2019 Project Abstract
For the Period Ending June 30, 2023

PROJECT TITLE: Benign Design: Environmental studies leading to sustainable pharmaceuticals
PROJECT MANAGER: William Arnold
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FUNDING SOURCE: Environment and Natural Resources Trust Fund
LEGAL CITATION: : M.L. 2019, First Special Session, Chp. 4, Art. 2, Sec. 2, Subd. 04b as extended by M.L. 2022, Chp. 94, Sec. 2, Subd. 19 (c.1) [to June 30, 2023]

APPROPRIATION AMOUNT: $415,000
AMOUNT SPENT: $415,000
AMOUNT REMAINING: $0

Sound bite of Project Outcomes and Results
This project provided insight into how fluorinated pesticides and pharmaceuticals present in Minnesota's waters degrade when exposed to sunlight was gained. Some compounds degrade to non-toxic fluoride, while others lead to fluorinated byproducts that may continue to impact the environment. The knowledge was used to help design new medically relevant fluorinated molecules.

Overall Project Outcome and Results

Many chemicals enter Minnesota's waters, and the adverse impacts of fluorinated compounds used as coatings and stain repellants have become apparent. Many other chemicals, including pesticides and pharmaceuticals, contain fluorine. When these chemicals break down in the environment, they may form persistent fluorinated products or non-toxic fluoride. The goal of this project was to evaluate how different fluorinated chemical structures degrade in sunlight and whether this information could be used to design chemicals that would limit environmental impacts. The first objective identified toxic and non-toxic fluorinated products formed during processing of pharmaceuticals in the environment or water treatment conditions. Experiments using sunlight were conducted to study the degradation of various fluorinated pharmaceuticals and pesticides that are known to be in Minnesota's waters. We identified several fluorinated byproducts using a robust analytical method that was developed. Several fluorinated groups may be harmful to the environment because they do not degrade to 'environmentally friendly' products and should be avoided in future chemical designs. The second objective was the synthesis of new fluorinated medical agents more likely to break down during water treatment or in the environment. The results indicate that degradation was successfully engineered to occur at the core of the structure, but some fluorinated groups remained intact, forming fluorinated byproducts. The third objective used computational chemistry methods to evaluate reaction rates of, and formation of products from, fluorinated pharmaceuticals and pesticides. The computations successfully predicted several experimentally observed results. Computational analysis will go together with experimental analysis to understand reactions of fluorinated compounds in water and wastewater, can assist in unknown fluorinated product identification, and can be used to help design more environmentally friendly fluorinated chemicals. The project outcomes can be used to better protect Minnesota's waters from a variety of fluorochemicals.

Project Results Use and Dissemination

The results of this work were disseminated by multiple presentations at conferences, public seminars, and discussions with stakeholders. Four journal papers were published, two more are in preparation, and student theses will be available in the University of Minnesota Digital Conservancy when they are completed. The published papers are available via the websites of William Arnold and William Pomerantz, respectively, or by request.

Environment and Natural Resources Trust Fund (ENRTF)
M.L. 2019 ENRTF Work Plan Final Report (Main Document)

Today's Date: March 9, 2023

Date of Next Status Update Report: Final Report

Date of Work Plan Approval: June 5, 2019

Project Completion Date: June 30, 2023

Does this submission include an amendment request? Yes

PROJECT TITLE: Benign Design: Environmental studies leading to sustainable pharmaceuticals

Project Manager: William Arnold

Organization: University of Minnesota

College/Department/Division: Civil, Environmental, and Geo- Engineering

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Location: Statewide

Total Project Budget: $415,000

Amount Spent: $415,000

Balance: $0

Legal Citation: M.L. 2019, First Special Session, Chp. 4, Art. 2, Sec. 2, Subd. 04b as extended by M.L. 2022, Chp. 94, Sec. 2, Subd. 19 (c.1) [to June 30, 2023]

Appropriation Language: $415,000 the first year is from the trust fund to the Board of Regents of the University of Minnesota to determine how to best remove harmful fluorinated pharmaceuticals during wastewater treatment and to develop alternate versions of these compounds that are medically useful but environmentally harmless. This appropriation is subject to Minnesota Statutes, section 116P.10.

M.L. 2022 - Sec. 2. ENVIRONMENT AND NATURAL RESOURCES TRUST FUND; EXTENSIONS. [to June 30, 2023]

I. PROJECT STATEMENT:

Many pharmaceuticals contain fluorine in their chemical structures. *There is limited information about how fluorine-containing pharmaceuticals are degraded during wastewater treatment or in the environment, and even less about the products that form.* This is important because one potential breakdown product is the **highly toxic** fluoroacetate while another is the non-toxic fluoride (which is in toothpaste). We need to understand which wastewater treatment and natural processes lead to toxic versus non-toxic breakdown products. Data will be needed for systems such as oxidation ponds in outstate Minnesota as well as in the wastewater treatment plants used in cities. *The objective of this proposal, therefore, is to gain the knowledge necessary to understand both how to best remove fluorinated pharmaceuticals from water and to allow the development of "benign by design" fluorinated chemicals.* Specific goals are to:

- Measure reaction rates and products of fluorinated pharmaceuticals when they are exposed to sunlight,
- Measure reaction rates and products of fluorinated pharmaceuticals in advanced treatment systems,
- Develop environmentally benign fluorinated magnetic resonance imaging (MRI) agents,
- Establish computational tools to predict the reactivity of fluorinated pharmaceuticals, and
- Disseminate the findings to water utilities and the MN Department of Health

There are fewer than 10 natural chemicals that contain fluorine. Because natural fluorinated organic compounds are few, the environmental pathways for processing synthetic fluorinated chemicals may not be as robust as those for other potential water pollutants. The presence of fluorinated chemicals in Minnesota's waters has received substantial attention. These compounds, however, are only a small subset of fluorochemicals used. In particular, a broad range of pharmaceuticals, including antibiotics, steroids, antidepressants, imaging agents, and statins contain fluorine. This could lead to accumulation of specific pharmaceuticals and their fluorinated degradation products in Minnesota's environment. Overall, we lack specific knowledge of
1) the **reaction intermediates and end products of synthetic fluorinated pharmaceuticals** in natural and engineered aquatic environments,
2) the level and type of fluorine incorporation that **maximizes utility and minimizes environmental impact of pharmaceuticals**, and
3) means to **predict the reactivity** and reaction pathways of fluorine-containing species under a variety of conditions.

Modern society requires effective pharmaceuticals, pesticides, and commercial/industrial compounds. The release of such chemicals into the environment is either necessary or inevitable, and having a sustainable society dictates that these chemicals be readily degradable after their desired function is achieved and that any degradation products are benign. This research project will provide critical knowledge that will lead to better wastewater treatment, prevent the accumulation of unanticipated and potentially toxic byproducts in the environment, guide the design of future pharmaceutical compounds, and protect Minnesota's water resources as well as human and environmental health.

II. OVERALL PROJECT STATUS UPDATES:

First Update January 15, 2020

Common pharmaceuticals that contain fluorine in the chemical structure were purchased. Photolysis rates of fluoxetine were found under various conditions, including pH 7, pH 10, addition of 0.5 mM sulfite, and 250 μM hydrogen peroxide. Dark controls were conducted to determine the effects of hydrolysis. Lansoprazole, another common pharmaceutical was studied under the same varying conditions, and the rate constants were found.

The rate constants for voriconazole were also found. Photolysis rates of 2-fluorophenol, 3-fluorophenol, 4-fluorophenol, 2-trifluoromethylphenol, 3-trifluoromethylphenol, and 4-trifluoromethylphenol were found at various pH values to look further into the photolysis of aromatic fluorine motifs. An NMR method was developed in and quantify the parent compound as well as any products that may form during photolysis. High resolution mass spectrometry methods were tested to determine any other major products that the NMR cannot detect.

Amendment Request: We previously budgeted for a graduate student to support synthesis of novel fluorinated materials as ^{19}F MRI agents and analysis of their environmental degradation products. The graduate student supported by this project is expected to be unable to continue his research efforts as of 06/01/2020. To continue progress, Dr. Anil Pandey has been identified as a postdoctoral researcher who has extensive experience in synthesizing fluorinated amino acids and fluorinated peptides and with fluorine NMR. We are requesting to rebudget $36,500 from graduate student salary and fringe benefits to postdoctoral salary and fringe benefits (a new personnel category) so Dr. Pandey can work on the project. Amendment Approved by LCCMR **2/7/2020**

Second Update September 1, 2020

Experiments have continued with a series of fluorinated pharmaceuticals and model compounds (fluorinated phenols and trifluoromethyl phenols). The NMR method was used to quantify the abundance of fluorine-containing reaction products, and mass balances were generally good. Fluoride is the major product observed under most conditions, particularly those generating hydroxyl radical and hydrated electrons, but organic products are also observed. Fluorine directly attached to an aromatic ring produces fluoride, and other fluorine motifs lead to some organic products. Work to identify the products is ongoing. The degradation results have provided guidance as to which MRI agents might be more degradable, with a new polyfluoroaromatic compound showing promise. Computational efforts have focused on predicting reactivity under oxidative conditions and predicting NMR spectra of potential reaction products.

Third Update March 1, 2021

Experiments have continued with three more model fluorinated organic compounds. Fluoride is the major product observed with some organo-fluorinated byproducts in advanced treatment systems with sulfite. A more robust NMR technique is being developed with changes in the internal standard compound. Sunlight photolysis with Celecoxib and Vornicazole has been started under advanced treatment conditions. Several additional fluorinated molecules have been synthesized and characterized to compare to our lead fluorinated temperature sensor. We have now also identified our lead fluorinated peptide for ^{19}F MRI and have optimized conditions to attach the peptide to a biological targeting agent for diagnostic imaging. Biological compatibility is now being investigated. If successful, this will be a second lead molecule for degradation studies.

Fourth Update September 1, 2021

During this phase of research, a more robust NMR method was developed for more reproducible and quantitative measurements. Photolysis experiments were continued with the herbicides sulfoxaflor and penoxsulam and the pharmaceutical voriconazole. Photolysis was conducted using both a mercury vapor lamp and a solar simulator under advanced treatment conditions with hydrogen peroxide, activated persulfate, and sulfite to mimic both engineered and natural aquatic systems. In the case of the herbicide sulfoxaflor, fluoride was not the major product at the end of photolysis. NMR spectra shifts showed that all byproduct structures were close to the parent compound structure in all photolysis matrices. Penoxsulam and voriconazole were photolyzed faster than sulfoxaflor and fluoride was a major product at the end of photolysis in addition to yet to be identified byproducts. Voriconazole is fluorinated on two aryl rings. We found the pyrimidine ring fluorine in voriconazole was more stable than the other aryl fluorines. To identify additional byproducts, we have commenced LC-MS and MS/MS fragmentation data collection. A final investigation has begun on a novel experimental fluorinated molecule for ^{19}F MRI. Solubility studies have identified a suitable organic co-solvent for analysis. An HPLC method is being developed to quantify the molecule along with previously discussed ^{19}F NMR

methods. Using UV visible spectroscopy the maximum absorbance of the molecule was found to be at 285 nm indicating that photolysis may be a possible route of degradation.

Amendment Request: Because of disruptions caused by the COVID-19 pandemic, we are requesting a one year extension of the project. The restrictions on laboratory work and limitations to laboratory facilities (NMR and mass spectrometry) on campus for analyses for extended periods has slowed progress on the experimental aspects of Activities 1 and 2. This, in turn, has led to a lack of data to drive the computations of Activity 3. The extension will allow full completion of the tasks now that normal operations of laboratories has largely resume. **Amendment pending further LCCMR and legislative action as of 10/6/21**

We are also requesting that $12,500 of the funds designated for analytical time be re-categorized as maintenance. These will still be used for costs related to analyzing samples on mass spectrometers for product identification, but we are able to now do this on an instrument we purchased that resides in our laboratory. Rather than pay service fees for use of an instrument in a central facility, we now need these funds to operate our own instrument. This does not change how the funds are used or the project scope but changes how they are categorized in the UMN accounting system, and such changes require an amendment request to be submitted. The maintenance costs are allocated based on instrument usage. **Amendment Approved by LCCMR 10/6/2021**.

Fifth Update March 1, 2022
Photolysis experiments were conducted on the pharmaceuticals florfenicol, ciprofloxacin, and enrofloxacin. Photolysis was conducted using a mercury vapor lamp under advanced treatment conditions with hydrogen peroxide and sulfite. Fluoride was found to be the major product for florfenicol under all conditions. The photolysis of the herbicides penoxsulam, florasulam, fluroxypyr, and the insecticide sulfoxaflor was completed with the mercury vapor lamp and a solar simulator. Heteroaromatic CF_3 and aliphatic CF_2 groups are stable and retained in most of the products while benzylic fluorine groups, and aryl fluorine groups are converted to fluoride and trifluoroacetic acid. Additionally, river water photolysis was performed on all agrochemicals and the role of reactive species from the dissolved organic matter was assessed. Based on the observation that aryl fluorine groups are more readily photolyzed under environmental conditions, a new fluorinated MRI-agent has been designed containing such groups. The long term goal, is to use such an fluorinated MRI agent for in vivo thermometry on patients. Two journal articles were published.

Amendment Request: We are requesting minor budget modifications. Our laboratory supplies were overspent, we realized that we re-categorized too much money to maintenance, and we will not need all of the travel funds allocated. It was also recognized that supporting an additional graduate student for summer 2022 will be helpful in completing project goals. Thus, we request that 1) $8,500 be moved from maintenance to personnel, specifically a graduate student researcher and 2) that $3,000 of travel funds and $2,000 of mass spectrometry time be moved to laboratory supplies. **Amendment Approved by LCCMR 4/18/2022**.

Update as of June 30, 2022:

Project extended to June 30, 2023 by LCCMR 6/30/22 as a result of M.L. 2022, Chp.94, Sec. 2, Subd. 19, legislative extension criteria being met.

Sixth Update as of September 1, 2022:
Photolysis experiments are being conducted on the pharmaceuticals florfenicol, flecainide, enrofloxacin, and pesticide saflufenacil. Photolysis is being conducted using a solar simulator and a mercury vapor lamp under advanced treatment conditions with hydrogen peroxide and sulfite. Fluoride was found to be the major fluorinated product for florfenicol and enrofloxacin under all conditions. Experiments on flecainide are currently being conducted. Three fluorinated molecules being used to develop magnetic resonance imaging (MRI) agents are being studied to determine their environmental stability using a mercury vapor lamp and solar simulator.

These molecules were redesigned based on preliminary findings in our studies that show aromatic fluorine groups are susceptible to favorable degradation pathways. All compounds were found to degrade under all conditions with fluoride being created. Preliminary computational results indicate that ^{19}F-NMR shift can be predicted with accuracy for parent and product structures.

Seventh Update as of March 1, 2023:
Photolysis experiments were conducted using a solar simulator on flecainide, enrofloxacin, and voriconazole under advanced treatment conditions with hydrogen peroxide and sulfite. Florfenicol was not subjected to solar simulator studies due to slow degradation rates. Fluoride was found to be the major photoproduct for voriconazole and enrofloxacin with modified parent compounds also detected at lower concentrations. Flecainide photolysis resulted in modified forms of the parent compound due to the stable aliphatic trifluoromethyl groups. Photolysis experiments were conducted with UV-Light Emitting Diodes (LEDs) at different wavelengths to understand wavelength dependence of fluorinated product formation. Eight different fluorinated compounds with different fluorinated functional groups were chosen. It was found that heteroaromatic-CF_3 and benzylic CF_3 have the largest wavelength dependence with observed variations in products and product quantities. The paper describing these results has been submitted. Computations of NMR shifts for 20 different fluorinated compounds were performed and fit linearly with their experimental NMR shifts. The computational calculations of NMR shifts for experimentally observed products is underway. Enthalpies of bond breaking in different CF_3 motifs were computed to explain trends that were experimentally observed. The environmental degradation studies of three fluorine-based magnetic resonance imaging (MRI) agents, have now been completed, and the results submitted for publication in the *Journal of Analytical Chemistry*. Combined, the findings to date have identified organofluorine motifs that are more susceptible to degradation, the processes that do and do not degrade fluorinated motifs, and ways to better incorporate fluorine into molecules that have utility (i.e., use as an MRI agent) while limiting their environmental persistence.

Overall Project Outcomes and Results as of June 30, 2023 (to be submitted before August 15, 2023):

Many chemicals enter Minnesota's waters, and the adverse impacts of fluorinated compounds used as coatings and stain repellants have become apparent. Many other chemicals, including pesticides and pharmaceuticals, contain fluorine. When these chemicals break down in the environment, they may form persistent fluorinated products or non-toxic fluoride. The goal of this project was to evaluate how different fluorinated chemical structures degrade in sunlight and whether this information could be used to design chemicals that would limit environmental impacts. The first objective identified toxic and non-toxic fluorinated products formed during processing of pharmaceuticals in the environment or water treatment conditions. Experiments using sunlight were conducted to study the degradation of various fluorinated pharmaceuticals and pesticides that are known to be in Minnesota's waters. We identified several fluorinated byproducts using a robust analytical method that was developed. Several fluorinated groups may be harmful to the environment because they do not degrade to 'environmentally friendly' products and should be avoided in future chemical designs. The second objective was the synthesis of new fluorinated medical agents more likely to break down during water treatment or in the environment. The results indicate that degradation was successfully engineered to occur at the core of the structure, but some fluorinated groups remained intact, forming fluorinated byproducts. The third objective used computational chemistry methods to evaluate reaction rates of, and formation of products from, fluorinated pharmaceuticals and pesticides. The computations successfully predicted several experimentally observed results. Computational analysis will go together with experimental analysis to understand reactions of fluorinated compounds in water and wastewater, can assist in unknown fluorinated product identification, and can be used to help design more environmentally friendly fluorinated chemicals. The project outcomes can be used to better protect Minnesota's waters from a variety of fluorochemicals.

Amendment Request: We are requesting minor budget modifications so that the final budget matches final expenditures. Our laboratory supplies and personnel each were overspent, and this allowed us to complete our project goals. The full amounts of maintenance and publications funds were ultimately not used, and there were a few hundred dollars left in the analytical time and travel lines. Thus, we request that a total of $9,406 be moverd from analytical time, maintenance, trael, and publication charges to personnel ($4,597) and laboratory supplies ($4,809). The revised budget sheet shows these changes and a zero balance.

III. PROJECT ACTIVITIES AND OUTCOMES:

ACTIVITY 1 Title: ***Identify toxic and non-toxic fluorinated products formed during wastewater treatment and environmental processing of pharmaceuticals***

Description: The rate at which fluorinated pharmaceuticals are degraded in wastewater oxidation ponds and rivers/lakes via photolysis and in advanced treatment systems for wastewater treatment will be measured as well as the fluorinated reaction products. The hypothesis to be tested is that fluorinated pharmaceuticals and imaging agents break down into fluorinated intermediate and product structures with the potential for environmental persistence and toxicity.

ACTIVITY 1 ENRTF BUDGET: $ 144,000

Outcome	Completion Date
1. Reaction rates of fluorinated pharmaceuticals wastewater and river water in sunlight	January 30, 2022
2. Reaction rates of fluorinated pharmaceuticals under advanced treatment conditions	October 31, 2022
3. Reaction product identification	January 30, 2023

First Update March 1, 2020
A robust NMR method was developed to accurately analyze and quantify parent compounds and the fluorine containing products that are formed. Photolysis rates of fluoxetine, lansoprazole, and voriconazole were measured under varying aqueous conditions. Conditions including varying pH, as well as the use of sulfite and hydrogen peroxide to simulate advanced treatment conditions Photolysis rates of ortho- para- and meta-fluorophenol as well as ortho- para- and meta-trifluoromethylphenol were found under basic, neutral, and acidic conditions to further study the aromatic fluorine motif and what fluorinated products are formed.

Second Update September 1, 2020
Work has continued with the selected pharmaceuticals and model compounds under various treatment conditions. Results have shown that simple model compounds (fluorophenols and trifluoromethyl phenols) predominantly form fluoride upon photolysis, but the trifluoromethyl phenols do form some organic fluorinated products. The more complicated pharmaceutical molecules form a variety of products. An important finding is that fluorine attached to an aromatic ring appears to be converted to fluoride. It will be necessary to test how many fluorines can be on the ring for this to hold. This information provided guidance for Activity 2. Preliminary reaction product identification with mass spectrometry was performed. Activities were limited from March – June were limited by the COVID-19 laboratory shutdown.

Third Update March 1, 2021
Photolysis work has continued with three more model compounds, specifically 2,5 difluorophenol, 3,5 difluorophenol and 2-trifluoromethyl anisole. The results have shown that most experimental conditions predominantly form fluoride. Addition of sulfite resulted in some organo-fluorinated byproducts. Photolysis rates were found for these model compounds for different pH conditions including advanced treatment conditions. The work on development of a more robust NMR technique with internal standard mixed in with the

analyte has started. Work on sunlight photolysis of the fluorinated pharmaceuticals celecoxib and vornicazole using the solar simulator under advanced treatment conditions has been started. Progress overall has been slower than expected due to effects and restrictions of the COVID-19 pandemic.

Fourth Update September 1, 2021
A more robust NMR analysis method was developed by recalculating the concentrations of internal standard hexafluorobenzene (HFB) after every NMR run. The overall mass balances were found to agree better than the previous method. Photolysis experiments were conducted with herbicides sulfoxaflor and penoxsulam, and the pharmaceutical voriconazole was also studied. Photolysis was conducted using a mercury vapor lamp and a solar simulator under advanced treatment conditions with hydrogen peroxide, activated persulfate, and sulfite. It was found that the fluoride is not the major product at the end of photolysis for the herbicide sulfoxaflor. NMR spectra shifts showed that all byproduct structures were close to the parent compound structure in all photolysis matrices. Penoxsulam and voriconazole undergo faster photolysis than sulfoxaflor, and fluoride is a major product at the end of penoxsulam and voriconazole photolysis along with yet to be identified byproducts. In voriconazole, an differential stability of aryl fluorine groups was identified. In this case, the pyrimidine ring aryl fluorine was more stable than the other aryl fluorines. LC-MS and MS/MS fragmentation data collection has been started to identify the stable byproducts.

Fifth Update March 1, 2022
Photolysis experiments were conducted on the pharmaceuticals florfenicol, ciprofloxacin, and enrofloxacin. Photolysis was conducted using a mercury vapor lamp under advanced treatment conditions with hydrogen peroxide and sulfite. Fluoride was found to be the major product for florfenicol under all conditions. Ciprofloxacin and enrofloxacin produced byproducts that are yet to be identified and their parent compounds degrade at a faster rate compared to florfenicol. The photolysis of the herbicides penoxsulam, florasulam, fluroxypyr, and the insecticide sulfoxaflor was completed with Hg Vapor and solar simulator lamps. Heteroaromatic CF_3 and aliphatic CF_2 groups are stable and retained in most of the products while benzylic fluorine groups are converted to fluoride and trifluoroacetic acid. Additionally, river water photolysis was performed on all agrochemicals and the role of reactive species from the dissolved organic matter was assessed. Mass spectrometry data collection has been completed for all agrochemicals.

Update as of June 30, 2022:

Project extended to June 30, 2023 by LCCMR 6/30/22 as a result of M.L. 2022, Chp.94, Sec. 2, Subd. 19, legislative extension criteria being met.

Sixth Update as of September 1, 2022:
Photolysis experiments are conducted on the pharmaceuticals florfenicol, flecainide, enrofloxacin, and pesticide saflufenacil. Photolysis is being conducted using a solar simulator and a mercury vapor lamp under advanced treatment conditions with hydrogen peroxide and sulfite. Fluoride was found to be the major fluorinated product for florfenicol and enrofloxacin under all conditions. Experiments on flecainide are currently being conducted. Fluoride is being found to be the major fluorinated photo product for all pharmaceuticals with other products being detected at lower concentrations. Results with saflufenacil back the observations that heterocyclic CF_3 forms stable products while Aryl-F is defluorinated.

Seventh Update as of March 1, 2023:
Photolysis experiments were conducted with UV-Light Emitting Diodes (LEDs) at different wavelengths to understand wavelength dependence of fluorinated product formation. Eight different fluorinated compounds with different fluorinated functional groups were chosen. It was found that heteroaromatic-CF_3 and benzylic CF_3 have the largest wavelength dependence with observed variations in products and product quantities.

Photolysis experiments were conducted using a solar simulator on enrofloxacin, voriconazole, and flecainide under advanced treatment conditions with hydrogen peroxide and sulfite. It was found that fluoride is the major product formed for enrofloxacin and voriconazole, with modified forms of the parent compounds found at low concentrations. Flecainide photolysis resulted with no fluoride production, and only modified parent compound products. This is due to the aliphatic trifluoromethyl groups which have previously been shown to be highly stable. This indicates this functional group should be avoided when designing molecules.

Final Report Summary as of June 30, 2023 (to be submitted before August 15, 2023):
Photolysis experiments were conducted for several model compounds including fluorophenols and trifluoromethyl phenols, pharmaceuticals (fluoxetine, sitagliptin, voriconazole, favipiravir, florfenicol, flecainide, and enrofloxacin), pesticides (penoxsulam, sulfoxaflor, florasulam, fluroxypyr, and 3-trifluoromethyl-4-nitrophenol (TFM)). Photolysis experiments were conducted using a mercury vapor lamp, solar simulator, and single wavelength LEDs to understand product formation under various conditions. A robust NMR method was developed for quantifying total fluorine in photolyzed solutions. The method can be used in future studies to identify fluorinated products and obtain accurate mass balances of fluorine. Overall, the use of integrated analyses using HPLC, ^{19}F-NMR, and untargeted, high resolution liquid chromatography–mass spectrometry methods allow for identification of all fluorinated reaction products including small modifications of the parent compound, quantification of these products, and assessment of the possible reaction pathways that lead to these byproducts. Several photolysis experiments and analyses using NMR indicate that heteroaromatic CF_3 groups are stable and retained in most of the products while benzylic-CF_3 groups are converted to fluoride and trifluoroacetic acid as the major degradation fluorinated products. Additionally, aryl- and heteroaromatic-F groups are converted fluoride as the major fluorinated product. It was observed that florfenicol's aliphatic CF group was converted completely to fluoride while flecainide's aliphatic CF_3 groups were stable and form byproducts that all retain the parent fluorine motif. These results show that heteroaromatic-CF_3 and aliphatic-CF_3 fluorines are resistant to photolysis in water and should be avoided when designing new molecules especially if the products retain any biological activity. Results with narrow-bandwidth LEDs showed a lesser number of fluorinated products as compared to the conventionally used mercury vapor or xenon lamps previously used to simulate sunlight, suggesting LEDs may be a means to limit the number of products formed in water treatment systems. A careful selection of wavelengths would be needed to minimize persistent products and accelerate defluorination. Results of this work will also assist in using UV-LEDs for water treatment, selecting the most efficient wavelengths, and informing future design of fluorinated compounds.

ACTIVITY 2 Title: ***Synthesis of new polyfluorinated MRI agents that breakdown during wastewater treatment or in the environment***

Description: Potential new MRI reagents with superior sensitivity and minimal environmental persistence will be synthesized. All synthesized compounds will be tested under the reaction conditions of Activity 1. Current clinical trials are using perfluorochemicals which will be environmentally persistent, and our work will provide critical knowledge about how to make fluorinated structures that are medical useful yet environmentally benign.

ACTIVITY 2 ENRTF BUDGET: $ 128,000

Outcome	Completion Date
1. Development of environmentally friendly MRI reagents	December 31, 2022
2. Evaluation of sunlight and advanced treatment of MRI reagents	June 30, 2023

First Update January 15, 2020
Perfluoro-15-crown-5-ether was purchased, and an NMR method has been developed to quantify the compound as it degrades. Preliminary work on synthesizing new MRI regents has begun.

Second Update September 1, 2020

Several new ^{19}F MRI agents have been synthetized and magnetic resonance properties characterized. Significant effort has been placed on the synthesis of novel fluorochemicals for sensitive in vivo thermometry applications. In this activity, seven new fluorochemicals have been synthesized and characterized for their thermoresponsive behavior and compared to theoretical predictions. We have now identified a lead molecule that is two-fold more responsive (0.02 ppm / °C) than the proton-resonance frequency, the gold standard for temperature calibration. Importantly, this new molecule is based on a perfluoroaromatic scaffold. Based on our preliminary environmental simulations using fluorinated aromatic model systems, we predict these fluoroaromatic groups, will be more easily degraded, primarily through the elimination of fluoride ions. We have developed nanoparticle materials that can suspend these fluorinated molecules in aqueous solution, and will begin investigating their stability under sunlight and advanced treatment conditions. In parallel, several fluorinated peptides are being developed for ^{19}F MRI applications; however, a lead has yet to be identified for evaluating their environmental degradation behavior.

Third Update March 1, 2021

Several additional fluorinated molecules have synthesized and characterized to compare to our lead fluorinated temperature sensor with sensitivity of (0.02 ppm / °C) for ^{19}F MRI temperature sensing. Our prior sensor remains the leading candidate molecule. An initial report is currently being written to communicate our findings in the *Journal of Fluorine Chemistry*. Theoretical and experimental studies have continued to aid in our understanding of the origins of the sensitivity. Such an understanding will lead to further improvements in magnetic resonance properties, as we prepare for degradation studies. We anticipate the fluoroaromatic groups will be more readily degraded based on Activity 1 studies. We have now also identified our lead fluorinated peptide for ^{19}F MRI and have optimized conditions to attach the peptide to a biological targeting agent for diagnostic imaging. Biological compatibility is now being investigated. If successful this will be a second lead molecule for degradation studies.

Fourth Update September 1, 2021

A new experimental fluorinated molecule containing eight aryl fluorines and 34 aliphatic fluorines has been subjected to solubility studies and compared via UV-Vis with a maximum absorbance found at 285 nm. An advanced draft describing the magnetic resonance behavior for MRI-based thermometry, and is anticipated to be communicated within the next two months. The MRI agent was found to be soluble in chloroform, and is approximately 10x less soluble in acetonitrile and methanol, and insoluble in water. Methods to quantify the molecule have been explored via HPLC and data is still being collected. Direct photolysis of the molecule under varying conditions in an acetonitrile and buffer solution is also being investigated, and will be quantified via ^{19}F NMR and HPLC. Advanced oxidation studies will be conducted using sulfite and hydrogen peroxide in a stirred buffer solution.

Fifth Update March 1, 2022

Based on the observation that aryl fluorine groups are more readily photolyzed under environmental conditions, a new fluorinated MRI-agent has been designed containing such groups. The long term goal, is to use such a fluorinated MRI agent for in vivo thermometry on patients. While our original designs were described in prior updates, we have now published this report this year (Lee et al. Analytical Chemistry, *in press*). These new fluorinated molecules improve upon the state of the art, and are envisioned to be more environmentally compatible. We now hope to continue to study their environmental stability as well as new analogs informed from this study.

Update as of June 30, 2022:

Project extended to June 30, 2023 by LCCMR 6/30/22 as a result of M.L. 2022, Chp.94, Sec. 2, Subd. 19, legislative extension criteria being met.

Sixth Update as of September 1, 2022:
Our recent manuscript on fluorinated MRI agents for thermometry has been published. (Lee et al. Analytical Chemistry, 2022). However, despite the significant number of arylfluorine groups for degradation, this molecule possesses a long fluorinated tail containing seven carbon atoms. Due to concerns of environmental persistence, this has been redesigned to contain only two, two carbon atom chains in the tail with fluorine to reduce the environmental persistence concern but maintain MRI performance. Three fluorinated MRI agents based on these designs are now being studied to determine their environmental stability using a mercury vapor lamp and solar simulator. All compounds were found to degrade under environmentally relevant conditions with the production of fluoride and other fluorinated compounds at low concentrations. Advanced oxidation experiments using a mercury vapor lamp and quantum yield experiments using a solar simulator are being conducted.

Seventh Update as of March 1, 2023:

We have now completed our degradation studies of our fluorinated MRI agents under environmentally relevant conditions as well as advanced oxidation experiments for simulations of waste water treatment conditions. We concluded from these studies that our new molecular designs provide a mechanisms for facile degradation, while maintaining high magnetic resonance performance for future biomedical applications. These results have been submitted to the *Journal of Analytical Chemistry* for disseminating our research findings.

Final Report Summary as of June 30, 2023 (to be submitted before August 15, 2023):

We have now completed our studies on the degradation of fluorinated model compounds demonstrating a facile fluoride degradation pathway for fluorinated aryl groups. We have used this information to design new ^{19}F MRI-based thermometry agents, which have both improved performance over state of the art perfluorocarbons, while being more readily degraded. We have published this work, in two reports (Lee et al. *Journal of Analytical Chemistry* **2022** and Li et al. *Journal of Analytical Chemistry* **2023**). In the latter study, studies conducted under environmentally relevant photolysis conditions and using ozonation to represent advance drinking water treatment conditions were conducted on our fluorinated thermometry agents. Analysis using ^{19}F-NMR indicated that degradation occurred at the aromatic cores of the molecules resulting in the production of vinyl fluorine groups and fluoride via the aryl fluorines. Following degradation, the aliphatic CF_3 and CF_2 motifs remained stable and unchanged resulting in the formation of varying fluorinated degradation products, consistent with results of the pharmaceutical and pesticide studies. These results highlight how environmental degradation studies have informed on an improved design for biomedical applications and also demonstrate directions for future work to maximize defluorination.

ACTIVITY 3 Title: ***Assess the parameters that dictate reaction rates and products of pharmaceuticals containing fluorine***

Description: While it is known that many fluorinated compounds are unreactive, a better understanding of how reactions of fluorinated pharmaceuticals occur under a variety of conditions is needed. We will develop computational methods to predict how fluorinated compounds breakdown under water treatment conditions and in sunlight. The theoretical results will be tested during the experiments performed in Activities 1 and 2. This will facilitate prediction of which compounds may accumulate in the environment and which are likely to be degraded.

ACTIVITY 3 ENRTF BUDGET: $ 143,000

Outcome	Completion Date

1. Modeling of reactive states/energies of reactions	October 31, 2022
2. Development of tools to predict reactivity of fluorinated pharmaceuticals	June 30, 2023

First Update January 15, 2020
Work on this activity is not yet underway

Second Update September 1, 2020
The computation oxidation potentials of model compounds and pharmaceuticals is underway. A critical component of these calculations is assessment of how the presence of fluorine in the structure affects the computed values, which should give insight into reactivity when an electron is extracted from the molecule. Computations are also being used to predict NMR spectra of potential products, so that we can hypothesize the identities of the product peaks seen in spectra in Activity 1.

Third Update March 1, 2021
Computations as described above are continuing.

Fourth Update September 1, 2021
Protocols for computation of oxidation potentials and NMR spectra have been finalized. Computations are on hold as more experimental data is generated.

Fifth Update March 1, 2022
Work on this task was minimal in the past period, but computations to help identify products observed in NMR spectra will resume soon.

Update as of June 30, 2022:

Project extended to June 30, 2023 by LCCMR 6/30/22 as a result of M.L. 2022, Chp.94, Sec. 2, Subd. 19, legislative extension criteria being met.

Sixth Update as of September 1, 2022:
Computations on pesticides penoxsulam, florasulam, sulfoxaflor, fluroxypyr, sulflufenacil and pharmaceuticals fluoxetine have started. The one electron oxidation potential is being calculated for all the fluorinated compounds. Predictions of ^{19}F-NMR spectra for parent and experimentally determined products are being performed. The preliminary results indicate that computations are able to determine parent shifts with good accuracy and product shifts are being used to observe shifts in spectra with respect to different changes in structures.

Seventh Update as of March 1, 2023:
Computations of NMR shifts for 20 different fluorinated compounds were performed and fit linearly with their experimental NMR shifts. The computational calculations of NMR shifts for experimentally observed products is underway, this will be done to elucidate accurate structures using a combination of computations, NMR, and LC-HRMS. Enthalpies of heterolytic bond breaking in different CF_3 motifs were computed to explain trends that were experimentally observed. So far, computations show promise for explaining NMR shifts and some experimental results.

Final Report Summary as of June 30, 2023 (to be submitted before August 15, 2023):
Computational NMR shifts for 20 different fluorinated compounds were calculated and it was found that they fit linearly with their experimental NMR shifts. Computational shifts for the products identified in activity 1 were also calculated and compared to the experimental values observed. More experimentation on separation of products is underway to identify NMR shifts of individual products and compute their shifts by DFT to confirm that computations can predict products. Enthalpies for heterolytic bond cleavage of C-F bond for benzylic and

heteroaromatic-CF_3 groups were performed computationally using density functional theory and it showed that the enthalpies are consistently higher for heteroaromatic-CF_3 groups which agrees with the experimental observations from activity 1 that these motifs are stable and do not defluorinate. Currently, we are computationally studying the effect of electron densities on experimentally observed defluorination. Overall, computations are a helpful tool to predict NMR shifts of fluorinated compounds and their degradation products. Such computations will help in product identification to go hand in hand with experimental analysis. Because our computations agree with experimental results, the computational method can be used to study new compounds as and when they are designed.

IV. DISSEMINATION:

Description: Results will be disseminated by publication in peer-reviewed journals, presentations and conferences, and via a final report. Funds are requested to make journal articles open access. Data sets will be archived in the Data Repository for the University of Minnesota (https://conservancy.umn.edu/handle/11299/166578), a publically available collection of research data. ENTRF support will be acknowledged on all disseminated materials.

The Minnesota Environment and Natural Resources Trust Fund (ENRTF) will be acknowledged through use of the trust fund logo or attribution language on project print and electronic media, publications, signage, and other communications per the ENRTF Acknowledgement Guidelines.

First Update January 15, 2020
Nothing to report.

Second Update September 1, 2020
Planned conference presentations were cancelled due to the COVID-19 pandemic.

Third Update March 1, 2021
A manuscript is in preparation describing a new molecule, and photolysis results to date will be presented at the American Chemical Society National Meeting (virtual) in April.

Fourth Update September 1, 2021

An advanced draft of a manuscript describing the ^{19}F MRI agent has been prepared and will be communicated soon. "Development of a Highly Responsive Organofluorine Temperature Sensor for ^{19}F Magnetic Resonance Applications" Amani L. Lee, Anil Pandey, Sina Chiniforoush, Mukunda Mandal, Christopher J. Cramer, Christy L. Haynes, and William C.K. Pomerantz* *manuscript in preparation.*

Results of the photolysis studies were presented at the spring national meeting of the American Chemical Society: Whiting, Q.T., Bhat, A., Mundhenke, T., Pomerantz, W.C., Arnold, W.A. 2021. Fluorinated photoproduct formation from photolysis of pharmaceuticals and agrochemicals. American Chemical Society National Meeting (virtual), April 2021.

Quinn Whiting's MS Thesis was completed and will be available in the UMN Digital Conservancy.

Fifth Update March 1, 2022
A manuscript titled "Tracking Fluorine during Aqueous Photolysis and Advanced UV Treatment of Fluorinated Phenols and Pharmaceuticals Using a Combined ^{19}F-NMR, Chromatography, and Mass Spectrometry Approach" Akash P. Bhat, Thomas F. Mundhenke, Quinn T. Whiting, Alicia A. Peterson, William C.K. Pomerantz, and William A. Arnold* was published in **ACS Environmental Au and is available open access:** https://doi.org/10.1021/acsenvironau.1c00057

A second manuscript titled “Development of a Highly Responsive Organofluorine Temperature Sensor for ^{19}F Magnetic Resonance Applications” A. L. Lee, A. Pandey, J. Li, S. Chiniforoush, M. Mandal, J. Li, C. J. Cramer, C. L. Haynes, and W.C.K. Pomerantz* was published in **Analytical Chemistry**. (https://doi.org/10.1021/acs.analchem.1c04248)

Two talks will be presented at the national meeting of the American Chemical Society in March.

Update as of June 30, 2022:

Project extended to June 30, 2023 by LCCMR 6/30/22 as a result of M.L. 2022, Chp.94, Sec. 2, Subd. 19, legislative extension criteria being met.

Sixth Update as of September 1, 2022:

The results of the studies were presented in meetings as follows:
Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) “Degradation of fluorinated agrochemicals using photolysis-based processes and understanding the effect of fluorine motifs in the structures” *AEESP Research and Education Conference St. Louis.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) “Degradation of fluorinated pesticides using photolysis-based processes and understanding the effect of fluorine motifs in the structures” *Gordon Research Conferences: Environmental Sciences: Water at Holderness School.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) “Understanding fluorinated byproduct formation during direct and advanced-treatment based photolysis of fluorinated herbicides using ^{19}F-NMR” *American Chemical Society (ACS) National Meeting and Exposition Spring 2022 San Diego USA.*

Mundhenke T. M., Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) “Photoproduct formation, determination, and quantification of the photolysis of fluorinated pharmaceuticals” *American Chemical Society (ACS) National Meeting and Exposition Spring 2022 San Diego USA.*

A manuscript titled "Finding Fluorine: Photoproduct Formation during the Photolysis of Fluorinated Pesticides." Bhat A. P., Pomerantz W. C. K., and Arnold W. A.* was published in **Environmental Science & Technology. (**https://doi.org/10.1021/acs.est.2c04242)

Seventh Update as of March 1, 2023:

A manuscript titled "Wavelength-dependent UV-LED photolysis of fluorinated pesticides and pharmaceuticals." Bhat A. P., Pomerantz W. C. K., and Arnold W. A.* was submitted for consideration for publication in **Environmental Science & Technology.**

A second manuscript, “Fluorous Liquids for Magnetic Resonance-based Thermometry with Enhanced Responsiveness and Environmental Degradation” J. Li, T. F. Mundhenke, T. G. Smith, W. A. Arnold, W. C.K. Pomerantz*, was submitted for consideration for publication in the **Journal of Analytical Chemistry**.

Both papers have undergone the first round of peer review and revised papers will be submitted shortly.

Final Report Summary as of June 30, 2023 (to be submitted before August 15, 2023):

The results of this work were disseminated by multiple presentations at conferences, public seminars, and discussions with stakeholders. Four journal papers were published, two more are in preparation, and student

theses will be available in the University of Minnesota Digital Conservancy when they are completed. The published papers are available via the websites of William Arnold and William Pomerantz, respectively, or by request.

Manuscripts published:

Bhat, A. P., Mundhenke, T. F., Whiting, Q. T., Peterson, A. A., Pomerantz, W. C., & Arnold, W. A. (2022). Tracking fluorine during aqueous photolysis and advanced UV treatment of fluorinated phenols and pharmaceuticals using a combined ^{19}F-NMR, chromatography, and mass spectrometry approach. *ACS Environmental Au*, 2(3), 242-252.

Lee, A. L., Pandey, A. K., Chiniforoush, S., Mandal, M., Li, J., Cramer, C. J., ... & Pomerantz, W. C. (2022). Development of a Highly Responsive Organofluorine Temperature Sensor for ^{19}F Magnetic Resonance Applications. *Analytical chemistry*, 94(9), 3782-3790.

Bhat, A. P., Pomerantz, W. C., & Arnold, W. A. (2022). Finding fluorine: Photoproduct formation during the photolysis of fluorinated pesticides. *Environmental Science & Technology*, *56*(17), 12336-12346.

Bhat, A. P., Pomerantz, W. C., & Arnold, W. A. (2023). Wavelength-Dependent UV-LED Photolysis of Fluorinated Pesticides and Pharmaceuticals. *Environmental Science & Technology*, *57*(13), 5327-5336.

Li, J., Mundhenke, T. F., Smith, T. G., Arnold, W. A., & Pomerantz, W. C. (2023). Fluorous Liquids for Magnetic Resonance-Based Thermometry with Enhanced Responsiveness and Environmental Degradation. *Analytical Chemistry*, *95*(14), 6071-6079.

Manuscripts under preparation:

Mundhenke, T. F., Bhat, A.P., Pomerantz, W. C., & Arnold, W. A. (2023) Photolysis of fluorinated pharmaceuticals: Fluorine mass balances using ^{19}F-NMR.

Bhat, A. P., Pomerantz, W. C., & Arnold, W. A. (2023). Density functional theory computations to evaluate photolysis and photoproduct formation from fluorinated compounds.

Work presented at conferences:

Pomerantz W. C. K., Arnold W. A. (2023, upcoming) "New Fluorous Liquids and Synthetic Oligomers for ^{19}F MRI with Improved Degradation Profiles" *American Chemical Society (ACS) National Meeting and Exposition Fall 2023, San Francisco, CA.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2023, upcoming) "Shining some (LED) light on fluorinated compounds! UV wavelength dependent photolysis" *American Chemical Society (ACS) National Meeting and Exposition Fall 2023, San Francisco, CA.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2023, upcoming) "Density functional theory computations to evaluate photolysis and photoproduct formation from fluorinated compounds" *American Chemical Society (ACS) National Meeting and Exposition Fall 2023, San Francisco USA.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) "Degradation of fluorinated agrochemicals using photolysis-based processes and understanding the effect of fluorine motifs in the structures" *AEESP Research and Education Conference St. Louis USA*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) "Degradation of fluorinated agrochemicals using photolysis-based processes and understanding the effect of fluorine motifs in the structures" *Gordon Research Conference, Environmental Sciences: Water. Holderness, NH.*

Bhat A. P., Mundhenke T. F., Pomerantz W. C. K., Arnold W. A. (2022) "Fluorine beyond PFAS: Tracking fluorine during photolysis of fluorinated pesticides and pharmaceuticals" *Keynote speech at ACS Midwest Regional Meeting (MWRM) Iowa City, IA.*

Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) "Understanding fluorinated byproduct formation during direct and advanced-treatment based photolysis of fluorinated herbicides using ^{19}F-NMR" *American Chemical Society (ACS) National Meeting and Exposition Spring 2022 San Diego, CA.*

Mundhenke T. M., Bhat A. P., Pomerantz W. C. K., Arnold W. A. (2022) "Photoproduct formation, determination, and quantification of the photolysis of fluorinated pharmaceuticals" *American Chemical Society (ACS) National Meeting and Exposition Spring 2022 San Diego CA.*

Whiting Q. T., Bhat A. P., Mundhenke T. M., Pomerantz W. C. K., Arnold W. A. (2021) "Fluorinated photoproduct formation from photolysis of pharmaceuticals and agrochemicals" *American Chemical Society (ACS) National Meeting and Exposition Spring 2021 (virtual).*

V. ADDITIONAL BUDGET INFORMATION:

A. Personnel and Capital Expenditures

Explanation of Capital Expenditures Greater Than $5,000: N/A

Explanation of Use of Classified Staff: N/A

Total Number of Full-time Equivalents (FTE) Directly Funded with this ENRTF Appropriation:

Enter Total Estimated Personnel Hours for entire duration of project: 6108	Divide total personnel hours by 2,080 hours in 1 yr = TOTAL FTE: 2.93

Total Number of Full-time Equivalents (FTE) Estimated to Be Funded through Contracts with this ENRTF Appropriation:

Enter Total Estimated Contract Personnel Hours for entire duration of project: N/A	Divide total contract hours by 2,080 hours in 1 yr = TOTAL FTE: N/A

VI. PROJECT PARTNERS:

The project team will be led by William Arnold University of Minnesota; Dept. of Civil, Environmental, and Geo-Engineering) collaborating with William Pomerantz and Christopher Cramer (Dept. of Chemistry, UMN) . Dr. Arnold has expertise in the environmental analysis, fate, and transport of organic contaminants and has been studying the fate of pharmaceuticals in the environment for 20 years. Dr. Pomerantz is an expert in the development of new fluorinated molecules, and Dr. Cramer's expertise is in theoretical chemistry and predicting the environmental fate of pollutants. Two graduate students and an undergraduate students will conduct the research activities. Their duties will include collecting water samples, performing experiments, data analysis, and presenting the results at in-state scientific conferences.

A. Partners outside of project manager's organization receiving ENRTF funding: N/A

B. Partners outside of project manager's organization NOT receiving ENRTF funding: N/A

VII. LONG-TERM- IMPLEMENTATION AND FUNDING: The long-term goal of the project is to prevent wastewater treatment plants, whether they be oxidation ponds in out-state Minnesota or advances treatment plants in cities, from becoming hotspots of fluorochemical contamination. This project will provide information about specific chemicals that could be problematic, wastewater treatment techniques that result in non-toxic (fluorinated) reaction products, and means to new fluorochemicals that are of medical use but environmentally benign. The proposed study will help to safeguard Minnesota's lakes and rivers and human and animal health.

VIII. REPORTING REQUIREMENTS:

- Project status update reports will be submitted March 1 and September 1 each year of the project
- A final report and associated products will be submitted between June 30 and August 15, 2023

IX. SEE ADDITIONAL WORK PLAN COMPONENTS:

A. Budget Spreadsheet
B. Visual Component or Map
C. Parcel List Spreadsheet: N/A
D. Acquisition, Easements, and Restoration Requirements: N/A
E. Research Addendum

Attachment A:
Environment and Natural Resources Trust Fund
M.L. 2019 Budget Spreadsheet - Final
Legal Citation: M.L. 2019, First Special Session, Chp. 4, Art. 2, Sec. 2, Subd. 04b
Project Manager: William Arnold
Project Title: Benign Design: Environmental Studies Leading to Sustainable Pharmaceuticals
Organization: University of Minnesota
Project Budget: $415,000
Project Length and Completion Date: 4 years, June 30, 2023
Today's Date: August 7, 2023

ENVIRONMENT AND NATURAL RESOURCES TRUST FUND BUDGET	Revised Budget 04/18/2022	Revised Budget 08/07/2023	Amount Spent	Balance
BUDGET ITEM				
Personnel (Wages and Benefits)	$ 358,500	$ 363,097	$ 363,097	$ -
William Arnold, Project Manager (75% salary, 25% fringe benefits). 4% FTE for years 1 - 3. Overall project coordination, lead Task 1 studies, co-lead Task 3. $34,500				
William Pomerantz, co-Project Manager (75% salary, 25% fringe benefits). 4% FTE for years 1 - 3. Lead Task 2, co-lead Tasks 1 and 3. $20,000				
Christopher Cramer, co-Project Manager (75% salary, 25% fringe benefits). 2% FTE for years 1 -3. Lead Task 3. $22,400				
Graduate student Research assistant 1, Perform environment fate studies for Task 1, perform computations in Task 3 (55% salary, 45% fringe benefits) 50% FTE for years 1 &2, 25% for Year 3. $124,100				
Graduate student Research assistant 2, Synthesize new MRI regents in for Task 2, perform computations in Task 3 (55% salary, 45% fringe benefits) 25% FTE for year 1, 50% for Years 2&3. $88,000				
Postdoctoral Researcher, Synthesize new MRI regents in for Task 2, $36,500, 50% in Y2, 80% salary, 20% fringe benefits				
Undergraduate researcher. Assist with laboratory experiments. 10 hrs per week during academic year, 40 hours per week in summer. (100% salary). $24,900				
Equipment/Tools/Supplies				
Laboratory Supplies (chemical and isotopically labelled standards, chemical reagents, necessary glassware, solvents, consumable supplies, laboratory notebooks, software licenses, instrument operation)	$ 32,000	$ 36,809	$ 36,809	$ -
Analytical time for identification of breakdown products using NMR	$ 7,000	$ 7,000	$ 7,000	$ -
Analytical time for identification of breakdown products using mass spectrometry	$ 6,500	$ 6,195	$ 6,195	$ -
Maintenance for mass spectrometry equipment system components	$ 4,000	$ 924	$ 924	$ -
Travel expenses in Minnesota				$ -
University vehicle rental and hotel stays to collect water samples. Presenation of results at local conferences.Reimbursement will be according to University of Minnesota guidlines.	$ 1,000	$ 350	$ 350	$ -
Other				$ -
Publication charges to make to make published journal articles (2-3) immediately available via open access to maximize data availability and dissemination	$ 6,000	$ 625	$ 625	$ -
COLUMN TOTAL	$ 415,000	$ 415,000	$ 415,000	$ -

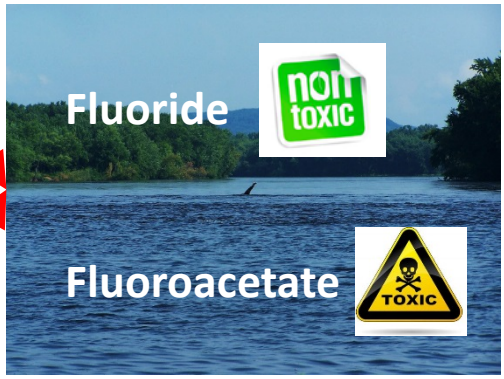
OTHER FUNDS CONTRIBUTED TO THE PROJECT	Status (secured or pending)	Budget		Spent	Balance
Non-State:		$ -		$ -	$ -
State:		$ -		$ -	$ -
In kind: Because the project is overhead free, laboratory space, electricty, and other facilities/adminstrative costs (54% of direct costs excluding permanent equipment and graduate student tuition benefits) are provided in-kind.	secured	$ 178,500		$ 178,500	$ -

PAST AND CURRENT ENRTF APPROPRIATIONS	Amount legally obligated but not yet spent			Spent	Balance
Current appropriation:				$ -	$ -
Past appropriations: N/A				$ -	$ -

Fluorinated pharmaceuticals and toxic byproducts in Minnesota lakes and rivers

Oxidation ponds

Antibiotics, statins, etc often contain fluorine



Advanced treatment

Outcomes:

1. Assess toxic byproduct formation
2. Identify wastewater treatment processes that lead to non-toxic products
3. Improve outstate and urban wastewater treatment
4. Develop rules for environmentally benign design of new compounds