Chemicals of Interest in Biosolids:

Summary of Key Information and Hazard Ranking

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Appendix A References for Literature Search in Biosolids Workbook

Executive Summary

TCEQ requested that ToxStrategies assist with the identification and prioritization of unregulated contaminants found in biosolids used for agricultural purposes. The scope of work for this project was outlined in the "*Work Plan for Work Order Under Umbrella Contract #582-20-10533 Between TCEQ and ToxStrategies, Inc., Comprehensive Literature Search on Potential Human Health Risks Associated with Sewage Sludge and Preliminary Risk Characterization"* (Work Plan), dated August 26, 2020.

This report summarizes the results of two tasks:

> Task 1 – Identify unregulated chemicals in biosolids, and review and document the available information for these chemicals. At the onset of this Task, TCEQ identified categories of chemicals for which they were most interested in gathering information.
>
> Task 2 - Develop and implement a ranking strategy to prioritize this list of chemicals. The chemical ranking is designed to allow TCEQ to focus their attention on chemicals that present the potential for the highest exposures and risks.

For Task 1, the list of unregulated contaminants in the categories of interest to the TCEQ was identified based on biennial reports for biosolids published by U.S. EPA. Each of these chemicals was then subject to a comprehensive literature search to gather critical information for use in prioritization. Key information gathered included concentrations, physical-chemical properties, and potential human health hazards associated with those chemicals. All of the information gathered was documented in the *Biosolids Workbook*. ToxStrategies reviewed and summarized information from U.S. EPA and other resources, as well as performed a series of literature searchs to supplement that information.

For Task 2, ToxStrategies developed a ranking system to prioritize the chemicals of interest to the TCEQ. This ranking scheme was based on the framework developed by U.S. EPA for the Toxic Substance Control Act (TSCA) (U.S. EPA, 2009), The ranking scheme considered potential human health risk based on three relevant categories: exposure, human health effects, and persistence/bioaccumulation. Potential for exposure was based on measured concentrations in biosolids, potential for human health effects was based on information on the Hazard Comparison Dashboard, and potential for persistence/bioaccumulation was based on estimates of these parameters in the U.S. EPA CompTox database, the Hazard Comparison Dashboard, and/or specific references identified in the literature search. Each category was scored with values from "1" to "3" with a maximum score across all categories of "9". The results of this effort are documented in the *Biosolids Workbook,* which was provided in an electronic format along with this report.

Of the 233 constituents identified as priority constituents by TCEQ, 175 constituents were ranked numerically. Chemicals were not ranked if information was missing from one or

more categories. Although comprehensive data collection efforts were undertaken, data is lacking in several categories for microbial and viral particles that were included in the final list of contaminants of interest. In some cases, groups of similar constituents were evaluated collectively (e.g., nonabromyldiphenyl ethers (BDEs) or PFAS). If one or more constituents in a group were not ranked, the general ranking of the group may be used to evaluate the group of constituents as a whole. A total of eight chemicals received the highest ranking of "9":

BDE-209 (2,2',3,3',4,4',5,5',6,6'- DeBDE)
Cholestanol
Cholesterol
Coprostanol (3-beta)
Desmosterol
Epicoprostanol
Stigmastanol, β-
Stigmasterol

It is important to note that these rankings are qualitative and do not provide a prediction of risk or specific health effects related to the presence of these constituents in biosolids. The presence of these highly ranked constituents in biosolids may warrant further evaluation to assess the potential for human health effects. For example, while exposure is related to concentration, concentration is not the only predictor of actual exposure, which may be mitigated by chemical form and application practices. While this study provides a means for comparing information for the constituents, no specific conclusions can be drawn regarding potential human health effects without further analysis.

1 Introduction

Although the U.S. EPA and TCEQ have promulgated regulations governing the use of biosolids (treated sewage sludge) as fertilizer for agricultural purposes (40 Code of Federal Regulations [CFR] Part 503 and 30 Texas Administrative Code [TAC] Chapter 312, respectively), the TCEQ has received inquiries regarding the potential human health risks associated with unregulated chemicals present in biosolids (U.S. EPA, 2018c). Pharmaceuticals, steroids, hormones, endocrine disrupters, flame retardants, and viruses may be present in biosolids, but the potential for human health risks related to exposure to these chemicals has not been assessed.

TCEQ has requested that ToxStrategies assist with the identification and prioritization of potential health risks associated with constituents in sewage sludge. To accomplish this request, ToxStrategies has performed two tasks:

Task 1: Literature search, information synthesis and reporting

Task 2: Preliminary ranking of potential human health risks associated with the constituents based on the results of Task 1.

The third task to compile a Texas-specific comprehensive, easy to understand guide for rules governing land application of biosolids is reported separately.

For Task 1, ToxStrategies has performed a literature search to gather information on the unregulated chemicals present in biosolids that were identified by the TCEQ as being of interest. Key information gathered included concentrations, physical-chemical properties, and potential human health hazards associated with those chemicals. Then, for Task 2 building upon a framework developed by U.S. EPA for the Toxic Substance Control Act (TSCA) (U.S. EPA, 2009), a ranking system was developed to prioritize the chemicals of interest to the TCEQ. Ranking was based on potential to present a human health risk based on ranking parameters representing exposure, human health effects, and persistence/bioaccumulation. The results of this effort are documented in the *Biosolids Workbook* that has been provided in an electronic format along with this report. ToxStrategies scope of work was outlined in the "*Work Plan for Work Order Under Umbrella Contract #582-20-10533 Between TCEQ and ToxStrategies, Inc., Comprehensive Literature Search on Potential Human Health Risks Associated with Sewage Sludge and Preliminary Risk Characterization"* (Work Plan), dated August 26, 2020.

This report provides the results of these efforts in two parts:

Section 2.0 Literature Search and Data Management
Section 3.0 Ranking Chemicals Identified in Biosolids

2 Literature Search and Data Management

While it is understood that potentially hundreds of unregulated chemicals are present in biosolids (U.S. EPA, 2018c), the focus of this research was a subset of unregulated chemicals and infectious particles, of interest to the TCEQ as defined in the Work Plan. Collectively referred to as priority substances herein, these include per- and polyfluoroalkyl substances (PFAS) and other flame retardants, pharmaceuticals, steroids, hormones, endocrine disruptors, and viral particles. The literature search and data management activities focused on these priority substances. However, when it was no additional effort (e.g., extracting information from a database), then information was gathered for all unregulated chemicals identified by U.S. EPA and recorded in the *Biosolids Workbook*.

The U.S. EPA has been publishing Biennial Reports summarizing available information concerning biosolids since 2006. These Biennial Reports were used as an initial reference for data gathering. In addition, a focused literature search was conducted to identify additional information available after 2017 for the priority substances identified by TCEQ. The literature search included problem formulation and scoping exercises, primary and secondary literature searching, and the compilation of identified information. Results of data gathering from the U.S. EPA Biennial Reports and the literature search were documented in an Excel workbook (*Biosolids Workbook*) provided along with this report. References for individual reports identified in the *Biosolids Workbook* are provided in Appendix A.

2.1 Problem Formulation and Scoping

Problem formulation exercises were undertaken to understand the current state of knowledge, develop a final compound list, and define a comprehensive strategy to identify relevant literature. As an initial step to the literature search, a targeted search of U.S. EPA's Biosolids Program website was performed (https://www.epa.gov/biosolids). Several relevant documents (secondary literature) were identified and reviewed in full for background information. Additionally, handsearching of the in-text citations and bibliography was performed to identify any related publications or reports. This information informed the scope and approach for searching the primary literature (i.e., peer-reviewed publications).

2.1.1 Final compound list

Based on problem formulation exercises and discussion with TCEQ, the unregulated constituent list used in this assessment was based on Appendix A of the most recent U.S. EPA Biennial Review (U.S. EPA, 2018b). This constituent list includes chemical and microbial constituents as identified in past or present Biennial Reviews, along with Chemical Abstract Service registry numbers (CASRN) and chemical categories as assigned by EPA. The final constituent list, comprised of 380 unique compounds and microbial constituents, is presented in the *Biosolids Workbook* as W-1. U.S. EPA CompTox Dashboard DTXSIDs were assigned to each constituent based on the constituent name and CASRN.

As outlined in the Work Plan, priority compounds included PFAS and other flame retardants, pharmaceuticals, steroids, hormones, endocrine disruptors, and viral particles. The EPA categories presented in the most recent U.S. EPA (2018b) Biennial Review were used to designate priority compounds. However, no EPA category existed for potential endocrine disrupting compounds. Thus, the UN Draft List of 45 Endocrine Disrupting Chemicals was used to identify constituents in this category (The International Panel on Chemical Pollution (IPCP), 2017). Of the 380 constituents identified in the compound list, 233 were designated as priority constituents based on their chemical category.

Information gathering efforts focused on TCEQ's list of priority constituents. If information was readily accessible for other constituents (e.g. a download from a database), then the information was also collected. If references were identified, the references were documented but the data was not collected.

2.1.2 Development of search strategy

Following the review of the targeted secondary literature, a search strategy was developed to identify primary literature published since the date of the most recent U.S. EPA (2019) Biennial Review. Search syntax was developed based on the syntax documented in the 2017 Biennial Review (U.S. EPA (2019). Revisions to key terms were employed to focus on priority substances and an English language-only filter applied. Similar to the search strategy reported by the U.S. EPA, separate searches were performed for chemicals and infectious particles rather than together in a concatenated fashion.

2.1.3 Inclusion and exclusion criteria

Development of inclusion and exclusion criteria for the review of primary literature was based on that of the most recent U.S. EPA (2019) Biennial Review. These criteria were then applied in a pilot exercise performed on a specified set of literature in order to identify potential challenges and refine criteria to fit the needs of the current effort. Based on the pilot exercise, literature was reviewed for the *Biosolids Workbook* if it reported constituent concentrations of priority substances in biosolids of any class, unless:

- Constituent concentrations were for non-priority substances in biosolids of any class.
- Concentrations were for spiked samples.
- Constituent concentrations of priority or non-priority substances were for media other than biosolids (e.g., biosolid-amended soil, air, wastewater treatment plant influent/effluent, spiked or cultured biosolids).
- Constituent concentrations were reported only in figures.
- Constituent concentrations were reported for sewage sludge explicitly described as "raw" or "untreated"

2.2 Secondary Literature Review and Primary Literature Search

2.2.1 Secondary literature review

A review of the secondary literature identified a number of regulatory resources that provided: biosolid concentrations, physical-chemical properties, human toxicity values, bioaccumulation factors, and bioconcentration factors. These secondary sources were reviewed for data relating to priority substances; however, if data were easily obtained for non-priority substances (such as values from the EPA CompTox Dashboard), these data were included in the *Biosolids Workbook*. Each of the secondary literature sources are described herein.

2.2.1.1 EPA Biosolids Biennial Reviews

The EPA collects and reviews "publicly available information on occurrence, fate and transport in the environment, and human health and ecological effects for constituents that (1) have been identified in the Targeted National Sewage Sludge Survey (TNSSS; U.S. EPA, 2009), or in the open literature as having been found in biosolids; and (2) have not been previously regulated or evaluated (e.g., as potentially causing harm to humans or the environment) in biosolids" (U.S. EPA, 2019). This process is undertaken every 2 years, and these Biennial Reviews are available for 2005, 2007, 2009, 2011, 2013, 2015, and 2017 (U.S. EPA, 2006, 2008, 2012b, 2015, 2018a, 2018b, 2019)

The Biennial Reviews employ a comprehensive literature screening that was used as the basis for the priority substance literature search. In addition to the information documented in the Biennial Reviews, primary literature identified as relevant by the EPA was reviewed by title and abstract for relevance to biosolid concentrations by applying the inclusion/exclusion criteria developed during problem formulations. Relevant publications were identified in the 2007, 2009, 2011, 2013, 2015, and 2017 Biennial Reviews; no sewage sludge concentration data were identified by the EPA for the 2005 Biennial Review.

2.2.1.2 EPA Targeted National Sewage Sludge Surveys (EPA TNSSS)

The EPA TNSSS program aims to identify the presence of constituents in biosolids using samples taken from wastewater treatment plants. While this data set was identified by the targeted secondary literature search, the reports contain empirical data, and thus, could be considered a primary data source. EPA TNSSS reports from 1989, 2001, and 2009 were identified and reviewed (U.S. EPA, 1989, 2007, 2009).

Sample concentration data were available in the 1989 and 2009 EPA TNSSS reports. Although the EPA also performed a TNSSS in 2001, the purpose was to obtain concentration data for dioxins and dioxin-like compounds (i.e., non-priority substances). Thus, no data were collected from the 2001 TNSSS report.

2.2.1.3 EPA CompTox Dashboard

The EPA CompTox Chemistry Dashboard (Williams et al., 2017) is a database of curated substances that provides access to data such as physicochemical, environmental fate and transport, exposure, usage, *in vivo* toxicity, and *in vitro* bioassay data. Additional public domain online resources are available through links to additional sources beyond the database. Using the list of chemicals procured from the EPA Biennial Reviews, a batch search for physicochemical data and availability of human toxicity values was performed. When available, data were was added to the *Biosolids Workbook*.

2.2.1.4 Hazard Comparison Dashboard

The Hazard Comparison Dashboard was identified as a resource in the EPA's CompTox Dashboard (https://hazard.sciencedataexperts.com). Vegosen and Martin (2020) describe

the Hazard Comparison Dashboard as a framework "to compile and integrate chemical hazard data for several human health and ecotoxicity endpoints from public online sources, including hazardous chemical lists, Globally Harmonized System hazard codes (H-codes), hazard categories from government health agencies, experimental quantitative toxicity values, and predicted values using Quantitative Structure-Activity Relationship (QSAR) models." Human health endpoints include acute toxicity (via the oral, inhalation, and dermal routes of exposure), carcinogenicity, genotoxicity/mutagenicity, endocrine disruption, reproductive toxicity, developmental toxicity, neurotoxicity (single exposure and repeat exposure), systemic toxicity (single exposure and repeat exposure), skin sensitization, skin irritation, and eye irritation. Fate endpoints include persistence and bioaccumulation. Further, while not relevant to this specific effort, ecotoxicity endpoints include acute aquatic toxicity and chronic aquatic toxicity.

While Hazard Comparison Dashboard was not developed under the umbrella of a specific U.S. EPA program, it is suggested that it may aid in chemical prioritization under TSCA (Vegosen & Martin, 2020). The data sources compiled for the database are explicitly described by Vegosen and Martin (2020) in Table 1. These data are arranged into a uniform structure to provide high-level categorization of human health, ecotoxicity, and fate endpoints ranging from low to very high. In the scenario that multiple sources provide data that result in different scores for the same constituent, the highest score is used as the database score.

When searched, the database outputs a matrix displaying the chemicals and associated ordinal hazard scores per hazard endpoint. For this report, this database was queried on December 9, 2020 via a batch search using the DTXSID as listed in the EPA CompTox Dashboard. The resulting data were integrated into the *Biosolids Workbook* as Worksheet W-3.

2.2.1.5 TCEQ Texas Risk Reduction Program (TRRP) RG-366/TRRP-19

The TCEQ TRRP guidance was used to identify quantitative human toxicity values. If values for unregulated constituents existed in the TRRP PCL tables, these were integrated into the *Biosolids Workbook* in Worksheet W-4. If the constituent was not listed in the TRRP PCL tables (168 priority constituents), the TRRP hierarchy was used to prioritize toxicity values from additional regulatory bodies. Specifically, the hierarchy was as follows:

- U.S. EPA Integrated Risk Information System (IRIS)
- U.S. EPA Provisional Peer Reviewed Toxicity Values (PPRTVs)
- U.S. EPA Health Effects Assessment Summary Tables (HEASTs)
- U.S. EPA National Center for Environmental Assessment (NCEA)
- TCEQ Toxicology Division Chronic Remediation-Specific Effects Screening Levels (RS-ESLs)
- Agency for Toxic Substances Disease Registry Chronic Minimal Risk Levels (ATSDR MRLs)

- Other scientifically valid sources as approved by the executive director on a chemical-specific basis.

2.2.1.6 European Chemicals Agency (ECHA) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Registration Dossiers

Following the application of the TRRP toxicity value hierarchy, constituents that did not have quantitative toxicity values were researched in the ECHA REACH Registrations (https://echa.europa.eu/information-on-chemicals/registered-substances). If available, systemic derived no effect levels (DNELs) were extracted for acute and long-term exposures via oral or inhalation routes. These DNELs are derived by the submitting party and are required in regulatory submissions for all registered substances.

2.2.2 Primary literature search

Following the review of the secondary literature, a primary literature search was undertaken to identify more recent literature since the publication of the 2016-2017 EPA Biennial Review, which evaluated literature published through the end of 2017. Two bibliographic databases, PubMed and Embase, were queried for literature published from 2018 to present using the search syntaxes developed during problem formulation (Box 1).

Box 1. Search syntax for chemical contaminant and infectious particle literature searches performed on 11/12/2020 in PubMed and Embase.

Chemical contaminant search:
PubMed: ("sewage sludge" OR "biosolids" OR "treated sewage" OR "sludge treatment" OR "sewage treatment") AND (pollutant OR toxic* OR chemical OR constituent OR contaminant* OR flame retardant* OR pharmaceutical* OR steroid* OR hormone* OR antibiotic* OR personal care product*) AND (occurrence OR concentration)*

Embase: ("sewage sludge"/exp OR "sewage sludge" OR "biosolids"/exp OR "biosolids" OR "treated sewage" OR "sludge treatment"/exp OR "sludge treatment" OR "sewage treatment"/exp OR "sewage treatment") AND ((pollutant OR toxic* OR chemical OR constituent OR contaminant* OR 'flame'/exp OR flame) AND retardant* OR pharmaceutical* OR steroid* OR hormone* OR antibiotic* OR 'personal care' OR (personal AND ("care"/exp OR care) AND product*) AND (occurrence OR "concentration"/exp OR concentration)*

Infectious particles search:
PubMed: ("sewage sludge" OR biosolids OR "treated sewage" OR "sludge treatment" OR "sewage treatment") AND ("land application" OR farm OR agriculture OR soil) AND (viral OR virus OR pathogen OR salmonella OR microb*) AND (occurrence OR concentration OR fate OR transport)*

Embase: ("sewage sludge" OR "biosolids" OR "treated sewage" OR "sludge treatment" OR "sewage treatment") AND ("land application" OR farm OR agriculture OR soil) AND (viral OR virus AND pathogen OR salmonella OR microb*) AND (occurrence OR concentration OR fate OR transport)*

Note: The asterisk (*) is used to allow searches to find words that begin with the letters indicated and end in any form.

Citation results for the chemical contaminant searches were deduplicated in EndNote (version X9.3.2) and subsequently imported into SWIFT-Review (version 1.43.10453) in order to utilize AI-driven text mining for prioritization of the most relevant citations. In order to prioritize the imported literature, a random seed selection of 52 articles (~5%) were designated as prioritization training documents and reviewed for relevance. The literature was then prioritized based on relevance to the training set on a scale of 0 to 1, with zero being the least relevant and 1 being the most. Prioritization of the primary literature in SWIFT-Review returned relevance scores of 0.16-0.86. Citations receiving a relevance score of >0.5 were then imported to DistillerSR for screening.

Due to the relatively low number of search results returned for the separate infectious particles search, all citation results were deduplicated in EndNote (version X9.3.2) and subsequently imported to DistillerSR for screening.

Citations were first screened by title/abstract based on the inclusion/exclusion criteria developed during problem formulation. If a citation was retained based on the title/abstract, the full text was obtained and reviewed in full. Concentration data and other information from relevant literature were then extracted.

2.3 Literature Search Results

Findings from the aforementioned efforts were compiled as a Microsoft Excel workbook, referred to herein as the *Biosolids Workbook*. The data obtained during the literature search are arranged in Excel worksheets, W-1 to W-8, which contain the extracted information as follows:

- W-1 Constituent List
- W-2 Biosolids Concentration
- W-3 Hazard Comparison Dashboard
- W-4 Human Toxicity Values
- W-5 Physical-Chemical Properties
- W-6 Bioaccumulation Factors
- W-7 Bioconcentration Factors
- W-8 Biosolids Hazard Ranking

Both TCEQ priority and non-priority compounds were retained in this *Biosolids Workbook*. While we did not investigate non-priority compounds, if we found information sources that were relevant, the information was recorded in the *Biosolids Workbook*. For example, during the primary literature review and extraction of biosolid concentrations,

concentration data were not collected for non-priority substances; however, the citation for the article was noted in the spreadsheet for potential future research needs.

2.3.1 Literature search and evidence identification

Primary literature and secondary information sources were reviewed for relevance to all data categories needed for hazard ranking. Figure 1 presents the data sources that had information for specific data categories.

Figure 1. Data sources reviewed and extracted for each data category

	Compound List	Biosolid Concentrations	Hazard Comparison Database	Physical-Chemical Properties	Bioaccumulation Factors	Bioconcentration Factors	Human Toxicity Values
EPA Biosolids Biennial Reviews	■	■		■	■	■	■
EPA TNSSS		■					
EPA CompTox Dashboard				■		■	■
EPA Hazard Comparison Dashboard			■				
TCEQ TRRP Guidance							■
ECHA REACH Registration Dossiers							■
PubMed/EMBASE Primary Literature		■					

In addition to the EPA TNSSS, primary literature was also reviewed for biosolid concentrations. Citations were obtained from two primary efforts: 1) review of the citations reported in the EPA Biosolids Biennial Reviews and 2) review of the results from the bibliographic database searches. A flow chart of this process is provided in Figure 2.

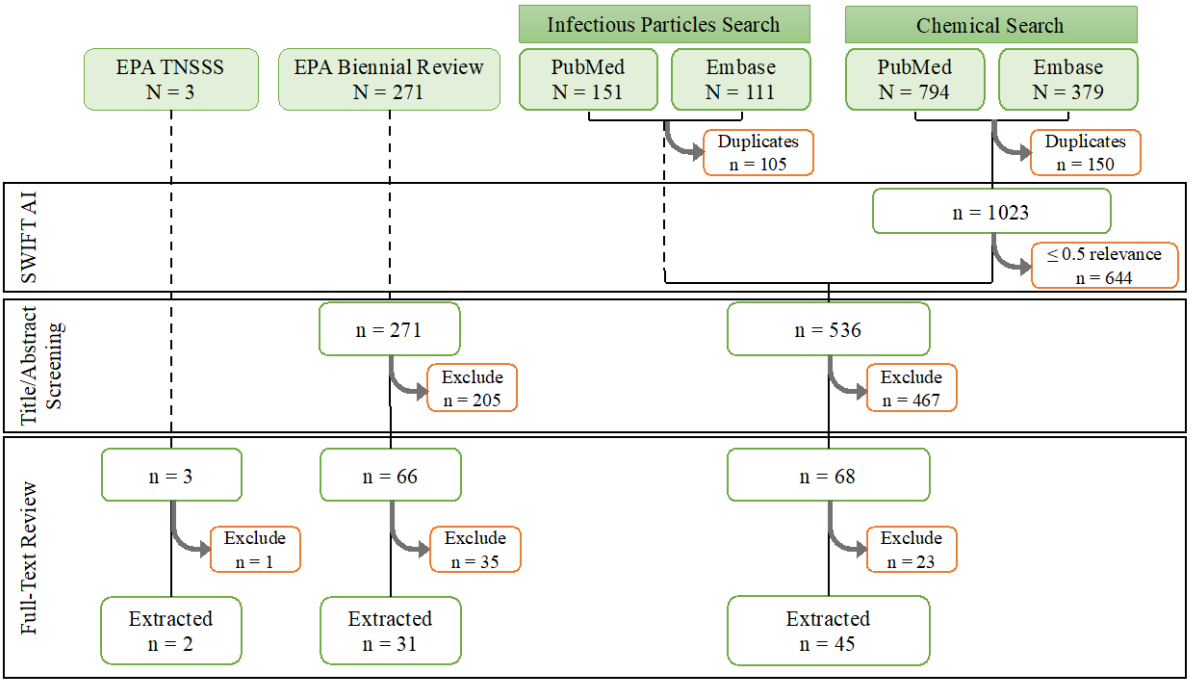

Figure 2. Primary literature search flow chart

2.3.2 Data gaps/availability

As indicated in the Biosolids Workbook, data was not found for all chemicals of interest to TCEQ. If data for one or more categories was not available, the chemicals were not ranked as noted in Worksheet W-8. Two specific categories of missing data are discussed below.

Although comprehensive data collection efforts were undertaken, data is lacking in several categories for microbial and viral particles that were included in the final compound list (Table 1). Contributing to this data gap is the absence of these constituents in the EPA CompTox Dashboard. As a result, categories for which these constituents have limited or no data include biosolid concentrations, the Hazard Comparison Database, physical-chemical properties, bioaccumulation and bioconcentration factors, and human toxicity values.

Table 1. Microbial and viral particles and associated EPA Category as listed in the final constituent list presented in the *Biosolids Workbook*, Worksheet W-1.

Microbial or Viral Particle	**EPA Category**
Aerobic endospores	Bacteria
Aeromonas spp.	Bacteria
Antibiotic-resistant bacteria (ARB) or Antibiotic-resistant genes (ARG)	Bacteria
Clostridia spp.	Bacteria
Coronavirus HKU1	Virus
Cosavirus	Virus
Endotoxin	Microbial toxin
Enterovirus	Virus
Escherichia coli (*E. coli*)	Bacteria
Giardia spp.	Protozoan parasite
Human adenoviruses (HuAdV)	Virus
Human norovirus (HuNoV)	Virus
Human polyomaviruses	Virus
Salmonella spp.	Bacteria

In addition to microbial and viral particles, information was not available in the EPA Hazard Comparison Dashboard for several of the listed constituents. These are listed in Table 2.

Table 2. Constituents not included in the EPA Hazard Comparison Dashboard

Constituent	**CASRN**	**DTXSID**
Dechlorane 603	13560-92-4	DTXSID30108225
Desmethyldiltiazem	130606-60-9	DTXSID601019739
Epianhydrochlortetracycline, 4-	158018-53-2	DTXSID80716137
Epianhydrotetracycline, 4-	4465-65-0	DTXSID40873790
Epitetracycline, 4-	23313-80-6	DTXSID80873794
Hydroxyamitriptyline, 10-	1246833-15-7	DTXSID201019737
Nitrate	14797-55-8	DTXSID5024217
Nitrite	14797-65-0	DTXSID5024219

Constituent	CASRN	DTXSID
Nonylphenol (branched), 4-	84852-15-3	DTXSID5029055
Norfluoxetine	57226-68-3	DTXSID4022529
Norverapamil	67812-42-4	DTXSID2023309
Phosphate (total)	14265-44-2	DTXSID7039672
Total Heptachlorodibenzofurans (HpCDF)	38998-75-3	DTXSID501019736
Total Hexachlorodibenzofurans (HxCDF)	55684-94-1	DTXSID50896899
Total Pentachlorodibenzo-P-Dioxins (PeCDD)	36088-22-9	DTXSID101019734
Total Pentachlorodibenzofurans (PeCDF)	30402-15-4	DTXSID801019735
Total Tetrachlorodibenzo-P-Dioxins (TCDD)	41903-57-5	DTXSID4051378
Total Tetrachlorodibenzofurans (TCDF)	55722-27-5	DTXSID3052147
Virginiamycin	11006-76-1	DTXSID40880080

3 Ranking Chemicals Identified in Biosolids

As discussed with TCEQ, ToxStrategies developed an approach for ranking constituents based in part on the approach used by the U.S. EPA for developing their list of chemicals for evaluation under the Toxic Substances Control Act (TSCA), also known as TSCA Work Plan Chemicals. In *TSCA Work Plan Chemicals: Method Document* (U.S. EPA, 2012), three criteria are considered for ranking chemicals: exposure, hazard, and persistence/bioaccumulation. The U.S. EPA developed a three-point scale for each of these categories (scores of 1 to 3) with a maximum potential cumulative score of 9.

The approach for ranking constituents in biosolids used herein relied on the same categories and ranking system as the TSCA Work Plan Chemicals: Method Document. The remainder of this section discusses each category, the information available for consideration, and the basis for the ranking within each category. A description of the final ranking is also provided.

3.1 Exposure Category Score

With respect to biosolids, exposure is directly related to the concentration of the constituent in the biosolid, as most other factors determining exposure are related to how a person is in contact with the biosolids and not specific features of the constituent. For

this reason, concentrations of the constituent in biosolids were used to provide an exposure score.

Concentration information was obtained in various units directly from the primary information source. Concentrations were converted to units of micrograms per kilogram (µg/kg) for most constituents where possible (excluding viruses and particles). In addition, concentrations of constituents were reported as dry weight, wet weight, or not specified. For materials with variable water content, such as biosolids, the most consistent and comparable measurement is to report results as dry weight measurement. When necessary, the primary reference was reviewed in detail to identify whether the text provided a specific indication of dry or wet weight measurements. For consistency and comparability, only concentrations reported as dry weight measurements were used to rank constituents for the exposure category. However, the other measurements are provided in the *Biosolids Workbook* for reference.

For viruses, however, units of µg/kg are not applicable. Table 3 presents the concentration information gathered on viruses, which is also included in the *Biosolids Workbook*. As discussed previously, information was not available for human health hazard or persistence and bioaccumulation/bioconcentration. Because of these differences, viruses were not ranked with the constituents in the *Biosolids Workbook*; rather, they should be considered independently with respect to additional regulatory activities.

Table 3. Concentrations of Viruses

Pollutant	TCEQ Priority	Minimum	Maximum	Median	Mean	Standard Deviation	Unit	Untreated	Class B	Class A	Reference
Enterovirus	Viral particles				7.70	0.81	log10 (copies per one dry gram)	X			Wong, et al., 2010
Enterovirus	Viral particles				5.91	1.13	log10 (copies per one dry gram)		X		Wong, et al., 2010
Human adenoviruses (HuAdV)	Viral particles				5.70		log10 (copies per one dry gram)		X		Viau and Peccia, 2009
Human adenoviruses (HuAdV)	Viral particles				3.86		log10 (copies per one dry gram)			X	Viau and Peccia, 2009
Human adenoviruses (HuAdV)	Viral particles				4.40		log10 (copies per one dry gram)			X	Viau and Peccia, 2009
Human adenoviruses (HuAdV)	Viral particles				5.15		log10 (copies per one dry gram)			X	Viau and Peccia, 2009
Human adenoviruses (HuAdV)	Viral particles	ND	5.33	3.94	3.39	1.42	log10 (copies per one dry gram)		X		Rhodes et al., 2015
Human adenoviruses (HuAdV)	Viral particles				5.70	0.60	log10 (copies per one dry gram)	X			Wong, et al., 2010
Human adenoviruses (HuAdV)	Viral particles				4.29	0.95	log10 (copies per one dry gram)		X		Wong, et al., 2010
Human norovirus (HuNoV)	Viral particles				4.39	2.23	log10 (copies per one dry gram)	X			Wong, et al., 2010
Human norovirus (HuNoV)	Viral particles				4.69	1.46	log10 (copies per one dry gram)		X		Wong, et al., 2010
Human norovirus (HuNoV)	Viral particles				4.22	1.35	log10 (copies per one dry gram)	X			Wong, et al., 2010
Human norovirus (HuNoV)	Viral particles				5.15	1.27	log10 (copies per one dry gram)		X		Wong, et al., 2010
Human polyomaviruses	Viral particles				5.40	0.49	log10 (copies per one dry gram)	X			Wong, et al., 2010
Human polyomaviruses	Viral particles				4.90	0.95	log10 (copies per one dry gram)		X		Wong, et al., 2010

– = not available
ND = not detected

As previously described, concentration data were obtained from primary sources that presented results for treated (Class A or Class B) and untreated biosolids. The term "untreated," as used here, refers to biosolids that did not require treatment prior to use for agricultural purposes. Concentration data for untreated sewage that entered the wastewater treatment facility were not recorded. Measurements for both treated and untreated biosolids, as recorded in the *Biosolids Workbook*, were used for the exposure category ranking.

A variety of concentration measurements were provided in the references reviewed (e.g., mean, median, maximum, etc.); concentration measurements were recorded in the

Biosolids Workbook as provided by the reference. A final comparison value was developed for each reference based on the following selection hierarchy:

1. 95% upper confidence limit
2. Mean
3. Median
4. Average of minimum and maximum
5. Single concentration measurement

If there were multiple measurements extracted from separate references for a single constituent, the maximum value among the interim values across all references was used to represent the concentration of the constituent for the purpose of ranking the exposure category. Table 4 identifies the priority constituents for which concentration data was unavailable.

Table 4. Priority constituents for which concentration data were not available

2,3,31,4,41-PeCB (PCB 105)	Bezafibrate	Mestranol
2,3,31,4,41,5-HxCB (PCB 156)	Clotrimazole	Methylenedioxymethamphetamine, 3,4-
2,3,31,4,41,5,51-HpCB (PCB 189)	Cyclophosphamide	Nonylphenol
2,3,31,4,41,51-HxCB (PCB 157)	Di-n-butyl phthalate (Butoxyphosphate ethanol, 2-)	Nonylphenol (branched), 4-
2,3,4,41,5-PeCB (PCB 114)	Di-n-octyl phthalate	Phenazone
2,31,4,41,5-PeCB (PCB 118)	Di-tert-butylphenol, 2,6-	Quinine sulfate
2,31,4,41,5,51-HxCB (PCB 167)	Diclofenac sodium	Sodium valproate
21,3,4,41,5-PeCB (PCB 123)	Dimethylaminophenazone	Sulfasalazine
3,31,4,41-TeCB (PCB 77)	Fenofibric acid	tert-Butyl-4-hydroxy anisole, 3-
3,31,4,41,5-PeCB (PCB 126)	Floxacillin	Tetrabromobisphenol A
3,31,4,41,5,51-HxCB (PCB 169)	Glyburide	
3,4,41,5-TeCB (PCB 81)	Indometacine	
Benzenesulfonic acid, 2,2'-(1,2-ethenediyl)bis[5-amino]	Mesalazine	

Numerical ranking in the exposure category was based on grouping final measured concentrations into three ranges to achieve an approximately equal number of constituents in each group:

- Concentrations <50 µg/kg were ranked as a 1 (62 constituents);
- Concentrations between 50 and 1,000 µg/kg were ranked as a 2 (58 constituents); and

- Concentrations greater than 1,000 µg/kg were ranked as a 3 (61 constituents).

While in this system, constituents close to the boundaries of the groups (e.g., 49 µg/kg and 52 µg/kg) would be ranked differently (1 and 2, respectively); those cases could be looked at more specifically for further analysis based on the detailed information in the *Biosolids Workbook*.

Several constituents were reported as non-detect in the various references. If a constituent was reported as non-detect and no numerical detections were reported, the constituent was given a ranking of "0" in the exposure category to acknowledge that we did find information on the concentration of that constituent but that it was non-detect.

3.2 Human Health Hazard Category Score

The hazard category was evaluated using the EPA Hazard Comparison Dashboard (the Dashboard) developed by Vegosen and Martin (2020). The Dashboard provides qualitative rankings for the vast majority of constituents identified with respect to human health effects, ecotoxicity, and fate. This section provides a summary of the information provided in the Dashboard and how it was used to develop a hazard rank on a scale of 1 to 3 for this project. Additional detail regarding the dashboard is available on the website and in their paper. The Hazard Comparison Dashboard is provided in Worksheet W-3.

We also recorded human toxicity data for constituents from references, such as the U.S. EPA's Integrated Risk Information System (2020); however, these data were not sufficiently complete to rank all chemicals on a consistent basis. These data were recorded for future reference in the *Biosolids Workbook,* Worksheet W-4.

Each of the categories ranked in the Hazard Comparison Dashboard are presented below. The first 15 categories relate to human health; the last four are for aquatic toxicity (2), persistence (1), and bioaccumulation (1).

1. Acute oral toxicity
2. Acute inhalation toxicity
3. Acute dermal toxicity
4. Carcinogenicity
5. Genotoxicity mutagenicity
6. Endocrine disruption
7. Reproductive
8. Developmental
9. Neurotoxicity – repeat exposure
10. Neurotoxicity – single exposure

11. Systemic toxicity – repeat exposure
12. Systemic toxicity – single exposure
13. Skin sensitization
14. Skin irritation
15. Eye irritation
16. Acute aquatic toxicity
17. Chronic aquatic toxicity
18. Persistence
19. Bioaccumulation

In the EPA Dashboard, each substance was ranked for each category using up to four classifications [very high (VH), high (H), medium (M), low (L), inconclusive (I)], or were left blank if there were no data or insufficient data. As described by Vegosen and Martin (2020), rankings were determined based on a review of 25 data sources, with each source providing information on at least one of the 16 hazard endpoints for one or more constituents. Specific criteria were set for each endpoint to develop the ranking. The data sources were further characterized as authoritative, screening, or predicted:

- Authoritative data sources were defined as those that "are considered to have a higher level of confidence" (Vegosen and Martin, 2020)
- Screening data sources were defined as estimated or not authoritative
- Predictive data sources were the least authoritative of the authoritative and screening data sources and applied to references that apply quantitative structure activity relationships (QSAR) methods to predict toxicity values (e.g., U.S. EPA Toxicity Estimation Software Tool [TEST]; U.S. EPA, 2016)

Hazard scores were derived for each source using the "scoring dictionary" as provided by Vegosen and Martin (2020). The scoring dictionary provides numeric or qualitative criteria for each ranking, derived from the Globally Harmonized System (GHS) of classification and labeling of chemicals (GHS codes) and the U.S. EPA's Design for the Environment (DfE) Alternatives Assessment Criteria for Hazard Evaluation (U.S. EPA, 2011), as described by Vegosen and Martin (2020). Vegosen and Martin (2020) identified a final qualitative ranking for each category by selecting the most conservative rank from the most authoritative data source.

The human health hazard category for this evaluation was scored by considering primary and secondary human health categories for chronic exposure. Primary categories represent chronic, severe, and potentially permanent effects (e.g., cancer), and secondary categories represent short-term, temporary, or less significant effects (e.g.,

skin sensitization). Acute health effects were not considered in the health ranking. The primary categories for human health hazard were carcinogen, genotoxic, mutagen, endocrine disruptor, reproductive toxicant, and developmental toxicant (Vegosen and Martin, 2020). The secondary categories for human health hazard were neurotoxicity, systemic toxicity, skin sensitization, and skin irritation.

The score for human health hazard was derived using a 2-step process:

Step 1:

A score was determined for each primary category using the following matrix (Table 5).

Table 5. Human Health Hazard Score for primary categories

Primary Human Health Hazard	Human Health Hazard Score			
	3	**2**	**1**	**No Score**
Carcinogenicity	VH or H	M	L	I or blank
Genotoxicity Mutagenicity	VH or H	M	L	I or blank
Endocrine Disruption	H*	Not applicable**	L	I or blank
Reproductive toxicity	H*	M	L	I or blank
Developmental toxicity	H*	M	L	I or blank

*Endocrine disruption, reproductive and developmental toxicity do not have very high (VH) hazard options
**Endocrine disruption does not have a medium score; only high or low options
H = high; vH = very high; M = medium; L = low; I = inconclusive data; blank = no data

A primary category score was selected for each constituent based on the highest ranking for all five primary human health hazard categories.

Step 2:

A score was developed for the secondary categories based on a scale of 2, 1, or no information, as indicated in Table 6. Secondary category rankings were for

Table 6. Human Health Hazard Score for secondary categories

Human Health Effects	Human Health Hazard Score		
	2	1	No Score
Neurotoxicity – repeat exposure	H, M	L	I or blank
Systemic toxicity – repeat exposure	H, M	L	I or blank
Skin sensitization	Not applicable*	L	I or blank
Skin irritation	H, M	L	I or blank
Eye irritation	H, M	L	I or blank

*Skin sensitization was only ranked as low or no information

The final human health hazard score was the higher of the primary or secondary category scores. Because the secondary categories had a maximum value of 2, the primary score would always be selected if the value was "3".

The Hazard Ranking Worksheet (W-8) provides the final ranking for the human health hazard category, with a note regarding the rationale (i.e., which endpoint contributed to the ranking). For example, if a constituent was a carcinogen, it would be ranked as a 3, and Worksheet W-8 would note that it was a carcinogen in the rationale column. To simplify presentation in Worksheet W-8, only one of the multiple primary categories that contribute to a ranking were noted as the rationale for the ranking. The rationale displayed in Worksheet W-8 were posted in the following order: carcinogen, mutagen, endocrine disrupter, reproductive, developmental. If a constituent was not rated as a "3" as a carcinogen or mutagen but was as an endocrine disrupter, then the rationale column says "endocrine disrupter." If a constituent was ranked based on a secondary category at a higher level than the primary category, the "secondary tier effect" appears in the rationale column on Worksheet W-8. The detailed information for the rankings is documented in Worksheet W-3.

3.3 Persistence/Bioaccumulation Category Score

As indicated by the category name, two factors impact this score: persistence and bioaccumulation. The scoring approach for both these categories was taken directly from TSCA methodology. Each of these two factors was ranked on a scale of 1 to 3, the rankings for each factor were then added together and divided by 2 to provide a final score

between “1” and “3” for the category. For example, if persistence was ranked as a “2” and bioaccumulation/bioconcentration was ranked as a “3,” the final score would be 5/2, or 2.5. Consistent with the TSCA Method, bioaccumulation and bioconcentration factors were used to develop the score for the bioaccumulation portion of this category.

The persistence score was based solely on half-life in the environment as provided in the CompTox database (Worksheet W-5). Half-lives were reported in $(days)^{-1}$ and converted to months by dividing by 30 days/month. Persistence (half-life) was ranked as follows:

- Half-lives < 2 $(months)^{-1}$ as a “1”;
- Half-lives between 2 and 6 $(months)^{-1}$ were ranked as a “2”; and
- Half-lives greater than 6 $(months)^{-1}$ were ranked as a “3”.

Bioaccumulation/bioconcentration was evaluated using multiple sources of information as shown in Worksheet W-8. The references included:

- Median bioaccumulation value from specific references
- Bioaccumulation rank from the Hazard Comparison Dashboard
- Bioconcentration value from the CompTox Database

The Hazard Comparison Dashboard provided a rank from 1 to 3 for each constituent. For the other two information sources, the bioaccumulation/bioconcentration was ranked as follows based on the TSCA Method:

- Bioaccumulation/bioconcentration values < 1000 were ranked as a “1”;
- Bioaccumulation/bioconcentration values >1000 and <5000 were ranked as a “2”; and
- Bioaccumulation/bioconcentration values >5000 were ranked as a “3”.

3.4 Cumulative Hazard Ranking

As shown on Worksheet W-8, each constituent was provided a cumulative ranking across the three categories evaluated: exposure, human health hazard, and persistence/bioaccumulation. In cases where a numerical ranking for one or more of these categories was not available, a final ranking was not calculated. In these cases, the primary reason for not ranking a constituent is posted in Worksheet W-8 in the “Notes” column; the primary reason was selected in the following order: exposure, human health hazard, persistence/bioaccumulation. If a chemical was not ranked because there was no ranking for human health hazard and persistence/bioaccumulation, only “human health hazard data was not available” would be presented. Because exposure is the first factor, most unranked chemicals have a note about absent chemical concentration data, but there may also be other missing information.

Of the 233 constituents identified as priority constituents by TCEQ, 175 constituents were ranked numerically. In some cases, groups of similar constituents were evaluated (e.g., nonabromyldiphenyl ethers (BDEs) or PFAS). If one or more constituents in a group were not ranked, the general ranking of the group may be used to evaluate the group of constituents as a whole. For example, 18 BDEs were flagged by TCEQ but two of them were missing information. The general ranking of the group could be applied to these additional two constituents for evaluation purposes.

Constituents with a ranking in all three categories were ranked in Worksheet W-8 between a "2" and a "9". A "9" represents a constituent with the highest score for each of the three categories.

Table 7: Highest ranked constituents (ranked as a "9")

BDE-209 (2,2',3,3',4,4',5,5',6,6'- DeBDE)
Cholestanol
Cholesterol
Coprostanol (3-beta)
Desmosterol
Epicoprostanol
Stigmastanol, β-
Stigmasterol

It is important to note that these rankings are qualitative and do not provide a prediction of risk or specific health effects related to the presence of these constituents in biosolids. These rankings are only a relative indicator among the constituents. Yet, the presence of these highly ranked constituents in biosolids may warrant further evaluation to assess the potential for human health effects. For example, further measurements in biosolids may help verify relevant concentrations in biosolids in Texas, which may be different than those in the literature cited in Worksheet W-2. Also, while exposure is related to concentration, concentration is not the only predictor of actual exposure, which may be mitigated by chemical form and application practices. Similarly, persistence/bioaccumulation is based on generic measurements for the constituents and are not specific to land-applied biosolids. While this study provides a means for comparing information for the constituents, no specific conclusions can be drawn regarding potential human health effects without further analysis.

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APPENDIX A

Biosolids Workbook Bibliographies

(organized by Worksheet in the *Biosolids Workbook*)

W-2 Biosolids Concentrations Bibliography

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