Guangdong, South China	GC -MS	Groundwater, Fishpond, Drinking Water	N-nitrosamines
Preiss et al., 2012	Kladow/Gatow, Southwest Berlin	GC - MS & LC - MS	Groundwater	Polar XOCs
Han Tran et al., 2013	Singapore	LC - MS	Groundwater, Surface Water & Wastewater	PPCPs, EDCs & Artificial sweeteners
Xu et al., 2013	Texas, USA	LC - MS	Groundwater & Surface water	Acidic Pesticides
Lange et al., 2012	USA, Canada, Europe & Germany	LC - MS	Groundwater, Surface water & Drinking water	Artificial Sweeteners
Vulliet et al., 2014	Guadeloupe/Guiana/Martinique/Mayotte/Reunion - French Departments	LC - MS & GC-TOF-MS	Groundwater	Pesticides, Pharmaceuticals, Hormones & Industrial substances
Fernández-Ramos et al., 2014	Colorado, USA	LC-TOF-MS	Groundwater	Prometon & Transformation products



Another objective of a hand full of studies was to determine the occurrence of compounds in samples through the use of LC/GS/TOF-MS (Jindal et al., 2015; Wolf et al., 2012). One study focused on identifying a contamination source (Castiglioni et al., 2015) while another focused on studying the chemicals behavior after being released from deep underground source (Kirishima et al., 2017). The studies that began in the early 2000s were focused mainly on finding the rate of occurrence of specific chemicals, while the studies that took place later in the decade shifted towards a focus on developing and validating study methods.

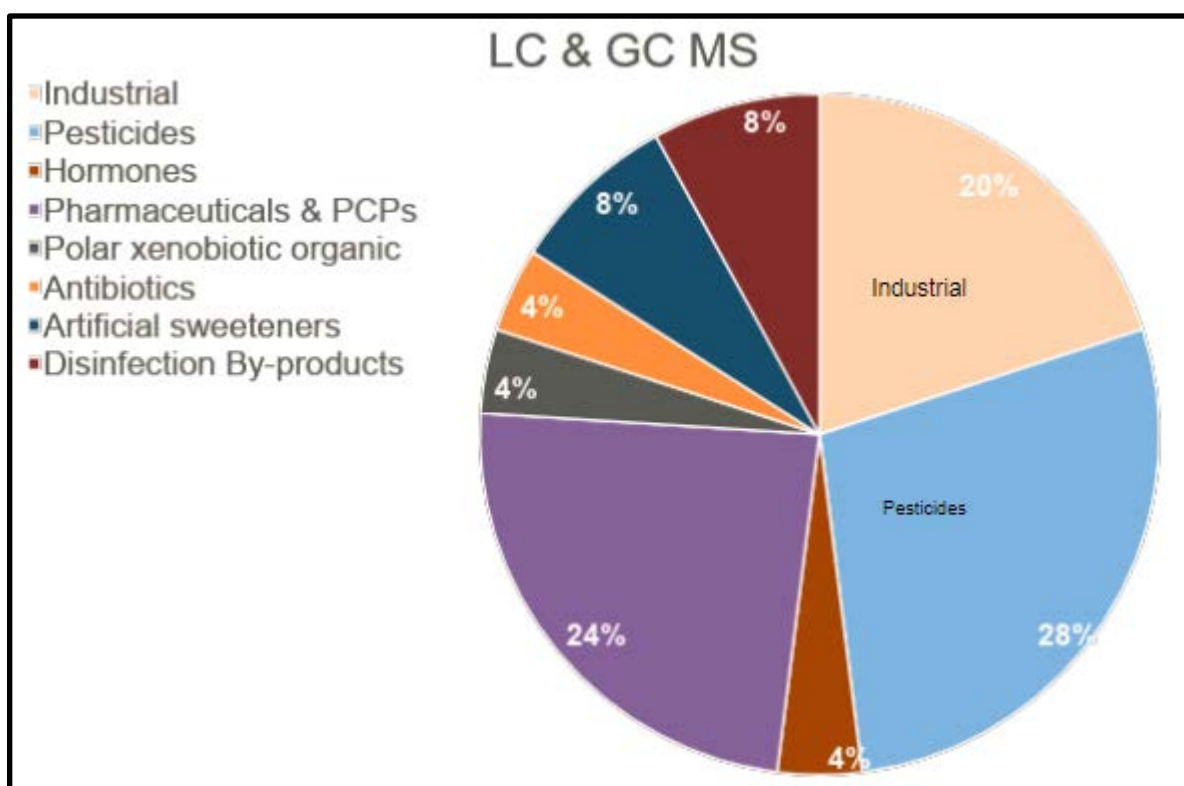
### **3.3 SPE vs POCIS**

Out of the total number of studies utilized for this review, 86% of them used a SPE technique with their sampling method, 10% used POCIS and the last 4% did not specify using either of the techniques for their sampling method. Of the 86% that used a SPE technique approximately 20% specified that they obtained grab samples. The few studies that used POCIS were those that aimed to identify the presence of organic compounds such as herbicides, insecticides, fungicides, antibiotics, antiepileptics, analgesics/anti-inflammatories, cardiovascular agents, psycholeptics and industrial compounds (Soulie et al., 2016). Whereas the studies that used SPE were those that focused on a vast array of chemicals, such as N-nitrosamines, caffeine, sucralose, ethylenethiourea and many more (Chen et al., 2017; Wolf et al., 2012).

### **3.4 Chemicals Screened**

Even though many of the studies had similar objectives there was a vast array of chemicals screened. The chemicals screened consisted of not only man made but of

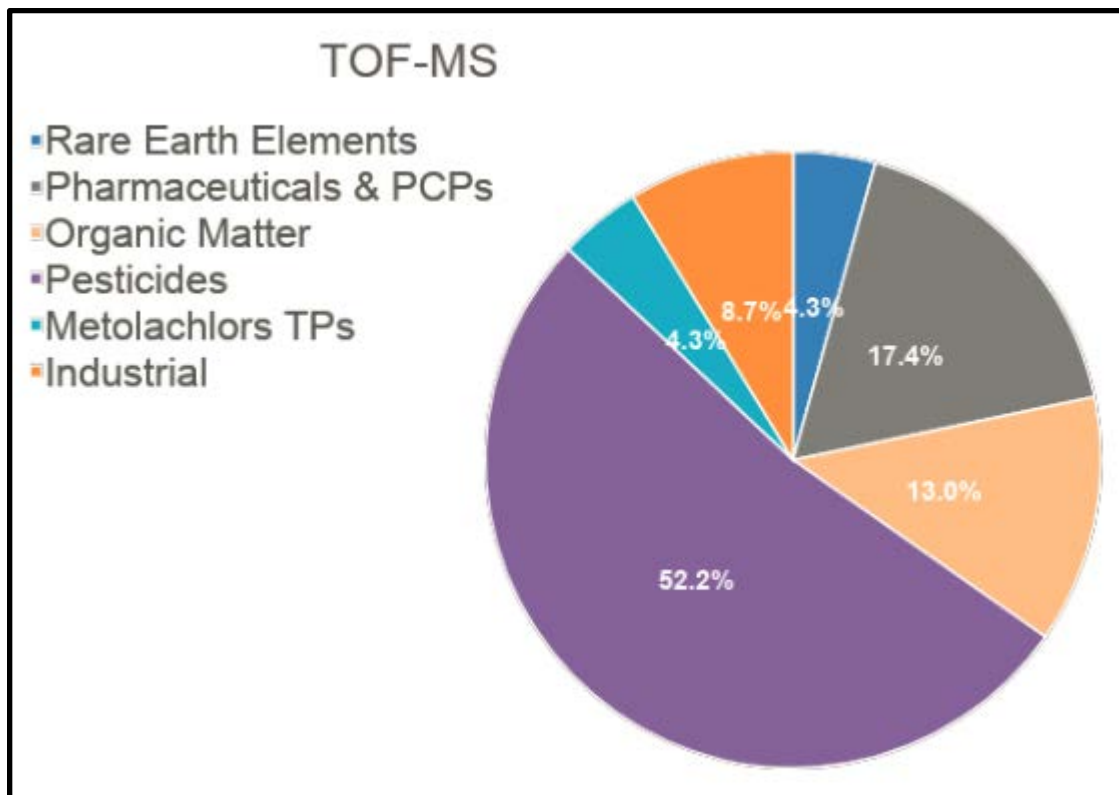
those that naturally occur in nature as well. In addition to these categories, some studies also aimed to identify and/or detect derivatives and by-products of chemicals from both major categories. This task however proved to be more challenging due to lack of references and limitations presented by the instrumentation. In both, **Figure 8** and **Figure 9**, the two main categories of chemicals screened, man-made and naturally occurring, were further categorized and are graphically represented based on the analysis type of the studies that screened for them. **Figure 8** focuses on the chemicals that were screened using the LC and/or GC MS, while **Figure 9** focuses on the studies that used TOF MS.



**Figure 8.** The chemical categories focused on by studies that used LC & GC MS.

For the studies that used LC and GC MS for analysis, the chemicals that were most often screened heavily and detected were pesticides. Additional chemicals that

were heavily screened for following pesticides were PPCPs and industrial chemicals. Likewise, the studies that focused on the use of TOF analysis also had the highest number of studies screening for pesticides and were again followed by PPCPs. For all analysis methods, pesticides were the chemicals screened for the most which was likely due to a majority of the studies being centered around urban and agricultural areas. The pesticides that were screened for were able to be even further classified as herbicides, insecticides and fungicides. Of note, for the studies that focused on these specific chemicals, sampling occurred in the Netherlands, India, Poland and the United States, which are all known for the highest expenditures and production of pesticides and PPCPs.



**Figure 9.** The chemical categories focused on by studies that used TOF MS.

In **Table 6**, the chemicals that were found in confined aquifers are listed. In Kapelewska et al., 2016, samples were taken from confined and unconfined aquifers located near the same landfill and it was found that the same chemicals were detected in both samples. Similarly, in Cherta et al., 2012, samples taken from different confined and unconfined aquifers in the same general area also found that the same chemicals were being detected.

**Table 6** - Chemicals detected in confined aquifers.

Study Reference	Chemicals detected
Kapelewska et al., 2016	Methylparaben (MP), ethylparaben (EP), propylparaben (PP), buthylparaben (BP), benzophenone (BPh), 3-(4-methylbenzylidene)camphor (4-MBC), N,N-diethyltoluamide (DEET), and two hormones: estrone (E1) and $\beta$ -estradiol (E2)
Sanchis et al., 2012	Glyphosate
Cherta et al., 2012	Naphthalenea, Acenaphthylenea, Acenaphthenea, Pentachlorobenzeneb, 4-t-Octylphenolc, Fluorenea, Chlorprophamd, Trifluralinc, Alpha-HCHc, Simazined, Atrazined, 4-n-Octylphenolc, Hexachlorobenzeneb, Terbutylazined, Beta-HCHc, Propyzamided, Lindanec, Phenanthrene, Anthracenea, 4-n-Nonylphenolc, Metribuzind, Endosulfan etherc, Alachlord, Metolachlord, Chlorpyrifosd, Aldrinc, Pendimethalind, Chlorfenvinphosd, Isodrinc, Fluoranthenea, Pyrenea, Endosulfan, p,p'-DDEc, Dieldrinc, Endrinc, BDE, p,p'-DDDc, Endosulfan, PCB, p,p'-DDTc
Lyczko et al., 2015	Thiotetronic Acids
Fernández-Ramos et al., 2014	Prometon and other Triazines

Ter Laak et al., 2012	N, N-diethyl-methylbenzamide (DEET), Phenazone, Popylphenazone, Tributylphosphate, Triethylphosphate, Triphenylphosphineoxide (TPPO), Tris (2-butoxyethyl) phosphate
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### 3.5 Detection Levels and Recovery

From the studies that used a non-targeted approach for analysis, several features were able to be identified due to the analysis techniques ability to reach low detection levels (Preiss et al., 2012). These studies obtained average recovery levels ranging from 70 - 90% (Zemo et al., 2017; Soulier et al., 2016; Sjerps et al., 2016; Preiss et al., 2012). Based on the lowest and highest detection percentages reached using the four methods, there appeared to be no significant distinction. As displayed in **Table 7**, almost all analysis methods had a detection limit of 52% and the highest detections were also extremely close in value. Furthermore, the exact number of unidentifiable features in the studies that did not specify their chemical targets the range of chemicals detected were either not specified or the total numbers varied (Zemo et al., 2017). When looking at all of the studies that used GC-MS and/or LC-MS, it was evident that the highest total number of chemicals that were detected by LC-MS. The LC-MS method was able to detect 109 more chemicals than the GC-MS. However, the studies that had the higher numbers of detection by the use of LC-MS also had up to 313 unidentifiable chemicals (Ter Laak et al., 2012; Wolf et al., 2012; Ripollés et al., 2012).

**Table 7.** The percentage ranges of detection by analysis type.

Analysis Type	Lowest (%) Detected	Highest (%) Detected
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GC - MS	52	110
LC - MS	52	118
GC - TOF - MS	52	90
LC - TOF - MS	39	119

**Table 8.** The highest number of chemicals detected by each analysis type.

<b>Analysis Type</b>	<b>Highest # Detected</b>
GC - MS	60
LC - MS	169
GC - TOF - MS	127
LC - TOF - MS	98

## 4.0 Discussion

The objective of this review was to summarize the current knowledge of non-targeted screening methods and to identify gaps in knowledge on these methods based on current studies. From the studies it was found that GC-TOF-MS was the best method to reach low detection limits as specificity of structures were more accurately and readily identifiable. This was the case despite the ability to detect more chemicals using LC-MS as several of the chemicals were not able to be as easily identified.

Another important finding that appeared to be evident from the studies, was that the recovery levels reached by the use of LC, GC and TOF mass spectrometry were on the higher end of the spectrum for pesticides and pharmaceuticals. This finding was probably due to the fact that so many pesticides and pharmaceuticals were imported,

exported and expended, during the time periods of these studies. Overall, when looking at all of the studies, all methods seem to be efficient and accurate for the purpose of monitoring groundwater for contaminants. Previous research had already established that these screening methods could be used to search for specific chemical compounds; however, the results of these studies have shown that these methods can be used to do more.

A large number of studies focused on LC methods as opposed to GC and TOF. Even though this is the case it would seem that more studies should have included GC and TOF due to the results of GC being more easily identifiable (Ter Laak et al., 2012; Wolf et al., 2012; Ripollés et al., 2012). The GC focused studies typically reached low detection limits with accuracy than the LC studies even though the result of both methods were significant (Cherta et al., 2012; Kapelewska et al., 2016; Planas et al., 2015; Chen et al., 2017). Additionally, of note, studies that used TOF reported a higher number of chemical compounds identified in their results even though studies that used GC and LC methods had in some cases a higher number of chemicals detected (Hernández et al., 2015; Lyczko et al., 2015).

#### **4.1 Limitations**

There were several limitations of note from the studies that used the different analysis methods. The most notable limitation which applied to almost all of the studies was due to SPE sampling. This is notable since SPE sampling only provides a snapshot of the contamination as opposed to POCIS sampling which was used by a few of the studies. POCIS sampling would have allowed the studies to capture a contamination

period over an extended time such as weeks, months and years. Another limitation in the past and on some of the non-targeted studies was the lack of reference standards available to compare the results to (Hernández et al., 2015; Brunswick et al., 2015). One of those limitations was not being able to compare the technique used in analysis to any other previous technology (Chen et al., 2017). Additionally, some of the labelled compounds may have exhibited different behavior than the analytes making the prospect of satisfactory results dubious (Ripollés et al., 2012). Another limit that was mentioned in one of the studies was a narrow mass window which only allows one single chromatography peak to be observed at the expected retention time (Hernández et al., 2015). A few additional limitations noted included: short term stability of the sample during transportation from the sampling source; instrumentation costs; overlapping of isometric peaks; and quantity and complexity of the data produced (Vulliet et al., 2014; Brunswick et al., 2015).

## **5.0 Conclusion**

From the current knowledge of mass spectrometry methods, it appears that the GC-TOF-MS would be the best place to start with development of standard procedure in monitoring groundwater. It would be highly beneficial for more studies to focus on this method as opposed to LC-MS based methods. This conclusion was drawn by the accuracy achieved using the GC-TOF-MS method in comparison to that of the LC-TOF-MS, LC-MS and GC-MS methods. Since this method has been identified with high potential for yielding significant data on groundwater analysis, this will allow for additional research to be conducted based on this benchmark.



Further research should be conducted on this method with targeted, suspect and non-targeted screening, in conjunction with newer reference standards. It would be beneficial to make a prioritization of the chemicals that were not identified in the studies based on the rate of their occurrence. After noting the rate of occurrence of these unidentified chemicals they ought to be added to the target and suspect database for further exploration on their properties and degradation in groundwater. Lastly, for the purpose of further developing the understanding surrounding the use of GC-TOF-MS with difference in sampling types and sampling periods should be examined.

## 6.0 References

- Alavanja, M.C.R. (2009). Pesticides Use and Exposure Extensive Worldwide. *Reviews on Environmental Health*, 24(4), 303 - 309.
- Bletsou, A. A., Jeon, J., Hollender, J., Archontaki, E., & Thomaidis, N. S. (2015). Targeted and non-targeted liquid chromatography-mass spectrometric workflows for identification of transformation products of emerging pollutants in the aquatic environment. *TrAC Trends in Analytical Chemistry*, 66, 32–44.
- Brunswick, P., Shang, D., van Aggelen, G., Hindle, R., Mark Hewitt, L., Frank, R. A., ... Kim, M. (2015). Trace analysis of total naphthenic acids in aqueous environmental matrices by liquid chromatography/mass spectrometry-quadrupole time of flight mass spectrometry direct injection. *Journal of Chromatography A*, 1405, 49–71.
- Castiglioni, S., Valsecchi, S., Polesello, S., Rusconi, M., Melis, M., Palmiotto, M., ... Zuccato, E. (2015). Sources and fate of perfluorinated compounds in the aqueous environment and in drinking water of a highly urbanized and industrialized area in Italy. *Journal of Hazardous Materials*, 282, 51–60.
- Chen, W., Li, X., Huang, H., Zhu, X., Jiang, X., Zhang, Y., ... Qi, S. (2017). Comparison of gas chromatography-mass spectrometry and gas chromatography-tandem mass spectrometry with electron ionization for determination of N-nitrosamines in environmental water. *Chemosphere*, 168, 1400–1410.
- Cherta, L., Beltran, J., Portolés, T., & Hernández, F. (2012). Multiclass determination of 66 organic micro pollutants in environmental water samples by fast gas chromatography - mass spectrometry. *Anal Bioanal Chem*, 402, 2301–2314.
- Fernández-Ramos, C., Ferrer, I., Mauch, K., Satinsky, D., & Michael Thurman, E. (2014). Identification of Prometon, Deisopropylprometon, and Hydroxyprometon in Groundwater by High Resolution Liquid Chromatography/Mass Spectrometry. *Science of the Total Environment*, 497-498, 459–466.
- Han Tran, N., Hu, J., & Leong Ong, S. (2013). Simultaneous determination of PPCPs, EDCs, and artificial sweeteners in environmental water samples using a single-step SPE coupled with HPLC–MS/MS and isotope dilution. *Talanta*, 113, 82–92.

Hernández, F., Ibáñez, M., Portolés, T., Cervera, M. I., Sancho, J. V., & López, F. J. (2015). Advancing towards universal screening for organic pollutants in waters. *Journal of Hazardous Materials*, 282, 86–95.

Jindal, K., Narayanam, M., & Singh, S. (2015). A systematic strategy for the identification and determination of pharmaceuticals in environment using advanced LC–MS tools: Application to ground water samples. *Journal of Pharmaceutical and Biomedical Analysis*, 108, 86–96.

Kapelewska, J., Kotowska, U., & Wiśniewska, K. (2016). Determination of personal care products and hormones in leachate and groundwater from Polish MSW landfills by ultrasound-assisted emulsification micro extraction and GC-MS. *Environ Sci Pollut Res*, 23, 1642–1652.

Kirishima, A., Kuno, A., Amamiya, H., Kubota, T., Kimuro, S., Amano, Y., ... Sato, N. (2017). Interaction of rare earth elements and components of the Horonobe deep groundwater. *Chemosphere*, 168, 798 – 806.

Kresinová, Z., Linhartová, L., Petru, K., Krejcová, L., Srdlová, K., Lhotský, O., ... Cajthaml, T. (2016). Method for analysis of psychopharmaceuticals in real industrial wastewater and groundwater with suspended organic particulate matter using solid phase extraction disks extraction and ultra-high performance liquid chromatography/time-of-flight mass spectrometry. *Journal of Chromatography A*, 1440, 15–22.

Lane, T. (2016). *Hydrology & Water Resources Engineering*. Retrieved from <http://slideplayer.com/slide/7016229>

Lange, F. T., Scheurer, M., & Brauch, H.-J. (2012). Artificial sweeteners - a recently recognized class of emerging environmental contaminants: a review. *Anal Bioanal Chem*, 403, 2503–2518.

Lava, R., Aimoa, E., Menegus, L., Pojana, G., & Marcomini, A. (2013). Determination of benzotrifluoride derivative compounds in groundwater. *Analytical Chimica Acta*, 804, 126 – 134.

Lyczko, J., Beach, D., & Gabryelshi, W. (2015). Detection, Identification, and Occurrence of Thiotetronic Acids in Drinking Water from Underground Sources by

Electrospray Ionization-High Field Asymmetric Waveform Ion Mobility Spectrometry-Quadrupole Time-of-Flight-Mass Spectrometry. *Analytical Chemistry*, 87, 9884 – 9891.

McEachran, A. D., Shea, D., Bodnar, W., & Guthrie Nichols, E. (2016). Pharmaceutical Occurrence in Groundwater and Surface Waters in Forests Land-applied with Municipal Wastewater. *Environmental Toxicology and Chemistry*, 35(4), 898–905.

McManus, S.-L., Moloney, M., Richards, K. G., Coxon, C. E., & Danaher, M. (2014). Determination and Occurrence of Phenoxyacetic Acid Herbicides and Their Transformation Products in Groundwater Using Ultra High Performance Liquid Chromatography Coupled to Tandem Mass Spectrometry. *Molecules*, 19, 20627–20649.

National Groundwater Association (NGWA). (2012, September 5). Information on Earth's water. Retrieved from <http://www.ngwa.org/Fundamentals/teachers/Pages/information-on-earth-water.aspx>

North Carolina Department of Environmental Quality (NCDEQ). (2013, April 1). NC\_Std\_Groundwater\_02LStandards. Retrieved from [https://files.nc.gov/ncdeq/documents/files/02L%20Groundwater%20Standards%20Table%205-21%202013\\_0.pdf](https://files.nc.gov/ncdeq/documents/files/02L%20Groundwater%20Standards%20Table%205-21%202013_0.pdf)

Planas, C., Ventura, F., Caixach, J., Martin, J., Rosa Boleda, M., & Paraira, M. (2015). Analysis of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone(MX) and its brominated analogues in chlorine-treated water by gas chromatography coupled to triple quadrupole tandem mass spectrometry (GC-QqQ-MS/MS). *Talanta*, 144, 145–156.

Preiss, A., Berger-Preiss, E., Elend, M., Gerling, S., Kuhn, S., & Schuchardt, S. (2012). A new analytical approach for the comprehensive characterization of polar xenobiotic organic compounds downgrading of old municipal solid waste (MSW) landfills. *Anal Bioanal Chem*, 403, 2553–2561.

Reilly, T. E., Dennehy, K. F., Alley, W. M., & Cunningham, W. L. (2008). Ground-Water Resources Program: Ground-Water Availability in the United States. Retrieved from <https://water.usgs.gov/watercensus/AdHocComm/Background/Ground-WaterAvailabilityintheUnitedStates.pdf>

Reemtsma, T., Alder, L., & Banasiak, U. (2013). A multi method for the determination of 150 pesticide metabolites in surface water and ground water using direct injection liquid chromatography - mass spectrometry. *Journal of Chromatography A*, 1271, 95–104.

Ripollés, C., Sancho, J. V., López, F. J., & Hernández, F. (2012). Liquid chromatography coupled to tandem mass spectrometry for the residue determination of ethylenethiourea (ETU) and propylenethiourea (PTU) in water. *Journal of Chromatography A*, 1243, 53–61.

Sanchis, J., Kantiani, L., Llorca, M., Rubio, F., Ginebreda, A., Fraile, J., ... Farré, M. (2012). Determination of glyphosate in groundwater samples using an ultrasensitive immunoassay and confirmation by on-line solid-phase extraction followed by liquid chromatography coupled to tandem mass spectrometry. *Anal Bioanal Chem*, 402, 2335–2345.

Sjerps, R. M., Vughs, D., van Leerdam, J. A., ter Laak, T. L., & van Wezel, A. P. (2016). Data-driven prioritization of chemicals for various water types using suspect screening LC-HRMS. *Water Research*, 93, 254–264.

Sobus, J. R. (2016). *Advancing Non-targeted Analysis Research within EPA/ORD*. U. S. Environmental Protection Agency.

Soulier, C., Coureau, C., & Togola, A. (2016). Environmental forensics in groundwater coupling passive sampling and high resolution mass spectrometry for screening. *Science of the Total Environment*, 563 - 564, 845 – 854.

Ter Laak, T. L., Puijker, L. M., van Leerdam, J. A., Raat, K. J., Kolkman, A., de Voogt, P., & van Wezel, A. P. (2012). Broad target chemical screening approach used as tool for rapid assessment of groundwater quality. *Science of the Total Environment*, 427-428, 308–313.

The Groundwater Foundation (TGF). (2017). GROUNDWATER CONTAMINATION. Retrieved from <http://www.groundwater.org/get-informed/groundwater/contamination.html>

U.S. Department of Commerce. (2016). 2016 Top Markets Report Pharmaceuticals. Retrieved from [https://www.trade.gov/topmarkets/pdf/Pharmaceuticals\\_Executive\\_Summary.pdf](https://www.trade.gov/topmarkets/pdf/Pharmaceuticals_Executive_Summary.pdf)

U. S. Environmental Protection Agency (US EPA). (2018, March 22). National Primary Drinking Water Regulations. Retrieved from <https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations>

U.S. Environmental Protection Agency (US EPA). (2017). Pesticides Industry Sales and Usage 2008 - 2012 Estimates. Retrieved from [https://www.epa.gov/sites/production/files/2017-01/documents/pesticides-industry-sales-usage-2016\\_0.pdf](https://www.epa.gov/sites/production/files/2017-01/documents/pesticides-industry-sales-usage-2016_0.pdf)

U.S. Geological Survey (USGS). (2018, March 20). Aquifers and Groundwater. Retrieved from <https://water.usgs.gov/edu/earthgwaquifer.html>

U.S. Geological Survey (USGS). (2017, December 6). Public-supply water use. Retrieved from <https://water.usgs.gov/edu/wups.html>

U.S. Geological Survey (USGS). (2011, January). Water-Quality Sampling by the U.S. Geological Survey: Standard Protocols and Procedure. Retrieved from <https://pubs.usgs.gov/fs/2010/3121/fs2010-3121.pdf>

Vulliet, E., Tournier, M., Vauchez, A., West, L., Baudot, R., Lafay, F., ... Cren-Olivé, C. (2014). Survey regarding the occurrence of selected organic micropollutants in the groundwaters of overseas departments. *Environ Sci Pollut Res*, 21, 7512–7521.

Wolf, L., Zwiener, C., & Zemmann, M. (2012). Tracking artificial sweeteners and pharmaceuticals introduced into urban groundwater by leaking sewer networks. *Science of the Total Environment*, 430, 8–19.

Xu, C., & Armstrong, D. W. (2013). High-performance liquid chromatography with paired ion electrospray ionization (PIESI) tandem mass spectrometry for the highly sensitive determination of acidic pesticides in water. *Analytica Chimica Acta*, 792, 1–9.

Xue, Q., Qi, Y., & Liu, F. (2015). Ultra-high performance liquid chromatography-electrospray tandem mass spectrometry for the analysis of antibiotic residues in environmental waters. *Environ Sci Pollut Res*, 22, 16857–16867.

Zemo, D. A., O-Reilly, K. T., Mohler-Renaie-Magaw, R. E., Espino Devine, C., Ahn, S., & Tiwary, A. K. (2017). Life Cycle of Petroleum Biodegradation Metabolite Plumes, and Implications for Risk Management at Fuel Release Sites. *Integrated Environmental Assessment and Management*, 13(4), 714–727.

**Appendix A: Synthesis of studies using targeted, suspect screening or non-targeted analyses of groundwater.**

**Table A-1.** Liquid & Gas Chromatography/Mass Spectrometry

<b>Chemical Class</b>	<b>Chemicals</b>	<b>Authors, Year</b>
Herbicides	Bentazone	ter Laak et al., 2012
	2,4-D, Bentazone, Bromoxynil, Dicamba, Triclopyr, and Mecoprop	McManus et al., 2014
	Glyphosate	Sanchís et al., 2012
	Clofibric acid	Tran et al., 2013
Fungicides	Ethylenebisdithiocarbamates - Ethylenethiourea, Propylenebisdithiocarbamate - Propylenethiourea	Ripollés et al., 2012
Hormones	Estrone, $\beta$ -estradiol	Kapelewska et al., 2016
Pharmaceuticals and personal care products (PPCPs)	Phenazone, Propylphenazone, N,N-diethyl-methylbenzamide	Ter Laak et al., 2012
	Ranitidine, Atenolol, Paracetamol, Xylometazoline, Ofloxacin, Ciprofloxacin, Ornidazole, Fluconazole, Repaglinide, Losartan, Omeprazole, Piroxicam, Ketoconazole, Olmesartan, Telmisartan, Clopidogrel, Imepenem, Ampicillin, Naphazoline, Metoprolol, Celiprolol, Antazoline, Mebeverine, Erythromycin, Eprosartan, Pioglitazone, Cetrizine, meloxicam, Valsartan, Diclofenac, Ranitidine, Doripenem, Amoxicillin, Amlodipine, Fluoxetine, Lornoxicam, Rosuvastatin, Atorvastatin, Pitavastatin, Fenofibrate, Loratidine	Jindal et al., 2015
	Caffeine, Carbamazepine 10,11-epoxide, Metoprolol, N-acetylaminoantipyrine, oxazepam, phenazone, propylphenazone, tramadol	Sjerps et al., 2016
	Methylparaben, Ethylparaben, Propylparaben, Butylparaben, Benzophenone, 3-(4-methylbenzylidene)camphor, N,N-diethyltoluamide	Kapelewska et al., 2016
	17-a ethynyl estradiol, 17-b estradiol, Estrone, Estriol, Progesterone, Testosterone, Sulfamethoxazole, lincomycin, Sulfamethazine, Tylosin, Trimethoprim, Triclosan, Erythromycin, Naproxen, Ibuprofen, Acetaminophen, Salicylic acid, Gemfibrozil, Meprobamate, Fluoxetine, Diltiazem, Paroxetine, Valsartan, Carbamazepine, Atenolol, Diphenhydramine, Triamterene Caffeine, Paraxanthine, N,N-diethyl-meta-toluamide, Cotinine, Bisphenol-A	McEachran et al., 2016
Acetaminophen, Caffeine, Carbamazepine, Ibuprofen, Ketoprofen, Fenoprofen, Naproxen, Propylphenazone, Gemfibrozil, Diclofenac, Indomethacin, Salicylic acid, Crotamiton, Trimethoprim, Diatrizoic acid, Diethyltoluamide, Bisphenol A	Han Tran et al., 2013	



Industrial	<p>Tributylphosphate, Triethylphosphate, Triphenylphosphine oxide (TPPO), Tris (2-butoxyethyl) Phosphate</p> <p>Benzotrifluoride, 4-Chlorobenzotrifluoride, 2,4-Dichlorobenzotrifluoride, 3,4-Dichloro-Benzotrifluoride, 3-Aminobenzotrifluoride, 4-Nitrobenzotrifluoride, 3-Amino-4-chlorobenzotrifluoride, 3-Nitro-4-chlorobenzotrifluoride, 4-Chloro-3,5-dinitrobenzotrifluoride</p> <p>Amidotrizoic acid, Carbamazepine, Acesulfame</p> <p>1,2-benzisothiazol-3(2H)-on, 4-Methyl-1H-benzotriazole, Benzotriazole, Tributyl phosphate, Triethyl phosphate, Triphenylphosphine oxide, Tris(2-chloro-1-methylethyl) phosphate</p> <p>Perfluoroalkyl substances</p>	<p>Ter Laak et al., 2012</p> <p>Lava et al., 2013</p> <p>Wolf et al., 2012</p> <p>Sjerps et al., 2016</p> <p>Castiglioni et al., 2015</p>
Polar xenobiotic organic compounds	2-Amino-5-chloro-4-methylbenzenesulfonate, Naphthalene-2-sulfonic acid, 1-Oxo-3,4-dimethyl-pyrrolo[1,2-a]pyrazin-2(1H)yl)acetic acid, 4-Methylcyclohexane-1,2-dicarboxylic acid, 2-(N-hydroxymethyl)-6-methyl-1H-indole-1,3-dione	Preiss et al., 2012
Antibiotics	Sulfonamides, Quinolones, Tetracyclines, Macrolides, Lincomycin, Chloramphenicol	Xue et al., 2015
Artificial sweeteners	<p>Acesulfame, Aspartame, Cyclamate, Neotame, Neohesperidine dihydrochalcone, Saccharin, Sucralose</p> <p>Acesulfame, Aspartame, Cyclamate, Saccharin, Sucralose, Neohesperidin dihydrochalcone</p>	<p>Lange et al., 2012</p> <p>Tran et al., 2013</p>
Disinfection By-products (chlorinated)	<p>3-Chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone, Brominated analogues</p> <p>N-nitrosamines</p>	<p>Planas et al., 2015</p> <p>Chen et al., 2017</p>
Pesticides	<p>Phenoxy acid pesticides (2,4-D, MCPA, 2,4,5-T, 2,4-DB, MCPB, 2,4,5-TB, cloprop, dichlorprop, fenoprop and mecoprop), Halogenated aliphatic acid pesticides (flupropanate, MCA, TCA and dalapon), Aromatic acidic pesticides (dicamba, 2,3,6-TBA, clopyralid, quinclorac and quinmerac)</p> <p>150 Pesticide metabolites</p>	<p>Xu et al., 2013</p> <p>Reemtsma et al., 2013</p>

**Table A-2.** Liquid Chromatography Time of Flight Mass Spectrometry

Chemical Class	Chemicals	Authors, Year
Rare Earth Elements	Y, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm & Yb	Kirishima et al., 2017

Pharmaceuticals and Personal Care Products	<p>Amitriptyline, Dosulepin, Chlorprothixene, Butamirate, Dosulepin carbinol, Melitracene carbinol</p> <p>Valsartan, Irbesartan, Venlafaxine, Carbamazepine, Tonalide, Octocrylene, Clindamicyn, Lincomycin, Ofloxacin, 4-aminoantipyrine-N-formyl and 4-aminoantipyrine-N-acetyl</p> <p>Caffeine, Carbamazepine, Ibuprofen, Progesterone, Acetaminophen, Diclofenac, 4-androstenedione, Ofloxacin, Testosterone, Drospirenone, Bezafibrate, Norethindrone, Estrone, Sulfamethoxazole, Levonorgestrel, Ethinylestradiol, Trimethoprim, Atenolol, Norfloxacin, Sulfamethazine, 17-beta-Estradiol, Ciprofloxacin, Metronidazole, Bisphenol A,</p> <p>Amitriptyline, Dosulepin, Chlorprothixene, Butamirate, Dosulepin carbinol, Melitracene carbinol, Thiepinon, 2-Isopropenyl-benzophenone, 2-Chloroprothioxanten-9-one</p>	<p>Kresinová et al., 2016</p> <p>Hernández et al., 2015</p> <p>Vulliet et al., 2014</p> <p>Křesinová et al., 2016</p>
Organic Matter	<p>Toluene, Dichloroethylene, Trichloroethylene,</p> <p>Thiotetronic Acids</p> <p>Anthracene, Fluoranthene, Pyrene</p>	<p>Křesinová et al., 2016</p> <p>Lyczko, et al., 2015</p> <p>Cherta et al., 2012</p>
Herbicides	<p>Prometon, Deisopropylprometon, Hydroxyprometon, Atrazine, Hydroxyatrazine, Deethylatrazine, Propazine, Simazine, Cyanazine acid, Deisopropylatrazine</p> <p>Tebutam, Atrazine, Benfluraline, Sebuthylazine, Terbutylazine, Metsulfuronmethyl, Chlorotoluron</p> <p>Diflufenican, Atrazine, Simazine</p> <p>Atrazine</p> <p>Atrazine, Diflufenican</p>	<p>Fernández-Ramos et al., 2014</p> <p>Soulier et al., 2016</p> <p>Hernández et al., 2015</p> <p>Cherta et al., 2012</p> <p>Vulliet et al., 2014</p>
Insecticides	<p>Carbosulfan</p> <p>Diazinon</p>	<p>Soulier et al., 2016</p> <p>Cherta et al., 2012</p>
Fungicides	<p>Azoxystrobine, Difeconazole, Metalaxyl</p> <p>Thiabendazol, Fenarimol, Carbendazim, Propiconazole, Imazalil</p>	<p>Soulier et al., 2016</p> <p>Hernández et al., 2015</p>
Metolachlors TPs	<p>Deschlorometolachlor, 2-Hydroxymetolachlor, Deschloroacetylmotolachlor, Metolachlor morpholinone</p>	<p>Soulier et al., 2016</p>
Pesticides	<p>Pirimicarb and 2-Aminobenzimidazole</p> <p>Naphthalene, Acenaphthylene, Acenaphthene, Pentachlorobenzene, 4-t-Octylphenol, Fluorene, Chlorpropham, Trifluralin, Alpha-HCH, Simazine, 4-n-</p>	<p>Soulier et al., 2016</p> <p>Cherta et al., 2012</p>

	<p>Octylphenol, Hexachlorobenzene-13C6, Hexachlorobenzene, Terbutylazine-D5, Terbutylazine, Beta-HCH, Propyzamide, Lindane, Phenanthrene, Anthracene, 4-N-Nonylphenol, Metribuzin, Endosulfan ether, Alachlor, PCB, Metolachlor, Chlorpyrifos, Aldrin, Pendimethalin, Chlorfenvinphos, Isodrin, Fluoranthene, Pyrene, Endosulfan I, p,p'-DDE-D8, p,p'-DDE, Dieldrin, Endrin, PCB, BDE, p,p'-DDD, Endosulfan II, PCB, p,p'-DDT</p> <p>Pentachlorophenol, Diuron, Carbendazim, Azoxystrobine, Metazachlor, Piperonyl butoxide, Phoxime, Fenarimol, Triadimenol</p>	Vulliet et al., 2014
Industrial	<p>Naphthenic acids</p> <p>Petroleum Metabolites</p>	<p>Brunswicka et al., 2015</p> <p>Zemo et al., 2017</p>

## **Appendix B: Instrumentation and Software**

**Table B-1.** Instrumentation and software for LC, GC & TOF-MS

Study Reference	Instrumentation	Software Utilized in Analysis
Ter Laak et al., 2012	LC LTQ FT Orbitrap MS with an electrospray ionization interface.	ToxID v.2.1.1 software; Xcalibur v.2.0 software.
Lava et al., 2013	Perkin Elmer Clarus 500 gas chromatograph; Thermo Finnigan Trace GC Ultra equipped with a DSQ single quadrupole mass detector; Velocity XPT sample concentrator Purge-and-Trap system equipped with a Teledyne Aquatek liquid autosampler	TurboMass® Perkin Elmer software; Xcalibur® Thermo software
Fernández-Ramos et al., 2014	GX-271 ASPEC fitted with a 25ml pump; Oasis HLB cartridges; Agilent 1290 series UHPLC system consisting of a binary pump, vacuum degasser, thermostatted column compartment, automatic autosampler; automatic injector; Coupled to an ultra-high definition quadrupole time-of-flight mass spectrometer Model 6540 Agilent with electrospray Jet Stream Technology; ZORBAX Eclipse XDB-C8 analytical column (150 mm × 4.6 mm, 3.5 µm particle size) from Agilent technologies.	Mass Hunter software
Preiss et al., 2012	Concentration Evaporator Workstation Turbovap II	Not specified
Reemtsma et al., 2013	Exactive mass spectrometer; Agilent 1200 HPLC-system coupled to an API 5500 QTrap mass spectrometer; Synergy Fusion-RP 100A 2.5 µm column, 50 mm × 2.0 mm;	Analyst 1.5 software
McManus et al., 2014	Strata-X 33 µm polymeric sorbent (100 mg/3 mL and 200 mg/6 mL), Strata-XL 100 µm polymeric reversed phase 100 mg/3 mL, Strata SDB-L Styrene-divinylbenzene polymer 500 mg/3 mL, Bond Elut ENV 200 mg/6 mL and Oasis® HLB 200 mg/6 mL Bond Elut ENV 200 mg/6 mL and Strata-X 100 mg/6 mL cartridges; Acquity UHPLC® system; Waters Quattro Premier XE triple quadrupole instrument operating in electrospray ionisation (ESI) mode (Waters).	MassLynx™ software; TargetLynx™ software
Soulier et al., 2016	Oasis® HLB (divinylbenzene/N-vinylpyrrolidone copolymer) extraction cartridges	ChromaLynx XS application; MarkerLynx XS application
Jindal et al., 2015	MicrOTOF-Q spectrometer; OASIS HLB SPE cartridges; system controller (SCL-10AVP), on-line degasser (DGu-14A), low-pressure gradient flow control valve (FCV-10ALVP), solvent delivery module (LC-10ATVP), auto injector (SIL-10ADVP), column oven (CTO-10ASVP), photodiode array (PDA) detector (SPD-M10AVP); LTQ XLTM linear trap mass spectrometer	Hystar (version 3.1); CLASS-VP software version 6.13; Xcalibur software (version 2.0.7 SP1) and LCQuan software (version 2.5.0).
Wolf et al., 2012	HPLC (Agilent 1100) coupled to a triple quadrupole mass spectrometer (API 3000, Applied Biosystems Sciex) with an electrospray ionisation source/ Phenomenex Synergi Polar-RP column; Agilent Zorbax Eclipse XDB-C8 column	Geographical Information System

Sjerps et al., 2016	OASIS HLB columns; Liquid Chromatography coupled to a Linear Ion Trap (LTO) Orbitrap High Resolution Mass Spectrometer; Accela UHPLC system and an Accela autosampler (Thermo Fisher Scientific); Omnisphere C18 column	MSXelator software
Lyczko et al., 2015	High field asymmetric waveform ion mobility spectrometry (FAIMS); Q-TOF micro mass spectrometer	Not specified
Hernández et al., 2015	Hybrid quadrupole-orthogonal acceleration-TOF mass spectrometer (Xevo G2 QTOF, Waters Micromass, Manchester, UK) was interfaced to a Waters Acquity UPLC system or to an Agilent 7890A GC system using a single instrument.	ChromaLynx XS (target mode) software (MassLynx v 4.1, Waters); MassFragment software (Waters)
Kapelewska et al., 2016	HP 6890 gas chromatograph with a mass spectrometric detector MSD5973; HP 7673 autosampler	Not specified
Cherta et al., 2012	Shimadzu QP2010 Plus GC system equipped with an autosampler (Shimadzu AOC-5000) and coupled to a single quadrupole mass spectrometer (Shimadzu GCMS-QP2010 Plus	Shimadzu software
Xue et al., 2015	UPLC column was coupled to a triple-quadrupole mass spectrometer (TSQ Quantum Ultra AM, Finnigan, USA) equipped with an electrospray ion source (ESI).	Masslynx V4.1
Vulliet et al., 2014	1290 Infinity HPLC system (Agilent Technologies); Kinetex XB-C18 (100×2.1 mm; 1.7 μm); Phenomenex with a KrudKatcher Ultra HPLC In-Line Filter from Phenomenex as a guard column; LC system was coupled to a triple-stage quadrupole mass spectrometer (Applied Biosystems Sciex/5500 QTrap) with an electrospray ion source (TurboV, Applied Biosystems); Agilent gas chromatograph equipped with a 7683B Series injector. The GC was coupled with a ToF mass spectrometer GCT Premier from Waters.	Analyst software (version 1.6.1); MassLynx software version 4.1 (Waters).
Sanchis et al., 2012	Photometric Analyzer II; Symbiosis Pico system equipped with a 5-mL sample loop; LC column Synergy 4 μ Hydro-RP 50×2.0 mm, 4 μm (Phenomenex, reference 00B-4375-B0); Symbiosis Pico LC system was coupled to a 4000 QTRAP hybrid triple quadrupole-linear ion trap mass spectrometer equipped with a Turbo Ion Spray source from Applied Biosystems-Sciex in the negative electrospray ionisation mode (ESI (-)); Synergy Hydro-RP (50×2 mm, 4 μm) analytical column	Analyst software version 1.5 (Applied Biosystems)
Planas et al., 2015	Integrated triple quadrupole GC-MS/MS Scion TQ	MS Workstation 8
Brunswick et al., 2015	Agilent Infinity 1290 HPLC system with Infinity 1260 autosampler (tray temperature set to 10 °C); Agilent 6550 iFunnel AJS Series Liquid Chromatograph Mass Spectrometer with Time of Flight detector (LC/MS-ToF); high mass resolution QToF instrument	MassHunter qualitative software; Agilent qualitative software; Microsoft Excel® software; GraphPad Prism® software;

Chen et al., 2017	Linear ion trap-orbitrap hybrid instrument at high mass resolution (LTO Orbitrap MS); HPLC-chemiluminescence; Termovap Sample Concentrator (BF-2000, Peta Instrument Co., China); Agilent 5975 quadrupole MS coupled with an Agilent 6890 N GC with an Agilent 7683B series auto liquid sampler; Agilent 7000 C triple quadrupole MS/MS coupled with an Agilent 7890 B GC with an Agilent 7693 series auto liquid sampler	Not specified
Xu et al., 2013	Finnigan LXQ (Thermo Fisher Scientific). Paired ion electrospray ionization was performed in the positive ion mode; Thermo Fisher Surveyor auto-sampler	Genesis Peak Detection Algorithm provided by the Xcalibur 2.0 software
Castiglioni et al., 2015	API 3000 triple quadrupole, equipped with a turbo ion spray source (AB-Sciex); XTerra MS C18, 100 × 2.1 mm, 3.5 μm column (Waters Corp); Thermo EQUAN system with a polar end-capped C18 pre-concentration column (Thermo Hypersil GOLD aQ 12 μm, 20 × 2.1 mm); Thermo Hypersil GOLD PFP analytical column (1.9 μm, 50 × 2.1 mm); QqQ mass spectrometer (TSQ Quantum Access MAX) equipped with a heated-electrospray ionisation (HESI-II) probe was used.	Excel (Microsoft Office Package); SigmaPlot (Sigmaplot Software Inc.); AB-Sciex software; Analyst 1.5; Excalibur 2.1 (Thermo Scientific).
McEachran et al., 2016	Thermo Scientific TSQ Quantum Ultra triple-quadrupole mass spectrometer configured with a Waters Acquity UPLC separation system	Not specified
Han Tran et al., 2013	Triple quadrupole mass spectrometer equipped with a Z-spray electrospray interface (LCMS-8030); XBridge™ C18 (100! 2.1 mm i.d; 3.5 μm particle size); Agilent ZORBAX SB-C18 (150! 2.1 mm i.d; 3.5 μm particle size); ZORBAX RRHD Eclipse Plus C18 (100! 2.1 mm i.d; 1.8 μm particle size)	Not specified
Kresinová et al., 2016	TOC analyzer (MULTI N/C 2100S, Analytik Jena); Waters Acquity UPLC System consisting of Acquity UPLC Sample Manager; Acquity UPLC Solvent Manager; Acquity UPLC Column Heater; Waters LCT Premier XE orthogonal accelerated ToFMS	MassLynx V4.0
Ripollés et al., 2012	LC-MS/MS with triple quadrupole (QqQ) analyzer; Acquity UPLC system (Waters) interfaced to a triple quadrupole mass spectrometer (TQD) (Waters Micromass); Waters 2777 Sample Manager, with a loop of 1 mL (Waters); Agilent 1100 binary pump; Acquity UPLC HSS T3 C18 (50 mm × 2.1 mm, 1.8 μm) column; UHPLC-MS/MS system with a QqQ analyzer and isotope-dilution analysis; Orthogonal Z-spray-electrospray (ESI) and atmospheric pressure chemical ion-ization probe (Ion Sabre APCI); Acquity UPLC system coupled to a Xevo TQ-S (triple quadrupole analyzer)	Masslynx v 4.1 software
Kirishima et al., 2017	Dionex ICS-1000 ion chromatograph; Inductively coupled plasma atomic emission spectrometer (Rigaku, CIROS-Mark II); NexION 300X ICP mass spectrometer (PerkinElmer Inc.; SEM-EDX (scanning electron microscope and energy dispersive X-ray analyzer)	MEDUSA software; HYDRA database