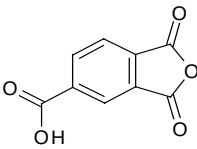
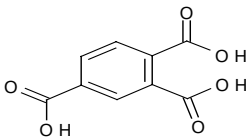


SIDS INITIAL ASSESSMENT PROFILE

CAS No.	552-30-7 528-44-9
Chemical Name	Trimellitic Anhydride (TMA) Trimellitic Acid (TMLA)
Structural Formula	TMA: $C_9H_4O_5$  TMLA: $C_9H_6O_6$ 

SUMMARY CONCLUSIONS OF THE SIAR**Category/Analogue Rationale**

Trimellitic anhydride (TMA) and trimellitic acid (TMLA) are considered to be structural analogues. In addition, in aqueous environments TMA is readily converted to TMLA. TMA rapidly forms TMLA under the conditions used to test its toxicity, the toxicities of TMA and TMLA are qualitatively believed to be the similar for systemic toxicity with these two chemicals being presented as analogues. The only difference being sensitization and potentially local effects/reactions at the initial point of contact (skin, eye, and respiratory irritation). The sensitization potential of TMA, may be directly attributed to the formation of haptens following a reaction with proteins. TMLA does not react with proteins to form haptens, and therefore does not share this mode of action for sensitization.

Human Health

TMA exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD_{50} has been reported to range from 2,030 to 3,340 mg/kg in male and female rats, with stomach lesions appearing as the most consistent lesion upon necropsy. In rats, the inhalation LC_{50} value was reported to exceed a concentration of 2,330 mg/m^3 , with lung lesions appearing as the most consistent lesion upon necropsy. The LC_{50} for TMLA was reported to be >3,750 mg/m^3 , with necropsy findings considered within normal limits. A dermal LD_{50} value of 5,600 mg/kg was reported for TMA. Because TMA rapidly converted to TMLA in the body, the acute toxicity of TMLA is expected to be similar to that of TMA. Both chemicals are considered to have mild skin and severe eye irritation potential. Studies on TMA suggest that these materials may also be respiratory sensory irritants. TMA but not TMLA should be considered a dermal sensitizer.

In repeated dose inhalation studies, the principal effects of TMA are on the immune system and the lung. In a 13-week inhalation repeat dose study, elevated antibody levels and lung foci were observed in rats following exposures to relatively low concentrations of TMA (0.002 – 0.054 mg/m^3), however a NOAEL was not identified. Elevated antibody levels, asthma, allergic rhinitis, and a late respiratory systemic syndrome (LRSS) are associated with

occupational exposures to TMA in some workers. The toxicity of TMA following repeated oral exposures is low, based on NOAELs of approximately 500 mg/kg-day identified for both rats and dogs. In a 13 week inhalation study, immunological and pulmonary effects were not associated with repeated exposures to TMLA; the NOAEL was determined to be 300 µg/m³ (the highest dose tested). *In vivo* genotoxicity data are not available however, three *in vitro* assays with TMA were negative. Although a reproductive toxicity test has not been conducted for TMA, histopathological changes to reproductive tissues have not been observed in rats following subchronic exposures, and it has been found to be neither teratogenic nor fetotoxic in developmental toxicity studies.

Environment

TMA has a melting point of 165°C, a boiling point of 390°C, a vapor pressure of 7.6×10^{-5} Pa @ 25°C, and assuming no hydrolysis a log K_{ow} of 1.95 and a water solubility of 1,036 mg/L. TMLA has a melting point of 219°C, an unknown boiling point, a vapor pressure of 3.8×10^{-6} Pa @ 25°C, a log K_{ow} of 0.95 and a water solubility of 21,000 mg/L. The half-life of TMA and TMLA in air is estimated to be 13.4 and 6.6 days, respectively, due to direct reactions with photochemically generated hydroxyl radicals. In the presence of water, TMA rapidly hydrolyzes (within 10 minutes) to form TMLA. Based on both chemicals physical chemical properties, TMA and TMLA are likely to partition to the water compartments in the environment. Acute toxicity testing in fish, invertebrates, and algae indicate a very low order of toxicity with measured No-Observed-Effect-Concentrations (NOECs) of 896, 792 and 739 mg/L, respectively. TMA and TMLA are readily biodegraded under aerobic conditions in sewage sludge, and are expected to biodegrade in soil and water as well. TMA and TMLA are not expected to bioaccumulate in food webs based on a BCF of 3.2.

Exposure

Approximately 100,000 metric tonnes/year TMA are produced worldwide, the majority of which (65,000 metric tonnes/year) are produced in the U.S. Most of the TMA produced (65%) is used in the synthesis of plasticizers for PVC resins, while smaller amounts (30%) are used as a reactant in wire and cable insulation enamels and polyester resins for powder coatings. When TMA is processed into the above materials, it is fully consumed and therefore, is not readily available for releases to the environment. All TMLA produced is used to make TMA. Occupational exposures to TMA and TMLA are likely to occur by the inhalation and dermal routes in settings where TMA is produced or used. Historical monitoring data have revealed mean concentrations ranging from 0.00051 to 0.77 mg/m³. Because TMA is rapidly hydrolyzed to form TMLA in the presence of water, consumer and environmental exposures to TMA are not anticipated. Data regarding these potential exposures to TMLA are largely lacking, but exposures are expected to be low outside of the workplace.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Although a reproductive toxicity study and an *in vivo* genotoxicity are not available for TMA or TMLA, sufficient data are available to address these endpoints. Therefore, no additional studies are recommended to meet the SIDS data set.