EXECUTIVE SUMMARY

Dodecanedioic Acid – Oral Risk Assessment CAS # 693-23-2			
PARAMETER	**LEVEL[1]**	**UNITS**	**DERIVED**
NOAEL (no-observed-adverse-effect level)	74	mg/kg-day	From a human oral bolus dose study supported by studies using intravenous infusion.
Oral RfD (oral reference dose)	70	mg/kg-day	From the NOAEL with a 1x total uncertainty factor.
TAC (total allowable concentration)	30	mg/L	A TAC of 500 mg/L was calculated from the oral RfD, the default 70 kg body weight and 2 L/day water consumption of an adult, and a 20% relative source contribution for drinking water. The TAC was limited by the 30 mg/L water solubility of dodecanedioic acid.
SPAC (single product allowable concentration)	30	mg/L	A SPAC of 50 mg/L was calculated from the TAC based on the default 10 sources of dodecanedioic acid in drinking water. The SPAC was limited by the 30 mg/L water solubility of dodecanedioic acid.
STEL (short term exposure level)	30	mg/L	A STEL of 700 mg/L was calculated from the NOAEL using the default 10 kg body weight and 1 L/day water consumption of a child. The STEL was limited by the 30 mg/L water solubility of dodecanedioic acid.

[1] The specified levels are based on the only available controlled human study by the oral route, supported by studies at higher levels using intravenous infusion. The existence of large food sources of dodecanedioic acid or its precursor dodecanoic acid and human tolerance of higher levels by infusion suggest these levels are likely conservative. Further, the TAC, SPAC, and STEL are limited by the water solubility of the chemical and are not based on any observed health effect.

KEY STUDY	Passi, S., M. Nazzaro-Porro, M. Picardo, G. Mingrone, and P. Fasella. 1983. Metabolism of straight saturated medium chain length (C9 to C12) dicarboxylic acids. J Lipid Res 24:1140-1147.
CRITICAL EFFECT	No critical effect was identified in humans or laboratory animals over the tested dose ranges.
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: • 1x for interspecies extrapolation • 1x for intraspecies extrapolation • 1x for subchronic to chronic extrapolation • 1x for LOAEL to NOAEL extrapolation • 1x for database deficiencies The total uncertainty factor is therefore 1x.
TOXICITY SUMMARY	Oral and parenteral studies in humans provided more direct representation of human response to dodecanedioic acid than animal studies. No signs of toxicity were seen in any of the volunteer subjects tested. Mild reductions in leukocyte (lymphocyte) counts were not considered adverse in the only repeated dose oral rat study. The single and repeated dose human and animal studies are in agreement regarding the lack of any health hazard from oral or parenteral exposure to this chemical. The mode of action of dodecanedioic acid is well understood. The chemical can be metabolized in the liver by the fatty acid β-oxidation pathway, and it can also be produced in the liver from dodecanoic acid, a common food oil component, by ω-oxidation. A *Salmonella typhimurium* reverse mutation assay produced negative results, as did a mouse bone marrow micronucleus assay. The only repeated dose oral study in laboratory animals was not adequate to address the carcinogenic potential of this compound. However, there is considerable human exposure to dodecanoic acid from food sources, and the human body is capable of producing dodecanedioic acid in the liver from dodecanoic acid by ω-oxidation. Based on negative findings for mutagenicity and clastogenicity, and on the extent of human exposure over time, dodecanedioic acid is *not likely to be carcinogenic to humans* based on U.S. EPA guidelines.
CONCLUSIONS	The existence of naturally occurring dodecanedioic acid or its precursor (dodecanoic acid) in edible plant and animal products as well as the existence of normal metabolic pathways for handling dietary dicarboxylic acids, which dodecanedioic acid has been shown to follow, suggest the potential for human toxicity is low. Based on the results of controlled human studies of the use of this chemical for parenteral nutrition, the drinking water action levels established in this document are protective of human health.