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Mineral hydrocarbons (MHC) are used in food, cosmetics, and pharmaceutical applications. Food-grade, high molecular weight, saturated MHC have generally been considered safe for intended uses based on an absence of evidence of human toxicity and a large body of evidence from toxicology data showing negligible systemic effects from long-term oral exposure.

Subchronic feeding studies of MHC in Fischer 344 (F344) rats have shown a dose-related increase in histopathologic observations in some treatment groups. Observations include granulomas and microgranulomas in the liver, which appear to result from an inflammatory response. Not all MHC studied produced granuloma in F344 livers. Studies conducted in F344 rats with granulomatous findings are in marked contrast to the negative findings reported in numerous subchronic and chronic toxicity studies on MHC conducted in several animal models, including Sprague–Dawley (SD) rats, Long-Evans rats and Beagle dogs.

The underlying mechanisms for species/strain differences in response to MHC is unknown, but is hypothesized to result from differences in absorption, metabolism, and inflammatory response. As with naturally occurring saturated hydrocarbons, MHC are primarily absorbed in the small intestine and transported to the body through the lymphatic system. Numerous studies suggest strain-dependent differences in MHC absorption leading to higher circulating MHC levels in F344 rats, as compared to SD rats. MHC undergo oxidative metabolism in the liver and numerous studies suggest strain-dependent differences in MHC metabolism.

SD rats appear to have a more efficient metabolism of saturated hydrocarbons and are less sensitive to MHC exposure as compared to F344 rats. This strain dependent difference in oxidative metabolism of hydrocarbons appears to be mediated through cytochrome P450 enzymes. Studies also suggest strain-dependent differences in inflammatory responses to MHC exposure. At similar target tissue concentrations of MHC, F344 rats exhibit inflammatory lesions, whereas no response is seen in SD rats. This may be due to differences with resident liver macrophages responsible for the secretion of vasoactive and toxic mediators involved in host defense mechanisms.

Saturated hydrocarbons from MHC and natural plant sources are found in human livers, in lipogranulomas. Human hepatic lipogranulomas are benign, circumscribed lesions, containing lipid droplets in the center. They show no evidence of inflammation or fibrosis and have not been associated with adverse clinical effects. These findings are in contrast to the hepatic granulomas observed in F-344 rats. Human exposure

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to MHC, under severe and abusive use exposures, do not result in F-344 rat-type epithelioid granulomas in the liver.

The European Food Safety Authority (EFSA) reviewed the data on the incidence of human hepatic lipogranuloma and concluded that "The current incidence is very low and do not appear to have any adverse consequences". It is unlikely that extrapolation of effects from F-344 rats are informative to human health risk assessments.