Statement of Sandra I. Sulsky, MPH, PhD, FACE to be presented at National Lime Association meeting with the Office of Management and Budget, scheduled for May 28, 2024.

I am an epidemiologist, and a Principal with Ramboll Americas Engineering Solutions, in our global Health sciences department.

Ramboll has provided the National Lime Association with assessments of the evidence regarding potential carcinogenicity of hydrochloric acid (HCl). We have submitted three reports:

1. In 2021 we assessed the evidence to determine whether HCl should be regulated as a non-carcinogen according to the Clean Air Act. This assessment used previous reviews by authoritative bodies as a starting point, supplemented with material published after those reviews were available. The bodies that have reviewed carcinogenicity of HCl are the International Agency for Research on Cancer (IARC), the Organization for Economic Cooperation and Development (OECD), and the International Programme on Chemical Safety (IPCS), part of the World Health Organization.

2. In February 2024, we updated the 2021 report with data from new publications and commented on the appropriateness of a health-based emissions limit, or HBEL, which is considered appropriate for regulating non-carcinogenic exposures.

3. In April 2024 we provided a summary of our prior assessments to correct the technical components of public comments regarding the proposed HBEL that were jointly filed by several advocacy groups (California Communities Against Toxics; Sierra Club; and Earth Justice). None of the comments filed by these organizations changed our conclusions.

Based on this work, I can say the following: HCl is used widely and has been used for a long time, in many industries. Studies of HCl-exposed worker populations have not raised strong signals of cancer risk. The few incidental findings reported can be attributed to mixed exposures that included chemicals that are known human carcinogens plus uncontrolled confounding, e.g., by cigarette smoking.

Moving down the chain of evidence: Animal studies have been conducted in rats and mice, which have been subjected to chronic exposures via inhalation, ingestion, and skin exposures. There were no increases in tumors in treated vs. control animals in these studies.

Even though there is no compelling evidence for cancer in humans or experimental animals exposed to HCl, some research has been done to investigate whether HCl *can* be carcinogenic. This is aligned with the EPA position that data regarding potential mechanisms of effect should be considered, especially when the animal and human data are limited.

There are two mechanisms for cancer causation: genotoxicity and neoplasia. Genotoxicity is the most direct mechanism - this is damage to DNA that might result in cancer if carried forward during cell replication. Genotoxicity studies are conducted in cell cultures. In all of the studies we identified, effects were only observed when the pH was highly acidic and this was often in studies that were conducted specifically to investigate the effects of an acidic environment - meaning the experiments were not undertaken to examine hypotheses related to HCl specifically, and the same effects were observed regardless of the agent used to produce the acidic environment. The experimental conditions are not relevant to human exposures, because the human body has innate buffering mechanisms to control acidity, and these levels of pH do not occur in the environment.

Cell proliferation or neoplasia is an indirect mechanism, in that increased cell replication leads to an increase in the chance for genetic error. Cell proliferation is always considered a threshold event - i.e., only occurs when exposure exceeds a certain concentration.

We identified only one study, a chronic inhalation study conducted in rats, in which hyperplasia was observed; this was in the rat trachea. Hyperplasia indicates excess cell growth, and this may be due to the irritation effect of breathing in an acidic environment. Acid concentration was high in this experiment, again leading to conditions that are highly unlikely to be relevant to humans.

Using the data from this study, EPA calculated an RfC of 0.2 mg/m^3. The RfC is an estimate of the continuous inhalation exposure that is *unlikely* to cause harmful health effects in humans, including in sensitive subpopulations. Using this estimate along with air modeling data, EPA estimated a health-based emission limit (HBEL) as 300 tons per year. They calculated this level of emissions would result in a hazard quotient of 0.2, five times below the level (HQ=1) at which adverse chronic health effects *might* occur. Cancer is considered a chronic health effect due to its long induction period. When the HQ=1, emissions sources are identified for further investigation - the HQ is a screening tool, it is not a means to identify an actual problem. So, basing the HBEL on HQ=0.2 builds in a wide margin of safety.

In summary, the weight of evidence does not suggest that HCl is carcinogenic to humans or animals, it does not suggest HCl *per se* is mutagenic, and cell proliferation occurred in rats in one inhalation study where the highly acid environment was not likely relevant to humans. EPA used these rat data to estimate the HBEL for HCl using an appropriately conservative and scientifically valid approach that accounts for unlikely events and incorporates a wide margin of safety for communities in proximity to emissions sources.