ITRC (Interstate Technology & Regulatory Council). 2023. *Contaminants of Emerging Concern Framework* CEC-1. Washington, D.C.: Interstate Technology & Regulatory Council, CEC Team. https://cec-1.itrcweb.org/.

This Case Study has been organized into the following subsections:

1. Introduction

The White Paper and the four associated contaminants of emerging concern (CEC) Fact Sheets are intended to provide a framework that states may consider when undertaking or developing a CEC program to identify, evaluate, and monitor potentially harmful substances in the environment. Addressing CEC is a complex process that requires consideration of many factors. This hypothetical case study shows how a CEC may be evaluated using the approach illustrated in the Identification of Key CEC Variables Fact Sheet Flowchart.

2. Background Information

Chemical Name: Chloro-α,α,α-trifluorotoluene
CASRN: 98-56-6
Chemical Formula: $C_7H_4ClF_3$
Molecular Weight: 180.56

The potential CEC was originally observed as a tentatively identified compound (TIC) in wastewater during full-scan GC-MS analysis with a >85% spectral match against the Wiley–National Institutes of Standards and Technology GC-MS mass spectral library (for example guidance on TICs see (USEPA 2020)). The potential CEC was also detected in the property well used as a drinking water source at the site. The laboratory identified the TIC as chloro-α,α,α-trifluorotoluene or para-chlorobenzotrifluoride, one of several compounds in a chemical mixture that is being used as a solvent substitute for xylene. This chemical is not listed in any of the Resource Conservation and Recovery Act, Comprehensive Environmental Response, Compensation, and Liability Act, or state lists of chemicals monitored or analyzed in environmental media (see the CEC Monitoring Programs Fact Sheet). A reference analytical standard was obtained to confirm the identity of the TIC. Once confirmed, the analytical method was updated using calibration information for the CEC to enable its quantitation (see the Analytical Methods Fact Sheet). With an identified CEC, evaluation can proceed using the process flowchart.

3. Key Variables Evaluation Using the Process Flowchart

3.1 Occurrence Criterion

The CEC was identified in wastewater and drinking well water samples but not measured in other environmental media. An additional four samples each from the wastewater and drinking well water including quality control samples were collected each month for three consecutive months and submitted to the laboratory that initially detected and identified the CEC.

Using the CEC prioritization flow chart, the following considerations indicate sufficient evidence of the presence of the CEC in the environment (wastewater and drinking water). Further evaluation of its hazards, physical-chemical properties, presence in other environmental media (soil and air), and presence at other sites is required:

- The wastewater data and the company's process and safety information indicate that the presence of the CEC in wastewater came from the waste stream of the industrial process used at the site.
- The CEC is a component of a solvent and an intermediate in pesticide production.
- The CEC was detected in all but one sample from the drinking water well, indicating groundwater contamination.
- Drinking water is a direct exposure route for the workers at the site. The extent of contamination on site and off site is not known and requires further investigation.
- Soil and ambient air concentrations of the CEC are not known and require further investigation.
- The volatilization from groundwater to indoor air pathways also requires evaluation. The CEC is a solvent used in some caulks, paints, and coatings and is found in some fabric stain removers. Therefore, it is possible that the chemical could migrate into indoor air.
- The European Chemical Agency reports this chemical is used (1) in consumer products such as coating products, inks, and toners; (2) in the manufacture of other chemicals, machinery and vehicles, plastic products, and mineral products (e.g., plasters, cement); (3) in scientific research and development; and (4) as an intermediate step in the manufacturing of another substance. Release to the environment of this substance can occur from industrial use and release to the environment may occur from indoor or outdoor use as a processing aid (ECHA 2022).

Recommendation

The CEC was detected in drinking water, but other environmental media were not analyzed. Exposure to a contaminant in drinking water is a direct human exposure. Proximity of the CEC to sensitive receptors (e.g., children) is a critical consideration for occurrence evaluation. The drinking water data quality is adequate; however, the environmental characterization of the site in relation to impact on soil, ambient air, and nearby surface water is lacking. The CEC evaluation should move to the evaluation and determination of other key variables (hazard/toxicity and physical-chemical properties) and additional occurrence characterization data to determine whether the CEC is a low-, medium-, or high-priority CEC. The occurrence of a contaminant in soil may lead to a higher priority assignment depending on several factors. See the Identification of Key CEC Variables Fact Sheet for additional explanation.

3.2 Human Health and Ecological Effects (Toxicity Criteria)

3.2.1 Available Human Health Toxicity Values (Hazard Criteria—Human Health)

Group 1 and Group 2 sources of toxicity values were searched. See the Identification of Key CEC Variables Fact Sheet for additional details on these sources. The Group 1 and 2 oral and inhalation toxicity values are available for this CEC (Table 1).

Table 1. Available toxicity values

Sources	**Chronic RfD**	**CSF**	**Chronic RfC**	**IURF**
Group 1	3×10^{-3} mg/kg-day (USEPA 2007)	NA	3.0×10^{-1} mg/m^3 (USEPA 2007)	NA
Group 2	NA	3.0×10^{-2} (mg/kg-day)$^{-1}$ (CalEPA, OEHHA. 2019)	NA	8.6×10^{-6} (µg/m^3)$^{-1}$ (CalEPA, OEHHA. 2020a)
Others	NA	NA	NA	NA

CSF = oral cancer slope factor; IURF = inhalation unit risk factor; mg/kg-day = milligrams per kilogram per day; mg/m^3 = milligrams per cubic meter; $\mu g/m^3$ = micrograms per cubic meter; NA = no information available currently; RfC = inhalation reference concentration; RfD = oral reference dose Note: The CSF value is an inhalation CSF. The National Toxicology Program (NTP. 2018) study used as the basis of the CSF and IURF is an inhalation study, and the inhalation CSF was developed by the California Environmental Protection Agency as part of the development of the IURF. The inhalation-based CSF may be used as a screening oral toxicity value to develop a drinking water screening value. Evaluation by toxicologists could be needed to determine whether route-to-route extrapolation (i.e., use of the inhalation CSF as an oral CSF) is scientifically supportable for development of a guidance value or criterion.

The United States Environmental Protection Agency's (USEPA's) Provisional Peer-Reviewed Toxicity Value (PPRTV) assessments (derivation details, (USEPA 2007)) developed subchronic and chronic noncancer oral reference dose (RfD) and inhalation reference concentration (RfC) toxicity values based on a 28-day oral study in rats (Macrí et al. 1987) and a 13-week inhalation study in rats (Newton et al. 1998), respectively. The critical noncancer effect was liver effects.

The California Office of Environmental Health Hazard Assessment (OEHHA) based its cancer toxicity values on the published chronic inhalation toxicity study by the National Toxicology Program (NTP 2018), NTP Technical Report on the Toxicology and Carcinogenesis Studies of p-chloro-α,α,α-trifluorotoluene (CalEPA 2020b). For chemicals with an oral cancer slope factor (CSF), inhalation CSF, or inhalation unit risk factor (IURF), the weight of evidence information or cancer classification (i.e., suspected/suggestive, likely/presumed, or known to cause cancer to humans) should be presented, if available. The OEHHA assessment did not specify a cancer classification.

3.2.2 Available Ecological Health Information (Hazard Criteria—Ecological Health)

According to the ECHA Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) registrations (ECHA 2022), the CEC is "toxic to aquatic life with long lasting effects" (see ECHA Brief Profile in the references section for more details). Hazards for aquatic organisms may be represented by the predicted no effect concentration (PNEC) values. The PNEC is the concentration below which adverse effects are not likely to occur (see the Risk Perception and Communication Fact Sheet for more information on ecological health endpoints). ECHA has listed PNEC values for aquatic and terrestrial (soil) organisms. Impacts to fish and aquatic invertebrates in relation to short-term toxicity (lethal concentrations) were also noted.

3.2.3 Hazard Information Summaries

Additional hazard information is summarized in Table 2 and the text below.

Table 2. ECHA identified hazards

Properties (Hazards)	Code	Hazard Description
Flam. Liq. 3	H226	Flammable liquid and vapor
Eye Irrit. 2	H319	Causes serious eye irritation
Skin Irrit. 2	H315	Causes skin irritation
STOT SE 3	H335	May cause respiratory irritation
Aquatic Chronic 2	H411	Toxic to aquatic life with long-lasting effects
Skin Sens. 1B	H317	May cause an allergic skin irritation
Carc. 2	H351	Suspected of causing cancer
Aquatic Chronic 3	H412	Harmful to aquatic life with long-lasting effects
STOT RE 2	H373	May cause damage to organs through prolonged or repeated exposure
Repr. 2	H361	Suspected of damaging fertility or the unborn child
Aquatic Chronic 1	H410	Very toxic to aquatic life with long-lasting effects
Skin Sens. 1	H317	May cause an allergic skin reaction
Carc. 1B	H350	May cause cancer (presumed human carcinogen)

STOT SE 3	H336	May cause dizziness or drowsiness

Information taken from https://echa.europa.eu/information-on-chemicals/registered-substances:
Hazard Class and Category Codes and Hazard Statement Codes

- California Environmental Protection Agency (CalEPA) (CalEPA 2019; 2020a):
  - Can pass from mother to baby during pregnancy.
  - Exposure occurs by breathing the CEC in air and skin contact with products containing the CEC.
  - Human cancer potency.

- ECHA (See ECHA Identified Hazards Table for breakdown of hazards and their classification):
  - Hazard classification and labeling: “Warning! According to the classification provided by companies to ECHA in REACH registrations this substance is toxic to aquatic life with long lasting effects, is a flammable liquid and vapor, is suspected of causing cancer, is suspected of damaging fertility or the unborn child, causes serious eye irritation, may cause an allergic skin reaction, causes skin irritation, and may cause respiratory irritation” (CalEPA, ECHA. 2022).

- Fluoride Action Network Project (Fluoride Action Network Project 2023):
  - Volatile, aromatic liquid used as a chemical intermediate in the manufacture of dinitroaniline herbicides. Also used as a dye intermediate, solvent, and dielectric fluid.
  - NTP 14-day toxicity studies on rats and mice indicated effects on the liver (liver hypertrophy), kidney (hyaline droplet nephropathy), and adrenal changes in rats (Jameson and Yuan 1992; USDHHS 2009).

Recommendation

Human health: The hazard/toxicity evaluation identified human health toxicity endpoints from Group 1 and 2 sources that could be used for calculation of risk estimates and preliminary risk characterization. The NTP study and ECHA information provide evidence of human health effects (developmental-reproductive and potential cancer effects) that require attention. The contaminant is detected in drinking water but not measured in other media. The detected CEC levels in groundwater should be evaluated against a cancer-based drinking water screening level or criterion developed using the Group 2 CSF to determine the risk of drinking the contaminated water. Note that the available CSF developed by CalEPA is an inhalation CSF; therefore, the extrapolation of inhalation toxicity data to develop an oral toxicity value requires further evaluation. The inhalation-based CSF could be used to develop an interim or provisional drinking water screening value. Environmental characterization of the site soil and ambient air for CEC concentrations is recommended. The detection of the CEC in surface water will require data on potential human indirect exposure through fish consumption, including information on bioaccumulation of the CEC in aquatic organisms. The CEC evaluation should move to the evaluation of physical-chemical properties. Additional studies are needed to more conclusively determine the human health toxicity relating to developmental-reproductive effects.

Ecological health: Based on data from REACH registrations for the CEC, ECHA concluded that the CEC poses a hazard for aquatic organisms and terrestrial organisms. Although there is no report of bioaccumulation, there is a potential short-term toxicity to fish and indirectly to human consumers of fish. To understand the direct effect on aquatic species and indirect risk to fish consumers, additional data on ecological impacts on fish and other aquatic species would be helpful.

Summary: Overall, the CEC poses human and ecological health effects of concern; however, noncancer toxicity data are not available to allow the evaluation of other potential noncancer endpoints (e.g., acute skin irritation [unlikely to be a concern at levels found in the environment] and reproductive-developmental effects). Because inhalation toxicity data indicate the importance of the inhalation exposure pathway, toxicity via indoor air inhalation exposure should be evaluated.

3.3 Physical-Chemical Properties Criterion

Further research on the chemical using the available database (Table 3) found the following physical-chemical information on the CEC. California (CalEPA 2020a) compared the vapor pressure and boiling point of the CEC to petroleum-based solvents and found similarities with xylene isomers and ethylbenzene (Table 4). This indicates that the CEC is a volatile compound.

Table 3. Properties

Source: PubChem (2023)

Chemical formula	**$C_7H_4ClF_3$**
CAS Number	98-56-6
EC Number	202-681-1
Synonyms	4-chloro-a,a,a-trifluorotoluene 4-chloro-α,α,α-trifluorotoluene 1 chloro-4-trifluoromethyl benzene benzene 1-chloro-4-(trifluoromethyl)- 4-chlorobenzotrifluoride para-chlorobenzotrifluoride p-chloro-a,a,a-trifluorotoluene
IUPAC Name	1-chloro-4-(trifluoromethyl)benzene
Molar Mass	180.55 g/mol
Appearance	colorless liquid
Odor	aromatic
Density	1.33 g/mL at 25°C
Melting Point	−33°C
Boiling Point	138.5°C
Vapor Pressure	7.6 mm Hg at 25°C
Solubility in Water	29 mg/L at 25ºC
Log Octanol/Water Partition Coefficient (6now)	3.60 at 25ºC (estimated)

Note: CAS . = Chemical Abstract Service, EC = European Community, g/mL = grams per milliliter, g/mol = grams per mole (molar mass), IUPAC = International Union of Pure and Applied Chemistry, mm Hg = millimeters of mercury.

Table 4. Vapor pressure and boiling point of similar compounds

Solvent	**Vapor Pressure (mm Hg, 25°C)**	**Boiling Point (°C)**
Ethylbenzene	9.6	136.2
p-Xylene	8.8	138.3
m-Xylene	8.3	139.1
Chloro-α,α,α-trifluorotoluene	7.6	138.5
o-Xylene	6.7	144.5

Note: mm Hg = millimeters of mercury.

Recommendation

In addition to solubility, other fate and transport properties that impact the CEC's mobility or ability to migrate (Henry's Law Constant, K_{oc}) and exposure potential (volatility, persistence half-life, bioaccumulation, and biomagnification factors) should be identified or estimated. The quality and correctness of the physical-chemical information gleaned from ECHA through its REACH registration data would need validation because ECHA emphasizes that the correctness of the REACH information is not guaranteed. Completion of the information gaps on the physical-chemical features of this chemical will inform its fate and transport characteristics (persistence, bioaccumulation, and mobility). Understanding fate and transport would lead to a better understanding of all potential exposure pathways and consequently the risk to sensitive human and ecological receptors.

3.4 Overall CEC Recommendation and Data Evaluation Based on Process Criteria

Based on the results of the evaluation of the CEC using the flowchart's three criteria (occurrence, hazard/toxicity, and physical-chemical factors), the CEC is: (1) found in drinking water, an exposure pathway of concern; (2) a hazardous substance (carcinogenic, irritant, and suspected reproductive toxicant); and (3) volatile and soluble in water. Occurrence in other environmental media (soil and air), noncancer health effects (especially those linked to reproductive and developmental impacts), and physical-chemical characteristics that may impact exposure through additional exposure pathways (indoor air) require further investigation. Therefore, we would classify this emerging contaminant as a **medium priority CEC** because additional information is needed to determine whether there is widespread concern, which would move it to a high priority. Such additional information would include characterization in other environmental media, continued drinking water monitoring and identification of the CEC in drinking water sources, investigation (toxicity and fate/transport), and data and risk reevaluation. The CEC classification does not negate the need to evaluate the extent of contamination in various environmental media and assessment of the risk posed by the CEC to human and ecological receptors. The three criteria provide a process for prioritizing CEC and identifying scientific information and data needed to fully characterize human health and ecological risks.

Throughout the evaluation of the CEC using the three criteria (see flowchart), this question is asked before proceeding to the next evaluation: ***"Are the data sufficient to make a technical assessment?"*** For occurrence data, this question seeks to answer analytical methods validity, data sufficiency, reproducibility, and other data-relevant issues (see Box 1 of the Identification of Key CEC Variables Fact Sheet). For toxicity or hazard data, this question will identify whether additional data are needed to support the health effects used to establish the toxicity values (cancer, skin irritation, or aquatic short-term toxicity) and identify other health concerns, especially those for sensitive humans (e.g., developmental effects). It is equally important that uncertainties, assumptions, and data sources are considered in the evaluation of hazard or toxicity data. Similarly, the physical-chemical properties of a contaminant reflect its potential to remain in the environment or cause increased exposure and risk to human and ecological receptors (see Box 2 of the Identification of Key CEC Variables Fact Sheet). Therefore, the data quality and sources supporting these physical-chemical properties should be part of the CEC evaluation.

For this case study, the basis of the toxicity endpoints are peer-reviewed studies, and the assessments were conducted by reliable scientific agencies. The oral and inhalation noncancer values derived from the PPRTV were based on oral and inhalation studies, but no cancer values were developed. CalEPA used an NTP 2018 inhalation study as basis for its inhalation cancer toxicity value (IURF). CalEPA also derived a CSF based on the NTP study to develop a No Significant Risk Level (CalEPA 2019). Because the CSF is based on an inhalation value (i.e., based on inhalation-to-oral route extrapolation), its use as an oral CSF may need to be evaluated for scientific validity. Although the California assessment did not specify a cancer classification, ECHA reported that this CEC is a likely or presumed human carcinogen. Health-based screening levels or criteria developed using this cancer toxicity value should be used to evaluate the risk posed by CEC levels in groundwater and other environmental media (e.g., air, soil) to human receptors. The findings of the evaluation should be used to inform regulators and decision-makers on the management of the CEC (e.g., source reduction, exposure prevention, etc.) to protect public health and the environment.

The ecological health impacts were based on data from REACH registrations. As ECHA indicated, the correctness or accuracy of these data may require validation. The physical-chemical information is not sufficient to characterize the chemical's properties and fate and transport characteristics. Characterization of the CEC occurrence in other media and at other sites is also needed. Overall, additional data are required to sufficiently evaluate this CEC and properly define whether the priority level of this CEC remains moderate or changes to high. High-priority substances are evaluated for additional steps that include expanded surveillance, additional risk evaluations and legislative actions (federal or state rulemaking). Regardless of priority level, CEC should be adequately characterized in various environmental media and evaluated for potential risks to human and ecological receptors.

4. Risk Perception and Communication

This part of the case study addresses risk communication messaging—specifically, the who, what, and when and the challenges and considerations, including uncertainties, unknowns, fast-evolving scientific information, and moving and varying risk estimates. As mentioned in the Identification of Key CEC Variables Fact Sheet, a CEC can be shifted between priorities (low, moderate, high) at any time depending on the unique circumstances of the CEC in relation to other competing communication priorities, and the risk communication challenges and strategies will be influenced by the resulting priority designation.

Based on available information identified in the key variables, evaluation, occurrence data, hazard/toxicity values, and physical-chemical factors are available for this chemical. The CEC is considered to be a medium priority CEC, and risk communication becomes more involved than for a low-priority CEC. At this stage, there may already be some public awareness and/or outrage.

For risk communication purposes, an updated version of the chemical Fact Sheet with the most recent occurrence, hazard/toxicity, and physical-chemical factors should be used. The Fact Sheet should also note that the chemical is not adequately characterized in various environmental media. Minimizing exposure by advising the community to not drink well water while the agency monitors drinking water for two consecutive rounds (3 weeks apart for the next 6 weeks) is recommended to the community at a community meeting along with next steps based on sampling results. The Fact Sheet is shared with decision-makers, internal agency stakeholders, and the community to educate them on both the knowns and unknowns about the chemical.

The goal of the risk communicator at this stage is to review and update any educational materials. A risk communicator focusing on precaution advocacy may continue to pressure decision-makers to find more data, but there is already enough information to recommend precautions that individuals can take to protect themselves. There may also be enough new data indicating that specific communities may be uniquely susceptible to the contaminant. At such a time, it is imperative to communicate both the knowns and unknowns to ensure honesty, transparency, and empathy for those involved. A Frequently Asked Questions document should also be developed to proactively address community comments, questions, and concerns. If not already developed, a communication team should be formed, and a communication plan completed. This will support effective communication of key messages. More information can be found in the Interstate Technology and Regulatory Council’s Risk Communication Toolkit (ITRC 2020).

More details on risk communication and risk perception challenges that may be considered are presented in the Risk Perception and Communication Fact Sheet.

References

CalEPA, OEHHA. 2019. “Initial Statement of Reasons: P-Chloro-α,α,α-Trifluorotoluene Proposition 65 Safe Harbors.” California Environmental Protection Agency Office of Environmental Health Hazard Assessment. October 18, 2019. https://oehha.ca.gov/media/pcbtfisor101719.pdf.

CalEPA, OEHHA. 2020a. “P-Chloro-α,α,α-Trifluorotoluene Cancer Inhalation Unit Risk Factor Technical Support Document for Cancer Potency Factor.” August 2020. https://oehha.ca.gov/media/downloads/crnr/pcbtfiur080720.pdf.

CalEPA, OEHHA. 2020b. “Fact Sheet—p-Chloro-α,α,α-Trifluorotoluene (Para-Chlorobenzotrifluoride, PCBTF).” California Environmental Protection Agency Office of Environmental Health Hazard Assessment. October 2020. https://www.p65warnings.ca.gov/sites/default/files/downloads/factsheets/pcbtf_fact_sheet.pdf.

ECHA. 2022. “Substance Infocard for 4-Chloro-α-α-α-TriFlurotoluene, A REACH Registered Substance Factsheet.” European Chemicals Agency. February 7, 2022. https://echa.europa.eu/substance-information/-/substanceinfo/100.002.438.

Fluoride Action Network Project. 2023. “CTFT: P-Chloro-a,a,a Trifluorotoluene (98-56-6). Adverse Effects. Fluoride Action Network Pesticide Project.” 2023. https://www.fluoridealert.org/wp-content/pesticides/epage.ctft.effects.htm.

ITRC. 2020. “Risk Communication Toolkit.” Washington, D.C.: Interstate Technology and Regulatory Council, Risk Communication Toolkit Team. https://rct-1.itrcweb.org.

Jameson, C. W., and J. Yuan. 1992. “NTP Technical Report on the Toxicity Studies of Para-Chloro-Alpha,Alpha,Alpha Trifluorotoluene (CAS NO: 98-56-6) Administered in Corn Oil and Alpha-Cyclodextrin to F344/N Rats and B6C3F1 Mice in 14-Day Comparative Gavage Studies.” *Toxicity Report Series* 14 (July): 1-C2.

Macrí, A., C. Ricciardi, A.V. Stazi, A. Mantovani, C. Vendramin Macrí, A. Piccioni, E. Badellino, M.P. Bianchi, M. Pepe, and M. Ceccanti. 1987. “Macri, A., C. Ricciardi, A.V. Stazi et al. Subchronic Oral Toxicity of 4-Chloro-α-α-α-Trifluorotoluene in Sprague-Dawley Rats.” *Food Chem. Toxicol.* 25 (10): 781–86.

Newton, Paul E., Henry F. Bolte, Ward R. Richter, James B. Knaak, and Ladd W. Smith. 1998. “Inhalation Toxicity, Neurotoxicity, and Toxicokinetic Studies of p-Chlorobenzotrifluoride.” *Inhalation Toxicology* 10 (1): 33–48.

https://doi.org/10.1080/089583798197862.

NTP. 2018. *NTP Technical Report on the Toxicology and Carcinogenesis Studies of P-Chloro-α,α,α-Trifluorotoluene (CASRN 98-56-6) in Sprague Dawley (Hsd: Sprague Dawley® SD®) Rats and B6C3F1/N Mice (Inhalation Studies)*. National Toxicology Program.

PubChem. 2023. “P-Chlorotrifluorotoluene.” 2023. https://pubchem.ncbi.nlm.nih.gov/compound/56632242.

USDHHS, NTP. 2009. “Chemical Information Profile for 1-Chloro-4-(Trifluoromethyl)-Benzene.” June 2009. https://ntp.niehs.nih.gov/sites/default/files/ntp/noms/support_docs/pcbtf060409.pdf.

USEPA, ORD. 2007. “Provisional Peer Reviewed Toxicity Values for 4-Chlorobenzotrifluoride.” May 21, 2007. https://cfpub.epa.gov/ncea/pprtv/documents/Chlorobenzotrifluoride4.pdf.

USEPA, ORD. 2020. “National Functional Guidelines for Organic Superfund Methods Data Review.” November 2020. https://www.epa.gov/sites/default/files/2021-03/documents/nfg_for_organic_superfund_methods_data_review_november_2020.pdf.