

West Virginia Chemical Spill: Mouse Dermal Irritation and Hypersensitivity Study

June 2015 NTP Update

Synopsis

The National Toxicology Program (NTP)¹ evaluated 4-methylcyclohexanemethanol (MCHM) and crude MCHM for their ability to irritate the skin or cause skin sensitization (hypersensitivity). Crude MCHM was the major constituent of the liquid spilled into the Elk River in West Virginia. It is a commercial product that contains primarily MCHM and a small amount of other chemicals. NTP found MCHM is a dermal (skin) irritant; however, it did not induce hypersensitivity, meaning it did not cause an allergic response in the skin. These findings on MCHM's effect on the skin are consistent with a previous study.²

NTP conducted two studies on crude MCHM. In both studies, crude MCHM caused skin sensitization. In one study, crude MCHM was also found to be a mild skin irritant. The hypersensitivity findings differ from a previous study in a different model system that did not find crude MCHM caused skin sensitization.³ The finding that crude MCHM irritated the skin is consistent with results from a previous study.⁴

Mouse Dermal Irritation and Hypersensitivity Study

Background on Irritancy and Hypersensitivity Study

Rashes and skin irritation were among the health effects reported by households following the chemical spill into the Elk River in West Virginia.⁵ The NTP conducted tests in mice to evaluate the potential for 4-methylcyclohexanemethanol (MCHM) and crude MCHM to cause dermal (skin) irritation and/or skin sensitization (hypersensitivity; i.e., allergic response) and to identify the concentrations at which such effects occurred. Dermal irritation results when a chemical causes localized skin inflammation by directly damaging cells. Skin sensitization results when a specific, structural component of a chemical causes changes in the immune system leading to an allergic response in the skin.

In these studies, MCHM and crude MCHM were each diluted in a mixture of acetone and olive oil to different concentrations (listed in Table 1) and applied to the ears of mice on study days 1, 2, and 3. The sample size was five mice per dose group.⁶ The mice were rested on days 4 and 5. On day 6, ear swelling at the site of application was assessed to determine any irritancy related effects. The proliferation (increase in number) of immune cells in the lymph nodes near the application site was measured to assess whether the exposure to either chemical caused skin sensitization by stimulating an allergic response. A second dermal irritancy and hypersensitivity study was performed on crude MCHM using different concentrations to verify the findings of the first study.

¹ NTP is a federal, interagency program whose goal is to safeguard the public by identifying substances in the environment that may affect human health. NTP is headquartered at the National Institute of Environmental Health Sciences, which is part of the National Institutes of Health. For more information about NTP and its programs, visit <http://ntp.niehs.nih.gov/>.

² http://www.eastman.com/Literature_Center/Misc/Pure_Distilled_MCHM-Acute_Toxicity_Battery_Containing_5_Study_Reports.pdf

³ http://www.eastman.com/Literature_Center/Misc/Crude_MCHM-Skin_Sensitization.pdf

⁴ http://www.eastman.com/Literature_Center/Misc/Crude_MCHM-Skin_Irritation_Study.pdf

⁵ <http://www.dhhr.wv.gov/News/2014/Documents/WVCASPERReport.pdf>

⁶ <http://ntp.niehs.nih.gov/testing/types/imm/methods/immunotoxicology-testing.html>

Table 1. Chemicals Tested in the Mouse Dermal Irritation and Hypersensitivity Study

CASRN*	Chemical name	Dose Levels (% chemical)	Notes
34885-03-5	4-Methylcyclohexanemethanol (MCHM)	2, 20, 50	a
NA	Crude 4-Methylcyclohexanemethanol (Crude MCHM)	First study: 1, 2, 5, 20, 40, 80 Second study: 1, 5, 25, 50, 75	b

* CASRN = Chemical Abstracts Service Registry Number; ^aMajor or minor constituent of the spilled liquid; ^bA commercial mixture containing greater than 70 percent MCHM along with lesser amounts of five other chemicals.

Study Findings

Treatment of mice with 20 percent or 50 percent MCHM resulted in an increase in ear thickness that was indicative of mild skin irritation. MCHM did not cause increased proliferation of immune cells, indicating that it did not cause hypersensitivity. These results are consistent with toxicity information from previous studies by the Eastman Chemical Company.⁷

In the first study of crude MCHM, mice treated with up to 80 percent of the chemical mixture showed minimal evidence of dermal irritation. However, as the concentration of crude MCHM increased, there was an increase in the proliferation of immune cells in the lymph nodes closest to the site of application in the mice. This increase in immune cells indicates that crude MCHM produced skin sensitization at concentrations greater than or equal to 20 percent. In the second study of crude MCHM, mild dermal irritation was observed at the site of application at the highest concentration tested and skin sensitization was observed at concentrations of 50 percent and higher. In these studies, crude MCHM is considered a mild skin irritant, and this finding is consistent with previous studies by the Eastman Chemical Company.⁸ Importantly, these data indicate that crude MCHM induces hypersensitivity at concentrations lower than those that cause dermal irritancy. The hypersensitivity findings reported here are inconsistent with results from a previous study by the Eastman Chemical Company using a different model system that found crude MCHM did not produce skin sensitization.⁹ The reasons for this inconsistency are not currently known, but may relate to the use of different methods and a different formulation of crude MCHM.

Next Steps

The studies to evaluate whether MCHM or crude MCHM can cause dermal irritation or hypersensitivity are complete. NTP will consider the findings from these studies in any future, overall assessment of the spilled chemicals.

⁷ http://www.eastman.com/Literature_Center/Misc/Pure_Distilled_MCHM-Acute_Toxicity_Battery_Containing_5_Study_Reports.pdf

⁸ http://www.eastman.com/Literature_Center/Misc/Crude_MCHM-Skin_Irritation_Study.pdf

⁹ http://www.eastman.com/Literature_Center/Misc/Crude_MCHM-Skin_Sensitization.pdf