

US DMF



# Vitamin E TPGS NF Grade

For Pharmaceutical, Nutraceutical and Personal Care Innovation

## Chemical Name

d- $\alpha$  tocopheryl polyethylene glycol 1000 succinate

## Synonyms/Acronyms

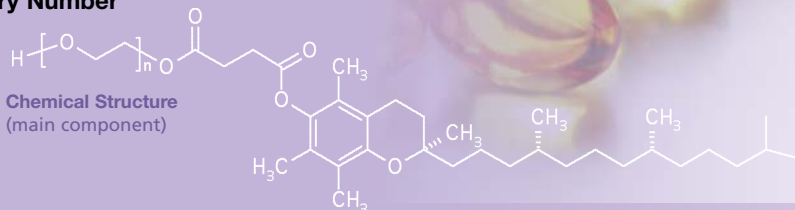
Vitamin E TPGS or TPGS

Tocophersolan (INCI and USAN)\*

Tocofersolan

## CAS Registry Number

9002-96-4



Isochem Vitamin E TPGS is a multi role excipient used in nutraceutical and pharmaceutical applications. Vitamin E TPGS has shown proven and recognized properties to improve **bioavailability** of poorly absorbed drugs acting as an **absorption and permeability** enhancer. As a water soluble compound, Vitamin E TPGS is also used as an efficient source of natural **Vitamin E**, both for therapeutic purposes and nutrition.

- Pharmaceutical and Nutraceutical application
- Food and beverage
- Cosmetic application
- Personal care
- Nutritional supplements

## Formulation using Vit E TPGS:

A lot of pharmaceutical companies have been incorporating Vitamin E TPGS mainly in oral dosage forms for years but new delivery applications are being investigated :

- parenteral delivery
- nasal delivery
- ophthalmic delivery
- dermal delivery
- ...

## Regulatory status

A monograph for Vitamin E TPGS is published in the current USP/NF.

Type II DMF for Isochem Vitamin E TPGS in the US (DMF includes impurities profile guaranty in addition to USP/NF standard).

**DMF number: 23823**

\* INCI: International Nomenclature of Cosmetic Ingredients - USAN United States Adopted Names

"THE KEY SOLUTION PROVIDER"



## Isochem: A recognized and established partner to serve your innovation

Isochem vitamin E TPGS is prepared by esterification of the carboxylic group of crystalline d- $\alpha$ -tocopheryl succinate with polyethylene glycol 1000. The manufacturing process is fully validated.

Isochem Vitamin E TPGS is manufactured in France in state of the art **FDA audited cGMP facilities**. Isochem has been granted a certificate of GMP compliance for the production of Vitamin E TPGS by the Drug French Authorities, AFSSAPS (Agence Française de Sécurité Sanitaire des Produits de Santé).

Isochem offers to the market a production capacity in **hundred of tons** scale added to supply chain security of **two qualified production sites**.

Isochem has multi sourced approvals of key raw materials complying with Pharmacopeia in order to secure its supply chain.

### Other quality statements

- Meeting kosher certification requirements
- Ingredients free of GMO (Genetic Modified organisms ) and BSE/TSE (Bovine Spongiform Encephalopathy / Transmissible Agents of Animal Spongiform Encephalopathy).
- Certificates are available upon request

### Safety and toxicology

A large number of studies to address the safety of Vitamin E TPGS have been conducted in the last decades both in humans and in animals (see references page 4). Studies to assess the safety and bioavailability of Vitamin E TPGS for use in food particularly for nutritional/medical purposes have been conducted by EFSA (European Food Safety Authority) (EFSA Journal (2007) 490, 1-20). From toxicology studies, an overall no-observed-adverse-effect level (NOAEL) of 1000mg/kg body weight per day can be derived. Vitamin E TPGS is not genotoxic.

### Packaging:

Isochem Vitamin E TPGS is available in :

- 1 kg in glass bottle,
- 20 kg in polypropylene drum with full opening lid,
- 100 kg in epoxy coated steel drum with full opening lid and 2 stainless steel bungs, 3/4" and 2".

All packages are heat resistant up to 65°C which enables the customers to mobilise the product for handling. The total opening and bunds offer versatile options of drum emptying. Internal and external coating complies with FDA, BAG, EC1895/2005 (Epoxy Derivatives restrictions), AP 96 (5) council of Europe Resolution (Surface coating intended to be on contact with food).

### Transport:

Material Safety Data Sheet disclosing safety precautions for handling and storage is available upon request.

Vitamin E TPGS is not classified as a dangerous good.



Samples for R&D work are available upon request





## Toxicology Data

<b>Oral LD-50</b>	Higher than 7,000 mg/kg in rat (highest dose tested) Ref: Journal of Agricultural and Food Chemistry (1977), 25(2), 273-8	
<b>Skin LD-50</b>	Higher than 2,000 mg/kg in rat (highest dose tested)	
<b>Skin Irritation</b>	No effect	
<b>Eye Irritation</b>	Slight effect	
<b>Skin Sensitization</b>	None (guinea pig)	

## Physical and chemical properties

### Chemical Abstract Index name:

Poly(oxy-1,2-ethanediyl),  $\alpha$ -[4-[[[(2R)-3,4-dihydro-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-2H-1-benzopyran-6-yl]oxy]-1,4-dioxobutyl]- $\alpha$ -hydroxy-

**Empirical Formula:**  $C_{33}O_5H_{54}(CH_2CH_2O)_n$

**Molecular Weight:** 1513 (approx)

### Physical form:

Vitamin E TPGS is water-soluble waxy solid with low melting point.

**Color:** White to light tan

### Gardner Color:

Less than 10 (generally less than 5)

### Vitamin E content (d- $\alpha$ -tocopherol):

25 % minimum weight basis; standard range 25-30 %

**Potency UI/g:** 428-446

**Acid Value:** 0.027 meq/g max

### Reactivity:

Vitamin E TPGS reacts with alkali or nucleophiles, very low reactivity with air

### Stability of aqueous solution:

Data of stability solution at various pH will be available soon.

**Specific Gravity:** 1.06 at 50°C to 1.03 at 90°C

**Melting Point:** 38 °C (range 37-41)

**Heat of melting:** 99.8J/g

**Heat capacity:** 1.7 J/g.K

### Solubility In Water:

up to 20 g/ 100ml of water at room temperature (3 hours)

**Specific Rotation [ $\alpha$ ]:** Not less than + 24°

**Viscosity:** 300-400cp at 50°C, data for higher temperatures will be available soon

### Amphiphilic (Surface-Active) Properties:

Vitamin E TPGS has amphiphilic properties with a polar hydrophilic head (polyethylene glycol 1000) and a lipophilic tail (phytyl chain of d- $\alpha$ -tocopherol).

**HLB (hydrophile/lipophile balance):** 13

### Critical Micellar concentration:

0.02 weight % at 37°C. Vitamin E TPGS forms various liquid crystalline forms with water. Numerous micron level particle size diameter of liquid emulsions and solid formulations with TPGS are reported

## Stability

Vitamin E TPGS is a highly stable form of vitamin E. It is stable when exposed to oxygen, heat, light, or oxidizing agents. It is unstable to alkali. Vitamin E TPGS is known to be stable excipient with a shelf-life of 4 years when stored in the original unopened container at room temperature. Nowadays, Isochem' stability study disclose data up to 3 years (on going study). Vitamin E TPGS is stable under the conditions of heat sterilization.

### Thermal degradation temperature

No exotherm up to 300 °C

### Oxydative thermal degradation

219°C

### Stability under repetitive heat/cool/cycles

Stable 20 cycles (between 0 to 85°C)

### Stability at 65°C

5 days

### Flash Point

278°C

### Sterilization

Stable when exposed to approximately 125 °C for 1 hour

### Shelf-life

Isochem Vitamin E TPGS FG and NF grades are labelled with a 4 year shelf-life from the date of manufacturing when stored in the original sealed unopened container



## References:

### Safety studies references:

Monice Zondlo Fiume, Final Report on the Safety Assessment of Tocopherol, Tocopheryl Acetate, Tocopheryl Linoleate, Tocopheryl Linoleate/Oleate, Tocopheryl Nicotinate, Tocopheryl Succinate, Dioleoyl Tocopheryl Methylsilanol, Potassium Ascorbyl Tocopheryl Phosphate, and Tocophersolan; *International Journal of Toxicology*, (2002), 21(Suppl. 3), 51-116.

National Cancer Institute, "One-Year Chronic Oral (Intubation) Study In Dogs and Rats", (National Institute of health, Bethesda M. D., 1994).

Friman, S., Leandersson, P., Tagesson, C., and Svanvik, J. Biliary Excretion of Different Sized Polyethylene Glycols in the Cat. *J Hepatology*, 1990, 11: 215-220.

Bland, J. and Prestbo, E. Vitamin E : Comparative absorption studies, *International Clinical Nutrition review*, 1984, 4(2), 82-86.

Krasavage W.J., Terhaar C.J., d-alpha-Tocopheryl poly(ethylene glycol) 1000 succinate. Acute toxicity, subchronic feeding, reproduction, and teratologic studies in the rat *Journal of Agricultural and Food Chemistry*, (1977), 25(2), 273-8.



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