

# Summary Report of Short-term Screening Level Calculation and Analysis of Available Animal Studies for MCHM

This summary report explains how the Centers for Disease Control and Prevention (CDC) used generally accepted scientific methods<sup>1</sup> to establish a short-term health advisory for drinking water in and around Charleston, West Virginia immediately after a chemical spill in the Elk River. The summary report also shows how CDC used animal studies—once they became available—to validate the initial short-term screening level of 1 part per million (ppm) calculated during the early stages of the emergency response.

## Background

On January 9, 2014, approximately 7500 gallons of an industrial chemical, 4-Methylcyclohexanemethanol (MCHM – CAS# 34885-03-5), spilled into the Elk River just upstream from the Kanawha County municipal water intake in Charleston, West Virginia. This municipal water system serves nearly 300,000 people whose water was affected by the chemical spill. Due to the uncertainty over the chemical levels in the water supply, the Office of the Governor issued a “Do Not Use” order at 6:00 pm on January 9, 2014. Later that evening, the West Virginia Department of Health and Human Resources contacted CDC about the release and requested assistance to review water sampling data and provide a drinking water screening level for MCHM. In response to this urgent situation, a screening level of 1ppm was recommended. Based on the information available, a level of 1ppm or below is not likely to be associated with any adverse health effects.

## Summary

The Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry (CDC/ATSDR) used the most relevant available information to provide a scientifically supported recommendation for the protection of public health. Initial actions in the Charleston area were based upon limited available information and resulted in a decision to issue a short-term public health alert regarding all municipal water use in the Kanawha water distribution area.

The initial short-term screening level that CDC/ATSDR recommended for the Elk River spill followed common practices for the interpretation of toxicological information for public health purposes (see Methodology section below). Often such information is incomplete; this was the case for MCHM in this incident. CDC/ATSDR analyzed additional information, once it became available, to verify the initial short-term screening level and health advisory.

## Data Review

On the evening of Thursday, January 9, 2014 emergency response staff from CDC/ATSDR, in cooperation with local and state health authorities, recommended an interim urgent short-term screening level based upon information available at the time. The short-term

screening level was used to issue a warning to users of the local water district to avoid all contact with municipal water.

Since CDC/ATSDR recommended the emergency short-term screening level, state and federal officials have acquired several additional proprietary studies on the toxicology of MCHM. When these studies became available, the U.S. Department of Health & Human Services convened a Federal expert workgroup including scientists from the National Institute of Environmental Health Sciences and National Toxicology Program, the National Library of Medicine, the Environmental Protection Agency, and CDC/ATSDR to review the available animal studies and the methodology for the short-term screening level calculation. This workgroup concurred that the 1 ppm short-term screening level was appropriate.

The studies of pure MCHM and crude MCHM are summarized below. For a more detailed description of these studies, please see the National Library of Medicine's Hazardous Substances Data Bank: <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@DOCNO+8182>.

**1) Crude MCHM. Ames test for mutagenic potential.** This test used multiple *Salmonella typhimurium* strains and one *E. coli* strain, with six doses, and with and without "S9 mix" to study the impact of possible metabolism of activity. No increase in revertants was noted. A repeat study confirmed these results.

**2) Crude MCHM. Two-week daily dermal application.** Male and female rats were dosed at 0, 100, 500, and 2000 mg/kg/day, 6 hours/day for 13 consecutive days. There was dermal irritation at all treatment levels and thus no No Observed Effect Level (NOEL) was identified. Because of the absence of significant histopathology and serum clinical chemistry changes, 2000 mg/kg was considered as the NOEL for systemic toxicity. One focus was to look at hematuria as a possible toxic effect seen in an earlier acute dermal study.

**3) Crude MCHM acute single dose dermal.** A single dose of 2000 mg/kg was applied to male and female rats, with a 14-day observation period. Dermal irritation was observed, and the dermal LD50 was greater than 2000 mg/kg.

**4) Crude MCHM acute single dose oral.** Male and female rats were dosed with 500, 1000, and 2000 mg/kg, followed by a 14-day observation period. The acute LD50 was calculated as 933 mg/kg for males and 707 mg/kg for females.

**5) Pure MCHM 28 day daily oral.** Rats received 0, 25, 100, and 400 mg/kg/day, 5 days a week, for 4 weeks. In this study, the administration of 400 mg/kg/day for 4 weeks was associated with erythropoietic, kidney, and liver effects, including increased liver weight, inflammation, and kidney tubular degeneration. The authors set a NOEL at 100 mg/kg/day. ***CDC used this study to establish the short-term health advisory for the MCHM spill in the Elk River.***

**6) Crude MCHM acute single dose oral (repeat of earlier study).** This is a study of a single oral dose to female rats (i.e., to look at hematuria as a possible toxic effect as seen in another study). The LD50 was calculated to be 500 mg/kg.

**7) Pure MCHM acute battery:**

**a) Acute single dose oral toxicity.** Male and female rats were dosed at 625, 1250, and 2500 mg/kg. The estimated LD50 was 1768 mg/kg in males and 884 mg/kg in females.

**b) Acute single dose dermal exposure.** Male and female rats were dosed at 2, 6, and 20 ml/kg. MCHM was irritating to skin at as low as the 2 ml/kg dose, but only in females at this dose.

**c) Acute single exposure dermal irritation.** Guinea pigs were dosed at 0.5 ml on the abdomen and covered with occlusive wrapping for 24 hours. They were observed for 48 hours after the wrap was removed. MCHM exposure led to strong skin irritation.

**d) Acute toxicity, repeated application to skin.** The backs of guinea pigs were exposed to 9 doses of 0.5 ml of MCHM “drop on” over 11 days. There was “... exacerbation of the irritant response with (multiple) application...”

**e) Acute toxicity, evaluation of skin sensitizing potential.** Male guinea pig footpads were exposed to 0.05 ml of a 1.0% solution MCHM in adjuvant (FCA) for induction. No sensitization was observed after a challenge application, and MCHM was concluded to have “a low potential to cause human sensitization.”

**f) Acute toxicity, eye irritation.** One dose of 0.1 ml of MCHM was placed onto the eyes of rabbits, followed by washing or no washing. The washed eyes showed slight irritation, and the unwashed eyes showed moderate irritation. MCHM was concluded to be a “moderate irritant.”

Together, these studies provide a much-improved (but still incomplete) understanding of MCHM's toxicology profile. In particular, one of the studies, the 4-week rat study (study 5 above), provides a NOEL in rats. This NOEL, established by the authors of the study, is 100 mg/kg/day. The 4-week NOEL represents a more scientifically sound study and point of departure for establishing a short-term health advisory for MCHM.

## Methodology

CDC/ATSDR used the following methodology to establish a short-term screening level of 1 part per million (ppm) for the MCHM spill in the Elk River:

$$DW\ Advisory \leq \frac{NOEL \times BW}{UF \times Intake}$$

Where:

- DW Advisory = Short-term Drinking Water Advisory
- NOEL = No Observed Effect Level in the experimental species (100 mg/kg/day)
- BW = Body weight of a child (10 kg)
- UF = Uncertainty factors that address differences between animals and humans (10X), address differences accounting for sensitive humans (10x), and account for weaknesses in the toxicological database (10X). For example, there are no developmental, neonatal, or transplacental studies available.
- Intake = The estimated intake from drinking water of a 10 kg child (1 liter/day).

NOEL (mg/kg/d)	BW (kg)	UF (unitless)	Intake (L/day)	Short-term DW Advisory (mg/L or ppm)
100	10	1000	1	1

<sup>1</sup> Donohue, J.M. and Libscomb, J.C. Health advisory values for drinking water contaminants and the methodology for determining acute exposure values. *Sci Tot Env.* 288 (2002) 43-49.