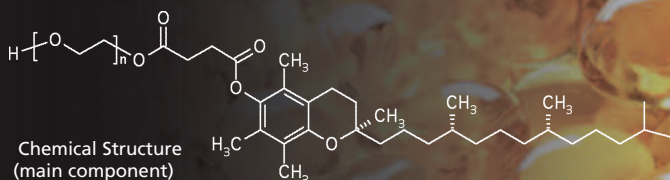


# Vitamin E TPGS

## NF\* and Food Grade



**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

PMC 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 vitamins micro-nutrients acting as an **absorption and permeability** enhancer and to develop Self-Emulsifying Drug Delivery System (SEDDS) for poorly soluble drugs as an emulsifier. 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. In Addition Vitamin E TPGS has physical properties that make it a relevant plasticizer for innovative technologies in the pharmaceutical industry such as hot melt extrusion.

#### APPLICATIONS

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

\*NF: National Formulary (US)

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

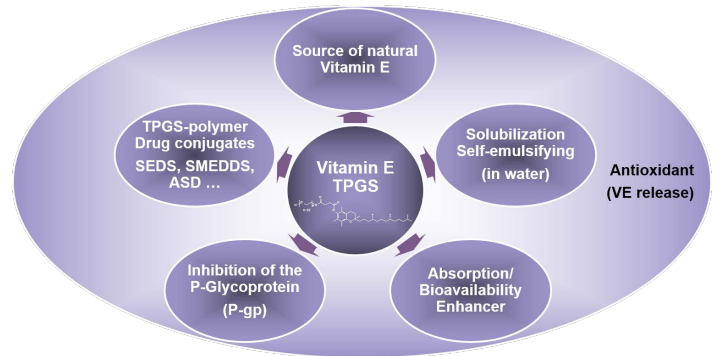
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### FORMULATION USING VITAMIN E TPGS

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

- parenteral delivery
- topical delivery
  - dermal
  - nasal
  - pulmonary



### REGULATORY STATUS

**FDA:** The FDA has not challenged a self affirmed GRAS (Generally Recognized As Safe) status made by Eastman and approved products containing Vitamin E TPGS. It is registered as Inactive Ingredient under the name **Tocophersolan (UNII: O03S90U1F2)**.

**USP :** Monograph for Vitamin E TPGS is published in the current USP-NF.

**CIR:** Expert Panel (US): safe as **used in cosmetic** formulation.

**PMC Isochem owns a Type II DMF** in the US for Vitamin E TPGS. PMC Isochem's DMF includes impurity profile guaranty in addition to USP/NF.

**PMC ISOICHEM's DMF number: 23823**



### PACKAGING

PMC Isochem Vitamin E TPGS is available in:

- 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 bungs offer versatile options of drum emptying. For R&D purpose, 1 Kg in glass bottle is available upon request.

### 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.

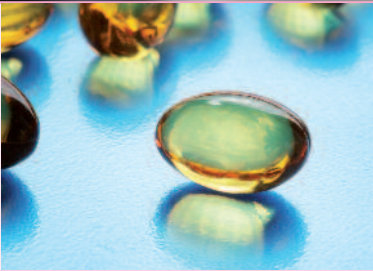
### HANDLING

Standard operating condition for melting, emptying drums and handling liquid TPGS is available upon request.

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:

$\alpha$ -[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]- $\omega$ -hydroxy-poly(oxy-1,2-ethanediyl)]

**Empirical Formula:** C<sub>33</sub>O<sub>5</sub>H<sub>54</sub>(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>

**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:

~ 20% at 20°C

Forms gels between 20 to 90% mixture with water.

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

**Viscosity:** ~ 390cP at 50°C, (See Viscosity = f(T°C) scheme page 4).

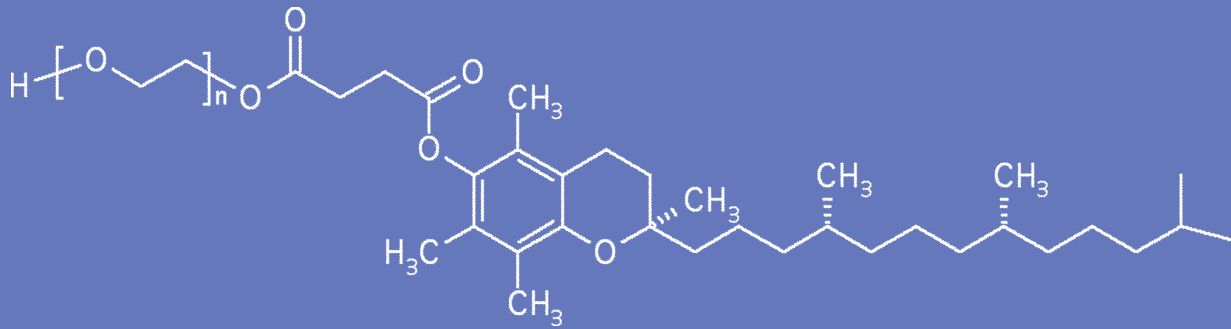
### Amphiphilic (Surface-Active) Properties:

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

### CMC (Critical Micelle 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.



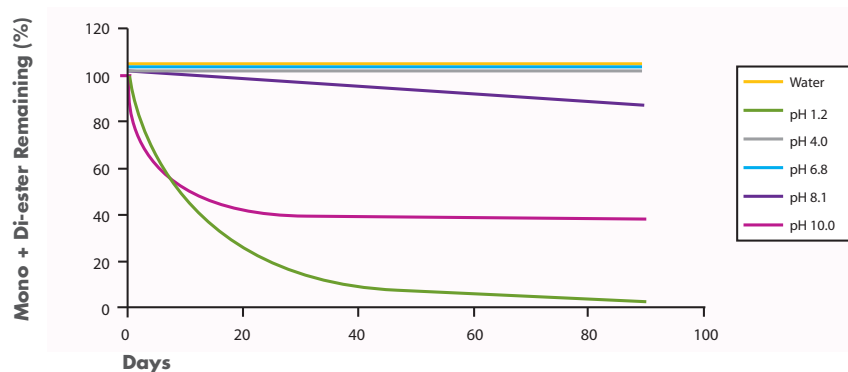
## STABILITY

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 a stable excipient with a shelf-life of 4 years when stored in the original unopened container at room temperature. (Statement available upon request)

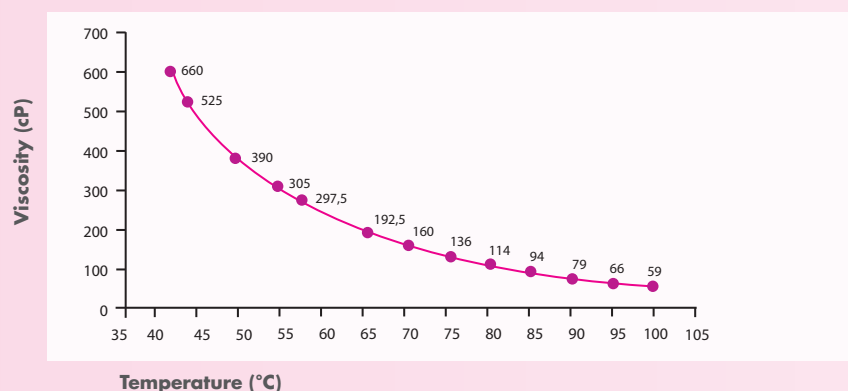
<b>Thermal degradation temperature</b>	No exotherm up to 300 °C
<b>Oxydative thermal degradation</b>	219°C
<b>Flash Point</b>	278°C
<b>Sterilization</b>	Stable when exposed to approximately 125 °C for 1 hour
<b>Stability under repetitive heat/cool/ cycles (Differential scanning calorimetry)</b>	Stable 20 cycles (between 0 to 85°C)
<b>ICH stability study</b>	48 months at 25°C 6 months at 40°C
<b>Stability in commercial packaging after 5 cycles heat at 60°C /cool at 20°C</b>	Conform to the specification

### Stability of vitamin E TPGS (10% aqueous solution at 37°C)



## VISCOSITY

### Viscosity values (cP) of Vitamin E TPGS



# Vitamin E TPGS

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### PMC ISOCHEM: A RECOGNIZED AND ESTABLISHED PARTNER TO SERVE YOUR INNOVATION

PMC 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.

PMC Isochem Vitamin E TPGS is manufactured in France in state of the art **FDA audited cGMP facilities**. PMC Isochem has been granted a certificate of GMP compliance for the production of Vitamin E TPGS by the French Drug Authorities, ANSM (Agence Nationale de Sécurité du Médicament).

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

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

#### Other quality statments

- Meeting kosher certification requirements
- Ingredients free of GMO (Genetic Modified organisms) and BSE/TSE (Bovine Spongiform Encephalopathy / Transmittable 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.



# Vitamin E TPGS

## NF and Food Grade

### REFERENCES

Further references are available on request

#### 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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