Human Health Risk Assessment for 1,4-Dioxane in Drinking Water Summary

NC Secretaries' Science Advisory Board - August 7, 2024

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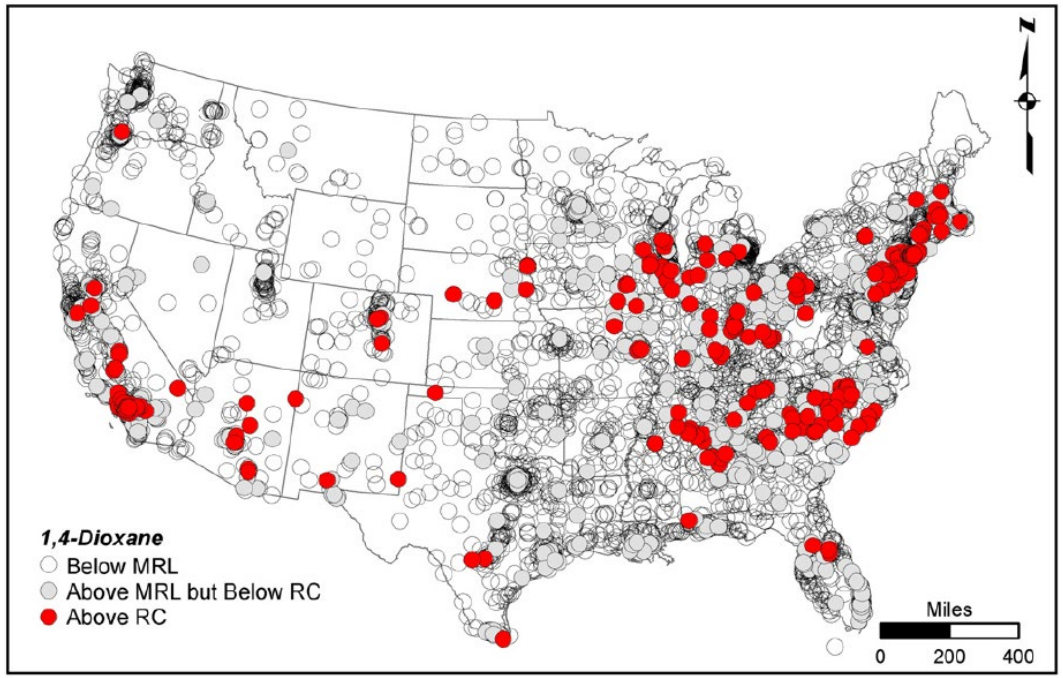
1,4-Dioxane History

- EPA issued the third Unregulated Contaminant Monitoring Rule (UCMR 3) on May 2, 2012.
  - UCMR 3 required monitoring for 30 contaminants (28 chemicals and two viruses) in drinking water between 2013 and 2015.
  - 1,4-Dioxane was included in UCMR3.
  - Results were published in 2017



California (73 systems),
New York (31 systems),
New Jersey (30 systems),
North Carolina (24 systems), and
Illinois (21 systems)
had the most PWSs that
1,4-dioxane exceeded 0.35 µg/L.
(D.T. Adamson et al., 2017)

MRL = Minimal Reporting Level
RC = Reference Concentration; 0.35µg/L
PWS = Public Water Systems

1,4-Dioxane History

- UCMR3 led high ranking states to revaluate the industrial sources of 1,4-dioxane, rules related to water quality standards, and discharge limits in affected permits.

- DEQ began monitoring across the state and many sites began monitoring independently.

State	Number of Detects	% Detects	mean	min	max	sd
IL	185	14%	0.58	0.07	22.93	2.33
NY	318	20%	0.59	0.07	10.00	1.07
NC	49	4%	1.69	0.07	8.80	2.31
CA	863	13%	0.68	0.07	7.80	1.17
AZ	88	8%	0.37	0.07	6.70	0.85
PA	271	20%	0.24	0.07	6.20	0.53
NJ	293	20%	0.42	0.07	5.60	0.78
AL	190	18%	0.31	0.07	4.20	0.52
NH	5	4%	2.00	0.10	3.64	1.62

(D.T. Adamson et al., 2017)

1,4-Dioxane History

DWR 1,4-dioxane Discharge Sampling:

- Greensboro TZ Osborne WWTP
  - October 2019 through current (as part of a settlement agreement between the City of Greensboro, NC Environmental Management Commission, the Haw River Assembly, and Fayetteville Public Works Commission)
- Asheboro WWTP
  - July 2021 through present (ongoing)
- High Point Eastside WWTP
  - June 2022 through present (ongoing)
- Burlington East WWTP
  - November 2019 through April 2020 (when City entered agreement with Haw River Assembly that included routine sampling)
- Reidsville WWTP
  October 2019 through July 2023

Legislative Report Details and Timeline

Sept 2023:

NC General Assembly directed DEQ to prepare a human health risk assessment of 1,4-dioxane in drinking water supported by peer-reviewed scientific studies.

Dec 2023:

NC SSAB discussed the difficulty in meeting the legislative timeline and recommended a strategy to meet the requirements in the time given

Jan 2024:

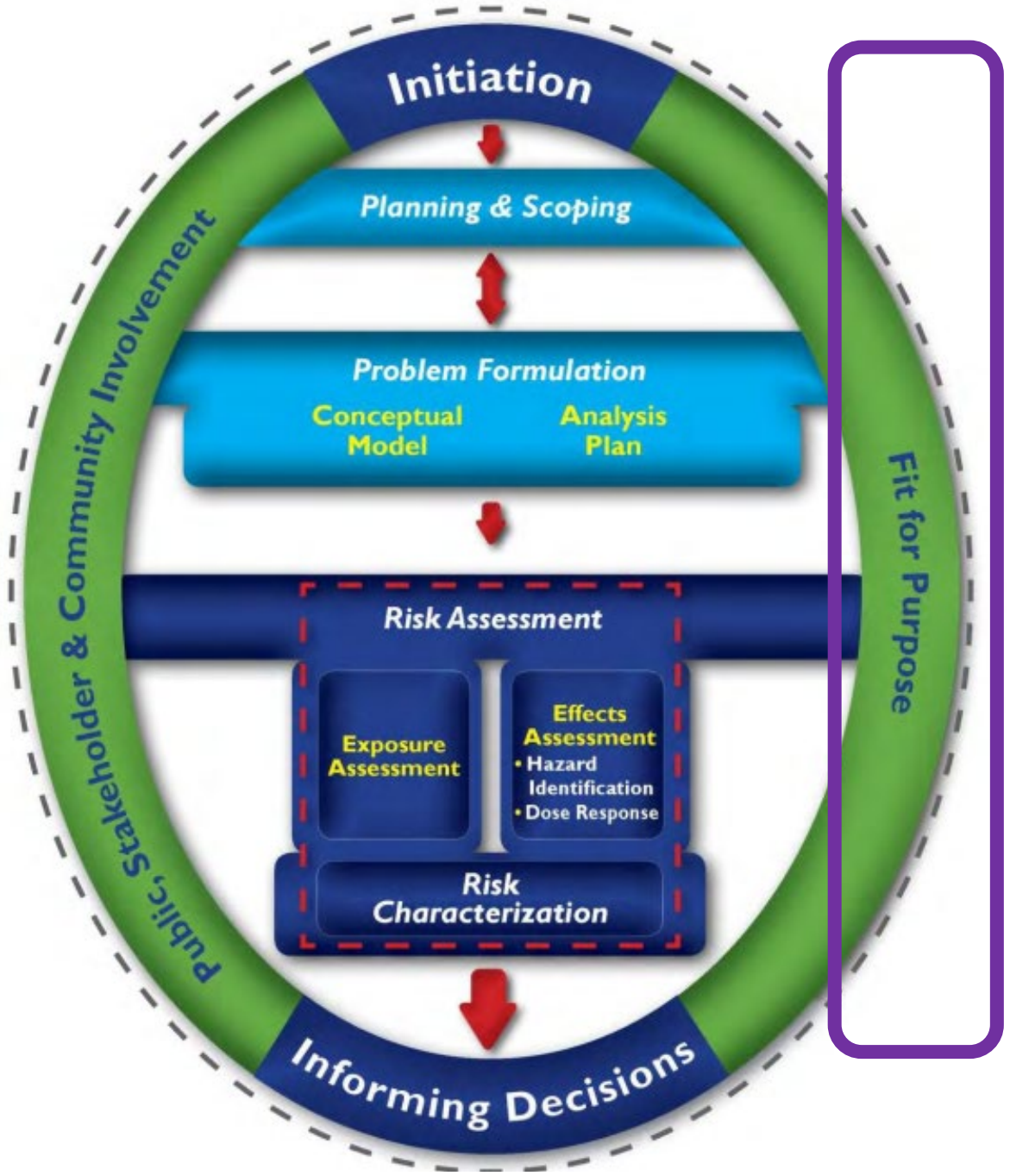
DEQ followed the strategy the SSAB suggested and convened a group of experts to begin the directive activities.

May 1, 2024:

DEQ delivered the assessment to the Joint Legislative Commission on Governmental Operations.

Overall Approach

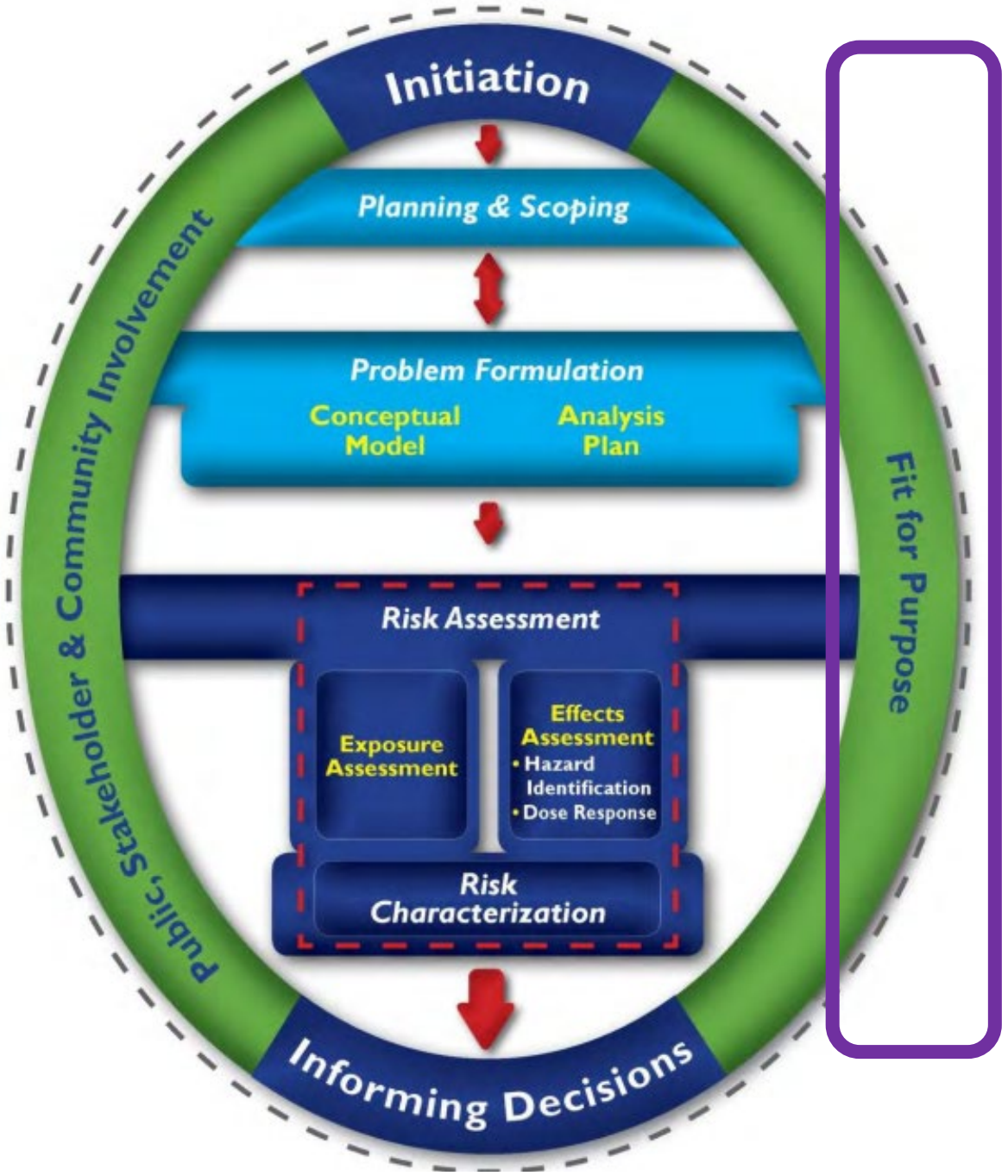
EPA's HHRA for Decision Making Framework



EPA's HHRA for Decision Making Framework

Approach: Follow EPA's Human Health Risk Assessment to Inform Decision Making Framework to evaluate the Cancer Risk of 1,4-Dioxane in Drinking Water in North Carolina.

Goal: Final report to legislature regarding carcinogenic risk of 1,4-Dioxane in NC drinking water on May 1, 2024.



1,4-Dioxane Work Group

Exposure Assessment Team Members

Person	Role	Responsibilities	Qualifications
Jared Wilson, MS (DEQ)	Team Lead	Data compilation and mapping	Geographic Information Systems Specialist, Data Analysis and Curation Resource.
Jenny Graznak (DEQ)	Occurrence Expert	Data provision and evaluation	1,4-Dioxane Consent Order Implementation, Monitoring, and Permitting Resource.
Tammy Hill (DEQ)	Exposure data specialist	Data provision and evaluation	1,4-Dioxane Monitoring and Data Curation Resource.

Effects Assessment Team Members

Person	Role	Responsibilities	Qualifications
Frannie Nilsen, PhD (DEQ)	Team Lead; Work Group Lead	Project Lead/Manager; compare existing CSF source information for evaluation	Environmental toxicologist
Elaina Kenyon, PhD (EPA)	Experimental Toxicology Data Expert	Evaluate models used to derive CSFs between difference information sources	Research toxicologist in the EPA's Center for Computational Toxicology and Exposure

1,4-Dioxane Work Group

Complete Assessment Review Panel Members

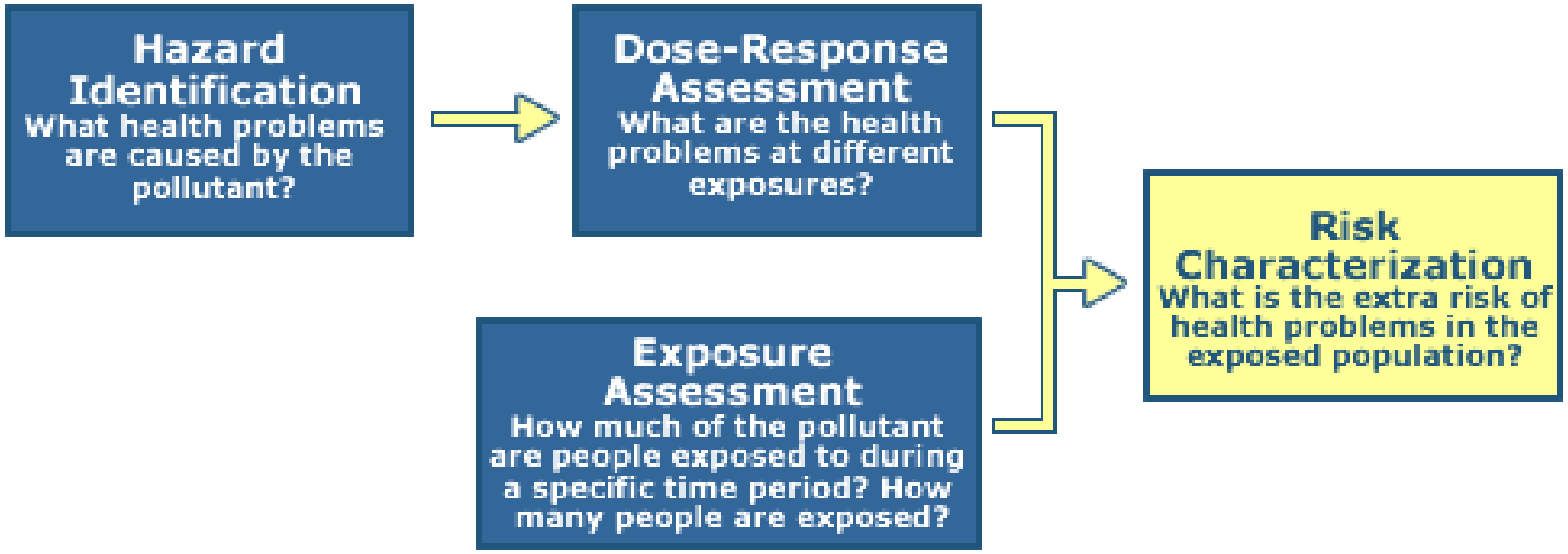
Person	Role	Responsibilities	Qualifications
Linda Birnbaum, Ph.D., D.A.B.T.	Human Health Expert	Evaluate data provided to inform risk	Human exposure and toxicokinetic expert
NC SSAB Members	Reviewer	Toxicology Expert Board	Toxicologists; Health Effects Experts

Advisory Committee Members

Person	Qualifications
Zack Moore, MD MPH	State Epidemiologist, NCDHHS
Betsey Tilson, MD MPH	State Health Director, NC DHHS
Sushma Masemore, PE	Assistant Secretary for the Environment, NC DEQ
Virginia Guidry, PhD MPH	Section Chief, Occupational and Environmental Epidemiology Branch, NCDHHS
Kennedy Holt, MSPH	Toxicologist, Occupational and Environmental Epidemiology Branch, NCDHHS

Risk Assessment Components

The 4 Step Risk Assessment Process



Exposure Assessment – Analysis Plan

Exposure Assessment Analysis Plan	
Approach	Describe prevalence and exposure to 1,4-dioxane and estimate the impacted population using all environmental occurrence and drinking water data available to DEQ.
Method	Compare environmental occurrence data to drinking water data and calculate the percent detections and percent detections above the national average value reported in the UCMR3 data.
Metric	Compare NC Exposure data to the National UCMR3 data to determine if the exposure experienced by NC is ‘average’ or ‘irregular’, based on mean value and standard deviation of the 1,4-dioxane concentrations reported in drinking water from both datasets.

Exposure Assessment – Data Quality

Data Quality Metrics

The EPA Framework data quality metrics were used to determine if the included data/assessments are appropriate for inclusion in the assessment (EPA Guidance 2014).

The metrics:

- Soundness – Scientific methods are consistent with application.
- Applicability and Utility – Dataset is relevant for this use.
- Clarity and Completeness – Assumptions, quality assurance information, data sources, and analyses used to generate information are documented.
- Uncertainty and Variability – Both described in dataset and methods used for analysis.
- Evaluation and Review – Data independently verified/ peer- reviewed.

Data Quality Metric	DEQ SW	DEQ WW	DEQ PWS	FPWC Data	CFPUA Data	Pittsboro Data	High Point Data	Cary Data	Sanford Data	UCMR3 Data
Soundness	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Applicability and Utility	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Clarity and Completeness	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Uncertainty and Variability	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Evaluation and Review	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Exposure Assessmer Data Analysis

- <u>Environmental Occurrence:</u> DEQ surface water (SW), DEQ wastewater (WW), drinking water utility raw/intake water (*i.e.,* surface or ground water) from 2013 through 2023,
- <u>Pre-Regulatory Efforts</u> – Drinking water utility finished water from 2014 through Dec 2021.
- <u>Post-Regulatory Efforts</u> – Drinking water utility finished water from Jan 2022 through present (most recent data retrieved January 2024).

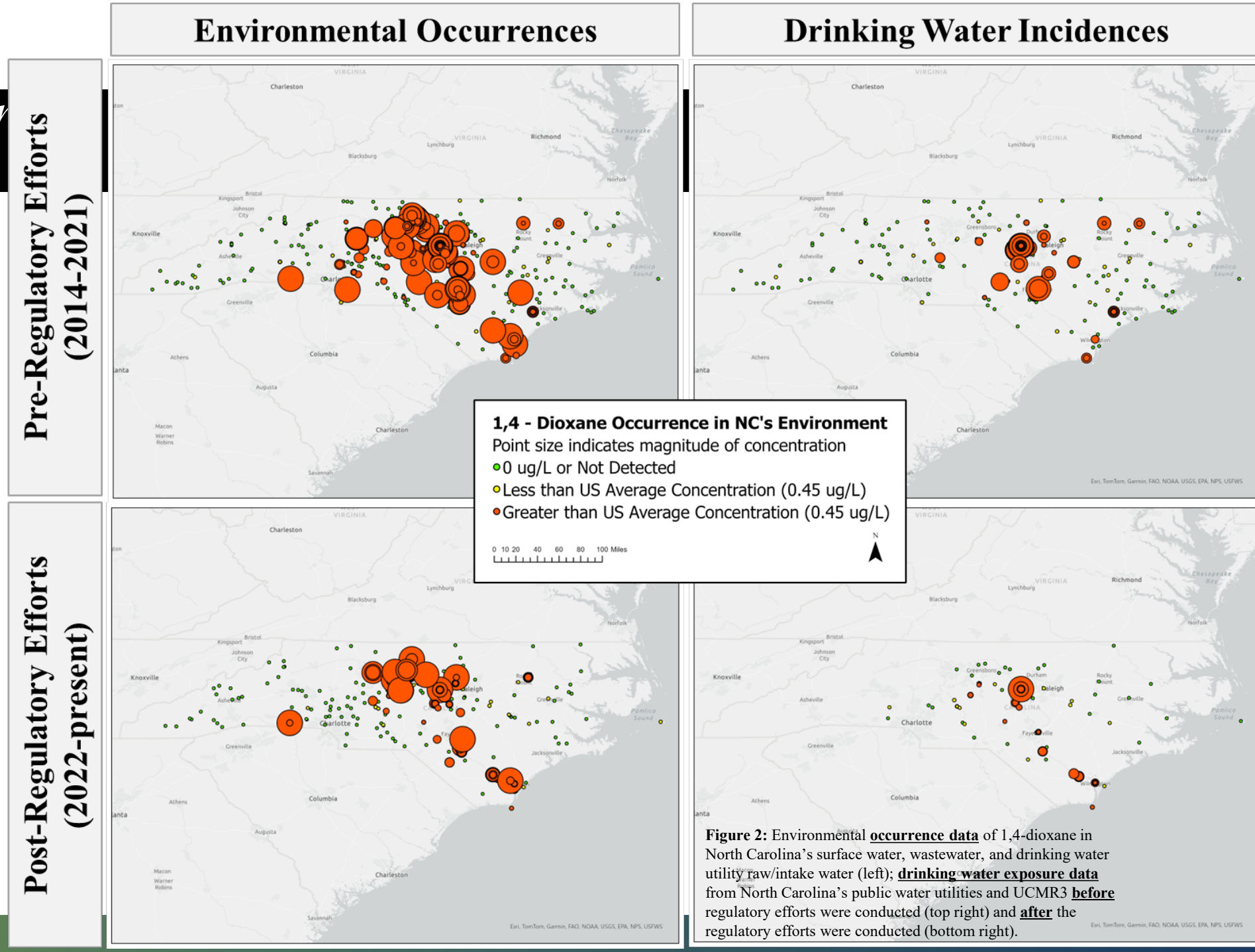


Figure 2: Environmental **<u>occurrence data</u>** of 1,4-dioxane in North Carolina's surface water, wastewater, and drinking water utility raw/intake water (left); **<u>drinking water exposure data</u>** from North Carolina's public water utilities and UCMR3 **<u>before</u>** regulatory efforts were conducted (top right) and **<u>after</u>** the regulatory efforts were conducted (bottom right).

Exposure Assessment – Summary

The data examined in this report indicate the following:

1. Most North Carolinians outside of the Cape Fear River Basin are not exposed to 1,4-dioxane at concentrations above the UCMR3 national average.
2. Some of those who are exposed within the Cape Fear River Basin are exposed to the third highest drinking water concentrations in the nation (UCMR3 Data).
3. Regulatory attention focused to reduce concentrations led to decreased 1,4-dioxane environmental and drinking water exposure in the Cape Fear River Basin in NC.
4. The public outreach efforts regarding 1,4-dioxane exposure in drinking water resulted in many locations in NC decreasing 1,4-dioxane exposure outside of the Cape Fear River Basin due to voluntary and/or other actions.

Effects Assessment – Analysis Plan

Effects Assessment Analysis Plan	
Approach	Compare existing assessments and evaluate quality of any new data for application of health-based guidance value for cancer endpoint calculations.
Method	Summarize existing and relevant new literature and compare data used to derive the health-based guidance values for cancer endpoint provided.
Metric	Compare any new data to EPA guidance for health-based guidance value for cancer endpoint derivation.

Effects Assessment – Data Quality

Data Quality Metrics

The EPA Framework data quality metrics were used to determine if the included data/assessments are appropriate for inclusion in the assessment (EPA Guidance 2014).

The metrics:

- Soundness – Scientific methods are consistent with application.
- Applicability and Utility – Dataset is relevant for this use.
- Clarity and Completeness – Assumptions, quality assurance information, data sources, and analyses used to generate information are documented.
- Uncertainty and Variability – Both described in dataset and methods used for analysis.
- Evaluation and Review – Data independently verified/ peer- reviewed.

Data Quality Metric	EPA IRIS 2010	EPA IRIS 2013	EPA TSCA 2023	EHCA 2021	Health Canada 2021
Soundness	✓	✓	✓	✓	✓
Applicability and Utility	✓	The inhalation update of 2013 is not applicable to the regulatory scenario	Not applicable to the regulatory scenario; includes occupational exposures, focused on dermal and inhalation routes of exposure.		✓
Clarity and Completeness	✓	✓	✓	✓	✓
Uncertainty/Variability	✓	✓	✓	✓	✓
Evaluation and Review	✓	No new oral exposure data was added to this assessment	The derived ECEL is for inhalation exposures. No ingestion limits derived in this assessment; risk criteria = 10^{-4}	The conclusions are related to occupational exposures	✓

Effects Assessment – Data Analysis

1. Hazard Identification: Comparison of existing 1,4-Dioxane data source information.
2. Dose-Response Analysis: An evaluation of current Cancer Slope Factor derivation and differences between sources

Assessment Type	EPA IRIS Assessment		Health Canada Non-Cancer Value (2021)	ATSDR Non- Cancer Value (2012)
	EPA Carcinogenicity (2013)	EPA Non-Cancer Value (2013)		
Species and Target Organ	Mouse Liver	Rat liver and kidney toxicity	Rat Liver	Rat liver
Endpoint and data used for dose-response modeling	Hepatocellular adenomas and carcinomas, female (Kano et al., 2009)	NOAEL (did not use benchmark dose modeling), male rat (Kociba et al., 1974)	Hepatocellular necrosis, combined male & female data (Kociba et al., 1974)	NOAEL (did not use benchmark dose modeling), male rat (Kociba et al., 1974)
Benchmark Dose Model Used	Log-logistic with linear low dose extrapolation	Not applicable (used NOAEL)	Log-Probit	Not applicable (used NOAEL)
POD	$BMDL_{50}$ = 32.93 mg/kg-day	NOAEL = 9.6 mg/kg-day	$BMDL_5$ = 5.4 mg/kg-day	NOAEL = 9.6 mg/kg-day
POD_{HED}	$BMDL_{50HED}$ = 4.95 mg/kg-day	Not calculated	Not calculated	Not calculated
Total UF applied	Not applicable	300 (UF_A=10, UF_H=10, UF_D=3)	1000 (UF_A=10, UF_H=10, UF_D=10)	100 (UF_A=10, UF_H=10)
Risk probability	1 in a million (10^{-6})	Not applicable	Not applicable	Not applicable
Low Dose Extrapolation method	Linear, no threshold	Assumes threshold, uses UFs[1]	Threshold (non-linear), uses UFs	Assumes threshold, uses UFs[1]
Health-based criterion	CSF = 0.1 mg/kg-day	RfD = 0.03 mg/kg-day	TDI = 0.0054 mg/kg-day	MRL = 0.1 mg/kg-day
Criterion description	Cancer protective factor for humans.	Lifetime (70 years) exposure can be experienced with no non-cancer effects occurring in humans.		

Effects Assessment – Summary

The Effects Analysis sections highlighted,

1. The EPA and Health Canada assessments agree that oral exposure to 1,4-dioxane causes carcinogenic effects in the liver, and that the carcinogenic liver effects MOA are the most well-understood.
2. The EPA IRIS assessment provides the most consistent value across regulated chemicals, and with federal and other state regulatory programs.
    1. There have been a few peer-reviewed scientific publications since both assessments were produced, but there are not enough additional data to support non-linear low-dose extrapolation approach for all target organs.
3. The CSF provided by the EPA IRIS assessment of 0.1 mg/kg-day was derived using the most health protective modeling approach and will provide science-based protection to North Carolinians from exposure to 1,4-dioxane in their drinking water.

Risk Characterization– Analysis Plan

Risk Characterization Analysis Plan	
Approach	Compare exposure data with drinking water values based on the health-based guidance value for protection from cancer.
Method	Risk will be determined based on the extent to which mean drinking water concentration, and the 95% confidence interval that people are exposed to is above a WQS derived using NC rule 02B.0208 based on the CSF of 0.1 mg/kg-day, and the Margin of Exposure (MOE) calculation to determine relative protectiveness of the derived WQS compared to other values examined.
Metric	The percent of exposure data that is above the derived WQS value will be related to the risk and magnitude of protection using the MOE calculation, the results will be compared to the UCMR3 data to determine how the risk in NC compares to the national risk.

Risk Characterization– Data Analysis

While the drinking water in NC is a source of 1,4-dioxane exposure at higher concentrations than the national values, the entire country is exposed to 1,4-dioxane in concentrations above the value that is predicted to cause one case of cancer in a million people (0.35 µg/L)

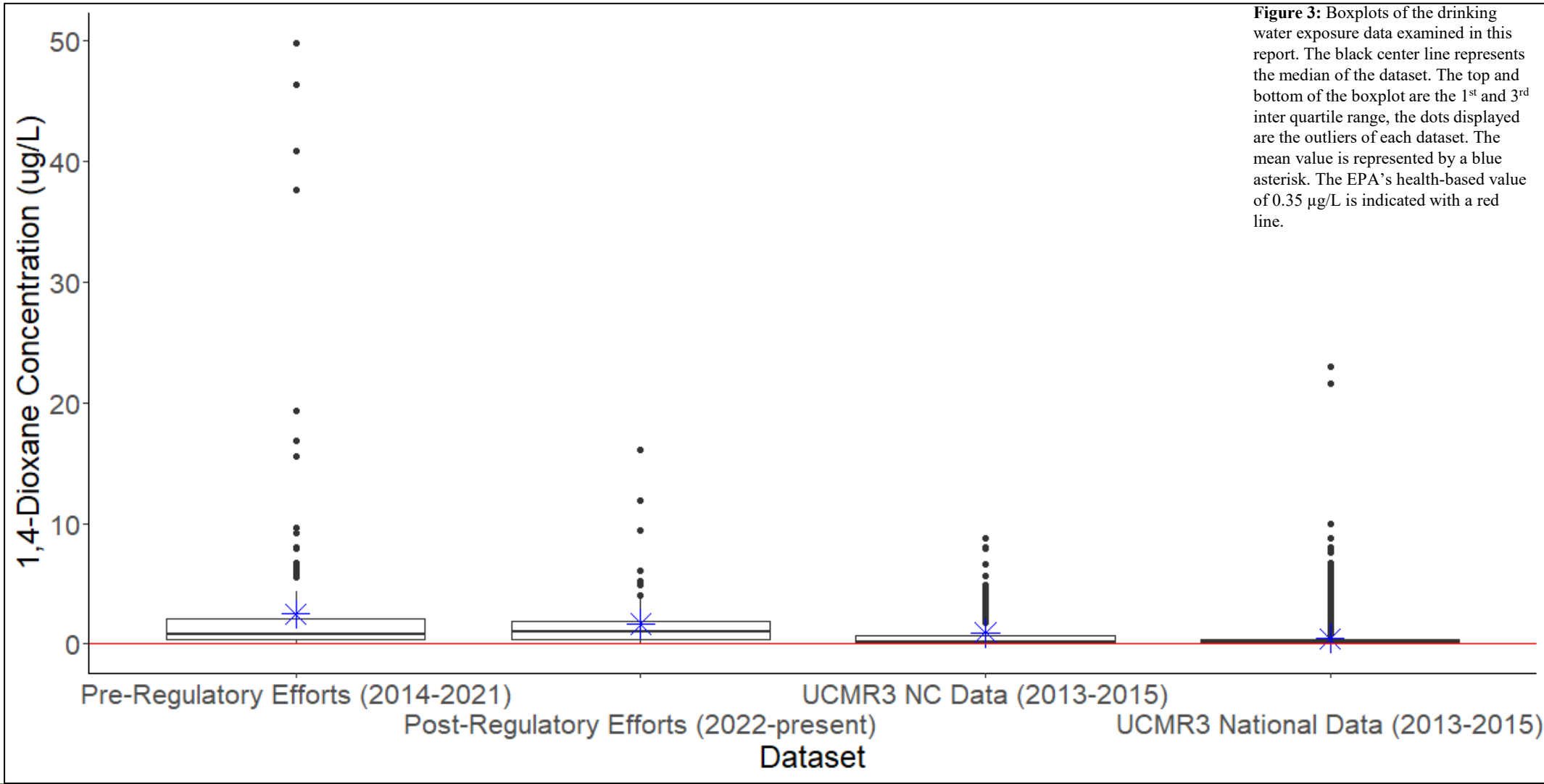


Figure 3: Boxplots of the drinking water exposure data examined in this report. The black center line represents the median of the dataset. The top and bottom of the boxplot are the 1st and 3rd inter quartile range, the dots displayed are the outliers of each dataset. The mean value is represented by a blue asterisk. The EPA's health-based value of 0.35 µg/L is indicated with a red line.

Risk Characterization– Data Analysis

Since all the mean values used in the *MOE Analysis* were considered protective, the MOE from each dataset was compared to the MOE from the derived WQS, to determine how protective each drinking water mean value is compared to the derived WQS that is based on the IRIS toxicity value (CSF = 0.1 mg/kg-day).

Exposure Assessment Drinking Water Dataset	Drinking Water (DW) Mean Value		Estimated Daily Exposure (mg/kg-day)	MOE ≥ 10,000 = Protective	MOE % Protectiveness
	(µg/L)	(mg/L)	= (DW mg/L * 2 L/day) / 70 kg	= BMDL / Estimated Daily Exposure	= MOE / 0.35 MOE
NC UCMR3	0.92	0.00092	0.00003	1,252,771	38%
Pre-Regulatory Efforts	2.49	0.00249	0.00007	462,871	14%
Post-Regulatory Efforts	1.67	0.00167	0.00005	690,149	21%
Derived WQS*	0.35	0.00035	0.00001	3,293,000	100%
National (US) UCMR3	0.45	0.00045	0.00001	2,561,222	78%

Table 4: The drinking water values examined in this report presented with paired toxicological values for Margin of Exposure (MOE) calculations.
*value is the derived WQS using the CSF of 0.1 mg/kg-day, not a mean measured value.

Risk Characterization – Summary

This report uses the exposure data and health-based values for cancer endpoint dose response information to determine how the risk in NC compares to the national risk.

Based on the risk assessment, it is concluded that NC's residents are exposed to 1,4-dioxane concentrations that may be two times the national average in drinking water and as much as 4 times national averages in surface and groundwater.

Based on the UCMR3 data, North Carolinians experienced approximately half the protection than the rest of the nation received from 1,4-dioxane in drinking water from 2013-2015 (NC UCMR3 = 38%; US UCMR3 = 78%).

Human Health Risk Assessment Report is Available

Report is available here:

https://www.deq.nc.gov/legislative-reports/14-dioxane-drinking-water-human-health-risk-assessment/open