



# Sulfolane: Research Efforts by the National Toxicology Program

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The Alaska Department of Environmental Conservation (DEC) Contaminated Sites Program oversees the cleanup of contaminated sites to protect against risk to public health and the environment.

**At DEC's request, the National Toxicology Program (NTP) is conducting new research to address uncertainties in sulfolane toxicity.**

This Fact Sheet summarizes the NTP's studies. A glossary is included to explain the scientific terminology used in the Fact Sheet.

Currently the public is not exposed to sulfolane. While the NTP studies are underway, Flint Hills is providing alternate water supplies to all properties with any detection of sulfolane in the water. Under the new Settlement Agreement, Flint Hills and the State will fund the expansion of the City's piped public water system to extend city water to all impacted properties, as well those expected to be impacted in the future.

## What is known about the toxicity of sulfolane?

Sulfolane is an industrial solvent used primarily in natural gas and petroleum refining. No studies have looked for health effects in people who have been exposed to this chemical. Most of what we know about how sulfolane might affect human health comes from studies in which laboratory animals were exposed to high levels of sulfolane for periods of time up to six months. In short-term studies, laboratory animals exposed to high doses of sulfolane showed effects on the central nervous system, such as hyperactivity, convulsions, and hypothermia. In longer studies, sulfolane was shown to affect the immune system and certain organs, including the liver, kidneys, and spleen in test animals. Animal studies also suggest that sulfolane at high doses can cause developmental problems in mice.

## What is the National Toxicology Program?

The NTP is a federal interagency effort of the National Institutes of Health, the Centers for Disease Control and Prevention, and the Food and Drug Administration to safeguard public health by conducting cutting edge toxicology research on substances in our environment. The NTP is advised by a Board of Scientific Counselors whose members are university and industry experts appointed by the Secretary of the U.S. Department of Health and Human Services.

Following DEC's nomination, sulfolane was accepted into the NTP program in early 2012. Supporting letters from the Fairbanks North Star Borough Mayor, the Alaska District F delegation, the Alaska Department of Health and Social Services, and others accompanied the nomination.

No long-term, or chronic, studies in animals have been conducted to determine if sulfolane might cause cancer or any other long-term health effects. In most laboratory tests with bacteria or animal cells, sulfolane did not cause cancer-like changes to the cells.

A more detailed review of the scientific literature on sulfolane can be found on DEC's website at <http://dec.alaska.gov/spar/csp/sites/north-pole-refinery/health.htm>.

### What new research is being conducted?

The NTP proposed a set of studies to answer questions about sulfolane toxicity. These questions include the health impacts of long-term exposure and effects on development and reproduction. Also, the effects of sulfolane on the immune system need further investigation.

In seeking to answer these questions, the NTP is conducting several studies in rodents, which are established laboratory animal models. The anatomy, physiology and even some genetic aspects of rodents are similar to humans, making them good predictors of human health outcomes. In the largest of these studies, rats and mice will be exposed to sulfolane in drinking water for 2 years.

Although there is no evidence that sulfolane causes cancer, there have been no studies conducted in animals or humans. The NTP will investigate this further in animals exposed to sulfolane in this 2-year study.

Four studies are being undertaken by the NTP (see text box for a more detailed description of each study):

- 1) **28-Day Toxicity Study – Awaiting Report**  
Mice, rats and guinea pigs were given a range of doses of sulfolane.
- 2) **ADME Studies – Awaiting Report**  
Mice and rats were given sulfolane and the distribution of sulfolane throughout the animal is studied.
- 3) **Subchronic Toxicity Study - Awaiting Report**  
Mice and rats from the 2-year study were assessed after 3 months of exposure.
- 4) **Chronic Toxicity Study – Currently Underway**  
This study will determine the effects of long-term exposure on rats and mice.

## NTP Studies on Sulfolane Underway

*(Glossary available, next page)*

1. **28-day Toxicity Study – Awaiting Report**  
Mice, rats and guinea pigs were given a range of doses of sulfolane. A number of toxicity endpoints were assessed, including the amount of sulfolane in the animals. Histology of multiple tissues and immunology were also evaluated. Goals of this study were 1) to determine if any of the animal species studied is more sensitive to sulfolane toxicity than the other species, and 2) to identify appropriate dosing levels for longer duration studies.
2. **ADME Study – Awaiting Report**  
Studies measure the absorption, distribution, metabolism, and excretion (ADME) of a chemical in male and female mice and rats. ADME studies help understand how a chemical moves around within the body, including whether there are any differences between sexes or rodent species.
3. **Subchronic Toxicity Study – Awaiting Report**  
Mice and rats from the 2-year study were assessed after 3 months of exposure. The study will look at effects on a number of toxicity endpoints including markers of development in the rats. In a separate study, the immune system of rats and mice exposed to sulfolane for 3 months were evaluated.
4. **Chronic Toxicity Study – Currently Underway, Began Spring 2015**  
Rats and mice are being given sulfolane in their drinking water for 2 years, consistent with how people would most likely come in contact with sulfolane. The purpose of this study is to determine the effects of long-term exposure to sulfolane including any potential carcinogenic effects.

## Glossary

**Absorption** – Process by which a chemical enters the body.

**ADME studies** – Studies that evaluate absorption, distribution, metabolism and excretion in the animals.

**Carcinogenicity** – A chemical's ability to cause cancer.

**Chronic Study** – A toxicity study designed to measure the effects of repeated, long-term exposure (usually 2 years in laboratory animals).

**Distribution** – Process of carrying the chemical to different parts of the body.

**Excretion** – Process of eliminating the chemical or its metabolites (or breakdown products) from the body.

**Histology** – Study of the structure of cells and tissues.

**Immunology** – Study of all aspects of the immune system such as white blood cells.

**Metabolism** – Process by which a chemical breaks down in the body.

**Subchronic Study** - A toxicity study designed to measure the effects of repeated exposure for greater than 30 days but up to around 10% of a lifetime (usually 90-days for laboratory animals).

**Toxicity** – The ability of a chemical to cause injury to cells and tissues.

## Contacts

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Information on the status of the cleanup project, current and future actions, newsletters, fact sheets and other project documents for the sulfolane investigation at the Flint Hills Refinery in North Pole can be found on the DEC website:

**[dec.alaska.gov/spar/csp/sites/north-pole-refinery](http://dec.alaska.gov/spar/csp/sites/north-pole-refinery)**