Effective: April 15, 2016
Supersedes: October 8, 2015

Dow Propylene Glycol PG USP/EP and PuraGuard™ (referred to as PG USP/EP)

Elemental Impurities/Metal Impurities

USP general chapter <232> "Elemental impurities - Limits" and USP <233> "Elemental Impurities – Procedure" are expected to become effective on January 1, 2018. ICH Q3D Guideline: "Impurities: Guideline for Metal Impurities" was published as an EMA guideline in early 2014 (EMA/CHMP/ICH/353369/2013) with implementation dates of June 2016 for new marketing authorization applications and December 2017 for all existing products on EU market. The revised European Pharmacopoeia chapter 5.20 is a verbatim reproduction of ICH Q3D with the same implementation dates.

While USP <232> and ICH Q3D are not mandatory for excipients, finished drug manufacturers and authorization holders must assess all sources of elemental impurities in their finished drug product.

This letter is intended to provide elemental impurity information for Dow PG USP/EP as per USP <232> and ICHQ3D. It is valid for Dow manufactured, factory packed and sealed material.

Dow currently performs the following elemental testing on PG USP/EP:

- Annually - Lead as per FCC method, NMT 1 mg/kg
- Quarterly - Heavy Metals as per USP, EP and JP. Substances that typically will respond to this test are lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver copper and molybdenum
- Iron as per ASTM E202, max. 0.30 mg/kg.

PG USP/EP from Dow is synthesized from propylene oxide and water without the use of metal catalysts or metal reagents, therefore no specific analysis for them is conducted. Elemental impurities are not intentionally added.

Based on the above, none of the metals listed below are known to be present in Dow PG USP/EP from residues of catalysts or reagents:

- Arsenic (inorganic), As
- Cadmium, Cd
- Mercury (inorganic), Hg
- Lead, Pb
- Cobalt, Co
- Nickel, Ni

- Vanadium, V
- Silver, Ag
- Gold, Au
- Iridium, Ir
- Osmium, Os
- Palladium, Pd
- Platinum, Pt
- Rhodium, Rh
- Ruthenium, Ru
- Selenium, Se
- Thallium, Tl
- Barium, Ba
- Chromium, Cr
- Copper, Cu
- Lithium, Li
- Molybdenum, Mo
- Antimony, Sb
- Tin, Sn
- Aluminum, Al

Results from limited spot analysis of PG USP/EP for heavy metals (Cd, Cr, Cu, Mo, Ni, Os, Pt, Rh, Ru, V, Hg, Ir, As, Pb and Pd) confirm the absence of these metals at a detection limit of 1 mg/kg. The analysis is performed by Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) and/or Cold Vapor Hydride Atom Absorption Spectrometry (CVAAS).

Should you have any questions or require further information, please contact us via our web site at http://dowac.custhelp.com/ (Answer Center, Ask a Question tab).

Effective: February 7, 2017
Supersedes: April 8, 2010

Dow Propylene Glycol USP/EP (PG USP/EP)
PuraGuard™ Propylene Glycol USP/EP

Composition and Trace Analysis Information – Absence of Melamine

For information on the components of our product(s) and their concentration, please refer to the Safety Data Sheet (SDS) and the Sales Specification. Hazardous constituents will be listed in the Composition Section of the SDS for this product if present at levels of 1% or above (by weight), or at any lower levels as required by applicable legislation, including but not limited to, carcinogens, mutagens, reproductive toxicants and sensitizers. In addition, consult the Hazardous Decomposition Products section of the SDS and the Sales Specification for further information.

Dow does not routinely analyze for additional materials that are not listed in the SDS or Sales Specification. Melamine is not used in the production process, is not intentionally added nor known to be present in factory packed and sealed PG USP/EP or PuraGard ™ from Dow.

Should you have any questions or require further information, please contact us via our web site at http://dowac.custhelp.com/ (Answer Center, Ask a Question tab).

Dow Answer Center

Propylene Glycol USP/EP - *Drug Master File* or Certificate of Suitability

Answer ID 7065 | Updated 08/12/2014 03:30 PM

Is there a *Drug Master File* (DMF) or Certificate of Suitability to the European Pharmacopoeia (CEP) for PG USP/EP?

Neither a *Drug Master File* (DMF) nor a Certificate of Suitability to the European Pharmacopoeia (CEP) exists for *Propylene Glycol* USP/EP (PG USP/EP) from Dow. DMF's and CEP's are optional and not common practice for an excipient like PG USP/EP in pharmaceutical applications. Instead of providing such detailed dossiers of information, Dow supports pharmaceutical customers by providing the specific information needed for submitting new *drug* applications. Dow PG USP/EP is manufactured in Dow facilities in the U.S., Germany, Brazil and Australia. Good Manufacturing Practice (GMP) principles, as published by the International Pharmaceutical Excipients Council (IPEC) and Pharmaceutical Quality Group (PQG) in the Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients 2006, are applied by Dow during the manufacturing and handling of PG USP/EP. The product is tested and complies with all items of the current USP, EP, JP and FCC. The production locations are ISO 9001:2000 certified. More information about PG USP/EP can be obtained from Dow's website at http://www.dowpg.com. A document entitled, Questionnaire Response Document; PG USP/EP Current Good Manufacturing Process, provides an overview of Dow's GMP program for PG USP/EP and is located at http://www.dow.com/propyleneglycol/tech/.

Print Email link to answer Notify Me

Dow Answer Center

Propylene Glycol USP/EP - Heavy Metal Content

Answer ID 7697 | Updated 03/04/2014 01:21 PM

Are heavy metals used in the manufacture of PG USP/EP?
European standard EN 71 regarding the safety of toys, and the U.S. equivalent standard ASTM F963, "Standard Consumer Safety Specification on Toy Safety", indicate maximum migration levels of the heavy metals; antimony, arsenic, barium, cadmium, chromium, lead, mercury and selenium.
None of the above heavy metals are used in the manufacture of PG USP/EP from Dow, therefore no specific analysis for them is conducted, nor are they included in the sales specification. Results from limited, spot analyses of PG USP/EP from Dow, confirm the absence of all the above metals with a detection limit of 1 ppm, well below the specified maximum values specified in EN 71 and ASTM F963.

This information is valid for *Propylene Glycol* USP/EP manufactured by Dow and delivered in factory packed and sealed containers.

Print Email link to answer Notify Me

Effective: March 4, 2014
Supersedes: September 12, 2011

Dow Propylene Glycol PG USP/EP

Residual Solvents

Dow Propylene Glycol USP/EP complies with the requirements for Residual Solvents per the current edition of the United States Pharmacopeia / National Formulary (USP/NF) General Chapter <467> and the current version of ICH Residual Solvents Guideline EMA/CHMP/ICH/82260/2006 (ICH 3Qc).

There are no Class 1, 2, 3, Table 4 or any other solvents not listed in USP/NF General Chapter <467> used or produced in making PG USP/EP. Based on Paragraph 6 of <467>, no analysis for solvents is conducted.

Should you have any questions or require further information, please contact us via our web site at http://dowac.custhelp.com/ (Answer Center, Ask a Question tab).

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Propylene Glycol USP/EP - Direct Food Additive

Answer ID 7243 | Updated 02/13/2011 04:29 AM

What direct food applications may PG USP/EP be used in as an additive for the food processing industry?

Propylene Glycol USP/EP is widely used in the food-processing industry as an additive. In direct **food** applications, PG USP/EP can **function** as a:

- Solvent and carrier in many **flavor** formulations for the processed **food** and beverage industry
- Solvent and carrier for colors, antioxidants, enzymes and emulsifiers
- Plasticizer and softening agent for food-contact items such as cork seals
- **Flavor** extraction solvent and processing aid in the isolation of natural **flavoring** materials, for example, extracting vanilla from vanilla beans
- Humectant and stabilizer in prepared fruits, vegetables and bakery goods (except in Europe)

When employed as a direct **food** additive, the caloric value of **propylene glycol** is defined as four calories per gram, according to the general definition for a carbohydrate given in the U.S. FDA 21CFR101.9(c)(1)(I)(B).

Dow Answer Center

Propylene Glycol USP/EP - Pharmaceutical Regulatory Status

Answer ID 7242 | Updated 12/11/2013 12:10 PM

What is the pharmaceutical regulatory status of PG USP/EP?
Dow PG USP/EP is tested against and complies with the specific requirements of:

- United States Pharmacopeia (USP)
- European Pharmacopoeia (EP)
- Japanese Pharmacopoeia (JP)

All original requirements of the different monographs are included in Dow's certificate of analysis for PG USP/EP. Comprehensive analyses for all pharmacopeia items are carried out on a statistical, quarterly basis. Dow PG USP/EP also meets the requirements and standards of the:

- U.S. Food and Drug Administration (U.S. FDA)
- Food Chemicals Codex (FCC)
- Brazilian Pharmacopoeia (Farmacopéia Brasileira)

Due to its extremely low toxicity and long history of safe use, PG USP/EP is "generally recognized as safe" (GRAS) by the U.S. Food and Drug Administration (U.S. FDA) for use in pharmaceuticals.

Dow PG USP/EP also complies with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guideline Q3C "Impurities: Guideline for Residual Solvents."[1] It is manufactured from hydrocarbon raw materials in a solventless process and does not contain any of the class 1, 2 and 3 solvents listed in this ICH guideline.

Dow PG USP/EP's certified premium purity of greater than 99.8 percent is maintained along the supply chain by producing and handling this pharmaceutical excipient according to Good Manufacturing Practice (also known as current GMP or cGMP) principles, as issued by the International Pharmaceutical Excipients Council (IPEC).[2]

[1] Impurities: Guideline for Residual Solvents, ICH Guideline Q3C, CPMP/ICH/283/95

[2] The Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients, International Pharmaceutical Excipients Council (IPEC) and Pharmaceutical Quality Group (PQG), 2006

Print Email link to answer Notify Me

The Dow Chemical Company
Midland, MI 48674
U.S.A.

July 1, 2008

CHANGE NOTIFICATION – PROPYLENE GLYCOL USP/EP SALES SPECIFICATION AND COA

Dear Customer:

We would like to announce that The Dow Chemical Company will change the following test item currently found on the Sales Specification 111814-S for Propylene Glycol USP/EP**.**

Specifically, “Organic Volatile Impurities” will be changed to “Residual Solvents.”

This change is in accordance to USP 31-NF 26 requirements which will become effective July 1, 2008.

The change does not affect the quality of the product.

This same change will also be reflected on any Certificate of Analysis (CoA) issued after July 1, 2008.

If you have any questions concerning this change, please contact Frank Schwerdtner or Dennis Reiswig.

Sincerely,

Frank Schwerdtner *Dennis Reiswig*

Frank Schwerdtner
Dow Deutschland, Stade, Germany
BAS; Quality Assurance/ Quality Control
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Dennis Reiswig
The Dow Chemical Company, Freeport, Texas
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DReiswig@dow.com

The Dow Chemical Company
Midland, MI 48674
U.S.A.

December 06, 2007

MODIFICATION OF DOW'S ASSAY TESTING METHOD FOR PG USP/EP

Dear Customer:

I would like to inform you of a change in the testing of Propylene Glycol USP/EP from The Dow Chemical Company. Effective December 15, 2007, testing values reported for Assay, currently using USP and FCC methods, will be determined using a validated Dow gas chromatography method, DOWM 100687, which relies on the latest analytical technology.

This change requires an amendment of the sales specification for Propylene Glycol USP/EP, number 111814-S, where the following note will be added:

Values reported for Assay under USP and FCC are determined using a validated Dow GC Method, DOWM 100687. Comparative validation to each Pharmacopeia listed is deemed impractical due to the following facts:

A. *Compendia methods require chromatographic equipment which is no longer readily available.*

B. *Dow's validated GC Method DOWM 100687 uses the latest technology.*

The change does not affect specification limits.

As soon as the specification is available, you will receive a copy for your documentation. The resulting Certificate of Analysis (CoA) will be changed accordingly.

Sincerely,

Dr. Frank Schwerdtner
Quality Control/ Quality Assurance
PO/PG Europe

The Dow Chemical Company
U.S.A.

March 23, 2011

Subject: Announcing DOW PuraGuard™ Propylene Glycol USP/EP and Third-Party Quality IPEA Certification

Dear Dow Distributor:

The Dow Chemical Company (Dow) is pleased to announce the launch of a new trade name for our current Propylene Glycol (PG) USP/EP product – **DOW PuraGuard™ Propylene Glycol USP/EP**. The DOW PuraGuard™ PG USP/EP name reflects our high-level product purity, quality standards and ***new*** **third-party IPEC Good Manufacturing Practices (GMP) quality certification from International Pharmaceutical Excipient Auditing (IPEA)** for our North American manufacturing facilities in Freeport, Texas and Plaquemine, Louisiana.

IPEA is a subsidiary of the International Pharmaceutical Excipients Council-Americas (IPEC), and is accredited by the American National Standards Institute (ANSI) and recognized by the FDA for excipient certification. IPEA Certification confirms that excipient manufacturers are in conformance with the IPEC-Pharmaceutical Quality Group (PQG) excipient GMP guide.

DOW PuraGuard™ PG USP/EP follows the same manufacturing process and meets the same product composition and impurity profile as PG USP/EP. This includes all product characteristics such as testing, assay specification of 99.8%, non-detectable MEG/DEG contents, two year shelf life, quality control and global documentation.

Currently, Dow is the *only* propylene glycol supplier to have received IPEA certification. In addition to this third-party quality certification, DOW PuraGuard™ PG USP/EP is reinforced by our Purity Plus program of high quality, application of IPEC-PQG GMP guidelines, global supply chain and exceptional solutions.

Be sure to visit our NEW website at www.dowpg.com to find a variety of resources:

- NEW - DOW PuraGuard™ PG USP/EP Purity Plus **overview brochure**
- NEW - DOW PuraGuard™ PG USP/EP **product application brochures** for pharmaceutical, food, personal care and animal feed
- NEW - **Video** highlighting the benefits of DOW PuraGuard™ PG USP/EP
- Online Answer Center
- Contact us to discuss obtaining a copy of our IPEA Certificate
- View a variety of technical datasheets, safety data sheets and fact sheets for propylene glycols

Dow remains committed to providing our customers with among the very best quality, supply chain and exceptional solutions for propylene glycol products. For more detail or answers to additional questions, please contact your sales professional.

Sincerely,

Paul Simons
PG Global Product Director & Strategic Marketing
The Dow Chemical Company

Erika Vergara
Business Quality Leader
The Dow Chemical Company

For more information about Dow's propylene glycol products, visit www.dowpg.com.

Enclosed: DOW PuraGuard PG USP/EP Distribution Q&A

For Reference: Distribution Q&A

QUESTION	ANSWER
Can a Dow distributor use the DOW PuraGuard™ trademark or Certificate of Analysis?	No, they may not. The trademark is a legally reserved name for exclusive use by Dow alone. When DOW PuraGuard™ PG USP/EP is purchased by the distributor, title and risk of loss transfers from Dow to the distributor; Dow cannot be held liable for the distributor's actions. Distributors will need to develop their own COA to be shared with and recognized by customers. In any kind of distributor product handling, (i.e. unloading and repackaging, unloading into a storage tank, or unloading into another transportation) all activities involving breaking bulk and transloading from one bulk container to another (i.e. from rail car to truck, truck to totes/drums, etc.) will be done under the distributor's COA and not Dow's. Dow is not responsible for quality level of the product once handled by the distributor.
Can customers purchase DOW PuraGuard™ PG USP/EP from Dow distributors?	In 2Q11 Dow will offer drummed DOW PuraGuard PG USP/EP. If a customer wants to purchase DOW PuraGuard™ PG USP/EP, they are still able to purchase it from the Dow distributor, but only if the distributor sells them the Dow-drummed DOW PuraGuard. Distributors may purchase bulk DOW PuraGuard PG USP/EP and break the bulk themselves, but are not able to sell the DOW PuraGuard brand name unless they sell the Dow-drummed DOW PuraGuard. The PuraGuard(TM) trademark belongs to Dow, and distributors need their own COA to document quality processes and product handling. If bulk must be broken, they can only certify they are selling PG USP/EP manufactured by Dow to their customers.
If a Dow distributor is not authorized to drum DOW PuraGuard™ PG USP/EP, can they buy drummed product from Dow for customers who want it?	Yes. In 2Q11 Dow will be offering drummed DOW PuraGuard PG USP/EP to customers. Distributors may purchase the drummed PuraGuard product and sell to their customers.
Will distributor customers still have the same lot control traceability from Dow?	Yes, the process is the same and lot control traceability are the same.
Who should I contact about distribution questions?	For answers to further questions regarding distributor sales, please contact: Paul Simons - PMSimons@dow.com or 989-638-7956 Patty Rogowski - PKRogowski@dow.com or 989-636-6561

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Propylene Glycol USP/EP - HACCP Plan Compliance

Answer ID 7063 | Updated 03/09/2011 10:46 AM

What is the HACCP plan for PG USP/EP?

Compliance with Hazard Analysis and Critical Control Point or HACCP is a systematic approach to the identification, evaluation, and control of food safety hazards.

Dow has determined that a HACCP plan for PG USP/EP is not necessary due to its existing quality and regulatory compliance programs.

PG USP/EP is an excipient in pharmaceutical products and is manufactured according to the guidelines defined in “The IPEC-PQG Good Manufacturing Practices Guide for Bulk Pharmaceutical Excipients” © 2006 The International Excipients Pharmaceutical Council, which are more stringent than the principles of HACCP.

PG USP/EP is manufactured from hydrocarbon raw materials in a closed, continuously-operated process utilizing dedicated equipment. The process is not open to the environment at any time during normal operations, prior to loading it into shipping containers, so contamination by foreign materials is unlikely. The material is tested for compliance with the U.S., European, and Japanese Pharmacopoeia plus the U.S. Food Chemicals Codex, all of which require that the material not be contaminated or adulterated.

The Dow Chemical Company
U.S.A.

Effective: 2/18/2008
New

Propylene Glycol USP/EP

Latex/Natural Rubber Content

The specification for the requested product has been reviewed for the origin of raw materials and specific ingredients. There is no "natural rubber" latex used in the manufacture or in the process for producing this product. This is a synthetically produced product.

If you have any questions or require further information, please contact us via our web site at www.dow.com.

Sincerely,

Connie L. Defoid

Global Director of Product Regulatory Management
The Dow Chemical Company
www.dow.com/propyleneglycol (Dow Answer Center)

The Dow Chemical Company
U.S.A.

July 15, 2010

Propylene Glycol USP/EP (PG USP/EP)

Availability of DMF or CEP

Neither a Drug Master File (DMF) nor a Certificate of Suitability to the European Pharmacopoeia (CEP) exists for Propylene Glycol USP/EP (PG USP/EP) from Dow. DMF's and CEP's are optional and not required for an excipient like PG USP/EP in pharmaceutical applications. Instead of providing such detailed dossiers of information, Dow supports pharmaceutical customers by providing the specific information needed for submitting new drug applications. Dow PG USP/EP is manufactured in Dow facilities in the U.S., Germany, Brazil and Australia. Good Manufacturing Practice (GMP) principles, as published by the International Pharmaceutical Excipients Council (IPEC) and Pharmaceutical Quality Group (PQG) in the Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients (2006), are applied by Dow during the manufacturing and handling of PG USP/EP. The product is tested and complies with all items of the current USP, EP, JP and FCC.

If you have any questions or require further information, please contact us via our web site at www.dowpg.com.

Sincerely,

Kim Bennett
NA Technical Service
Performance Products
The Dow Chemical Company
NA CIG Phone: (800) 447-4369 Fax: (989) 832-1465
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Dow Deutschland Anlagengesellschaft mbH
Postfach 1120
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January 25th, 2012

Microbiological Contamination and Propylene Glycol USP/EP

Dear Valued Customer,

The following statement should answer your questions about Dow Propylene Glycol USP/EP (PG USP/EP) and potential microbiological contamination.

Dow's Propylene Glycol USP/EP is manufactured from propylene oxide derived from synthetic hydrocarbons, and water from condensed steam, at high temperature and pressure in a closed process using dedicated equipment, without the use of additives or process aids. No material used in the production process is of animal or plant origin. PG USP/EP is transported in sealed containers that are either dedicated to its use or that have followed a strict policy for limiting prior cargoes, to prevent contamination.

PG USP/EP from all our production sites is tested for microbiological contamination regularly. The testing is performed following the guidelines given in the European Pharmacopoeia and meets the requirements of other pharmacopeias. No microbiological contamination has been detected at a 10 CFU/g detection limit in any sample of DOW Propylene Glycol USP/EP since the test program has been initiated in 1988.

I hope this information is helpful in your use of our product. For more detailed information, please visit our web site www.dowpg.com, visit our online Dow Answer Center, call our Customer Information Group (CIG) at +800 3 694 63 67 (toll free) or +31 11567 2626 (toll phone), fax CIG at +31 11567 2828 or email us at dowcig@dow.com.

Yours sincerely,

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