Propylene Glycol

- **Propylene Glycol Ph. Eur. / USP**
- **Propylene Glycol Ph. Eur. / USP / JP**
- **Propylene Glycol Ph. Eur. / USP / JP parenteral grade**

Aug. Hedinger GmbH & Co. KG

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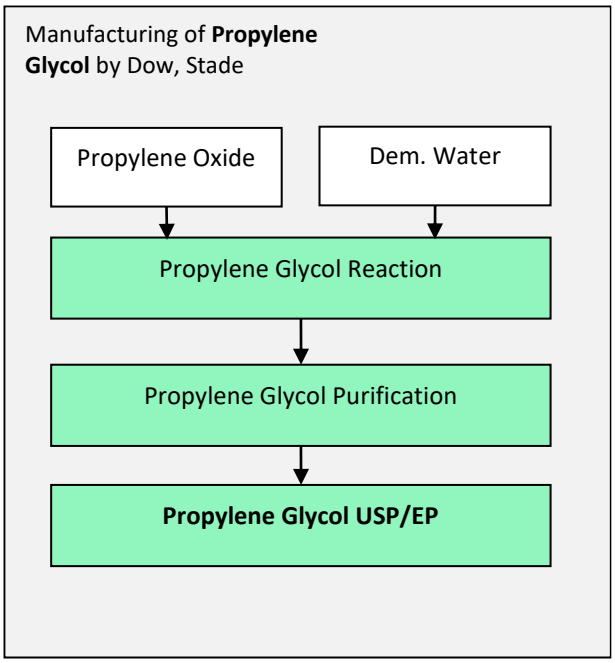
Manufacturing according to IPEC-PQG GMP* by Dow, Stade



- Manufactured by Dow Deutschland Anlagengesellschaft mbH at a dedicated facility in Stade, Germany
- Manufacturing complies with requirements of IPEC-PQG GMP Guideline for Bulk Pharmaceutical Excipients
- Dedicated process equipment
- Filtration unit before loading gantry to avoid particles
- Full traceability to raw materials and their analytical data

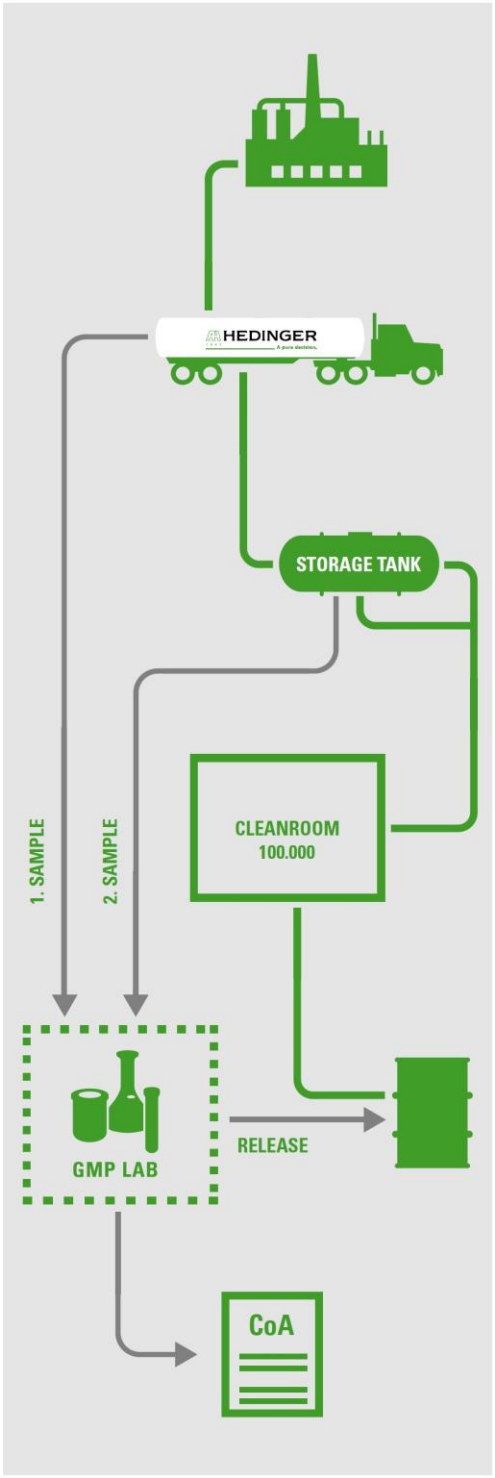
Propylene Glycol USP/EP is made from carefully monitored raw materials, and is itself manufactured and distributed under strictly controlled conditions.

* A GMP audit will be performed by a Qualified Person of Hedinger at the manufacturing facility approximately every three years. A report is available for customers after signing a Confidentiality Agreement.

Quality / Regulatory Compliance

- Dow sales specification
- Certification of each batch according to current pharmacopoeia monographs by Hedinger:
  - European Pharmacopoeia (Ph. Eur.)
  - United States Pharmacopeia (USP)
  - Japanese Pharmacopoeia (JP) on request
  - Chinese Pharmacopoeia (ChP) on request
- Questionnaire with regulatory information of the product provided by Hedinger
- Classified by the Food and Drug Administration (FDA) as Generally Recognized As Safe (GRAS)
- Fulfils requirements of current ICH Q3C Residual Solvents Guidelines
- Data on elemental impurity profile according to current ICH Q3D guideline available
- Complies with the compendial specifications of the Food Chemicals Codex (FCC)
- EU-approved food additive in accordance with E1520 (Commission Regulation (EU) No 231/2012)
- Kosher-certified
- Special grade for parenteral applications available (TAMC, TYMC, endotoxins specified)
- Confirmation for nitrosamine risk evaluation is available

Hedinger integrated GMP/GDP-System



Excipient Manufacturer
Verifiying of GMP compliance by Hedinger
via GMP audits of the manufacturing plant
"one product – one partner" strategy

Bulk Handling
(loading/transport/unloading)
Only dedicated Equipment
(for example own qualified tank trucks, hoses)
only dedicated storage tanks

Quality of Primary Packaging Material
Supplier qualification
Incoming control and release
Brand new packaging material only

Repackaging Under Controlled Conditions
in Clean Rooms Class D (100.000)
3-step air filtration
Air locks for personnel and packaging material
Repackaging in containers from 250 ml – 1.000 l

Batch-Related Full Analysis in
2 Internal GMP Laboratories
Full analysis according to all pharmacopoeias and GMP
Customised test methods
Batch release from a qualified person (QP)

Reduced Incoming Control at the
Drug Manufacturer
Hedinger's certificate of analysis enables
reduced incoming control (EU-GMP Part 1 Chap. 5)
Significant cost savings possible

Quality Assurance (QA)
Supporting all Levels
of the Supply Chain:

Documentation
According to GMP

–

Full Traceability at
Each Level

–

Training for all
Those Involved

–

Change Control

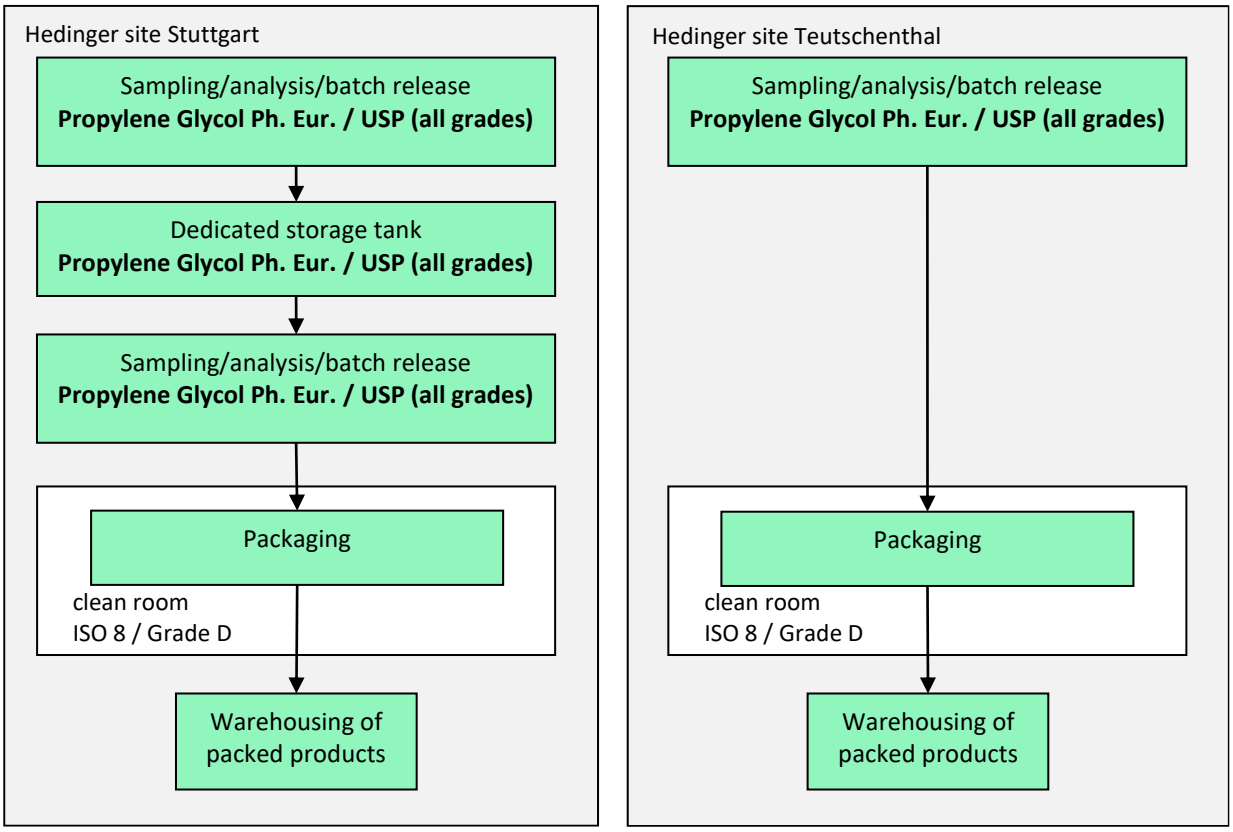
–

Regulatory Information

–

QA Agreements

Handling of Propylene Glycol by Hedinger



- Sampling by qualified sampling personnel under the responsibility of Quality Control department
- Full analysis according to Ph. Eur. and USP (JP and ChP on request) in a GMP laboratory in compliance with EU-GMP Part I, Chapter 6
- Release by Qualified Persons according to EU-GMP
- Dedicated storage tank for Propylene Glycol Ph. Eur. / USP on Hedinger site Stuttgart
- Manufacturing and repackaging in classified cleanrooms Grade D / ISO 8 (classification and operating conditions according to EU-GMP Part I, Annex 1 and ISO 14644)
- Qualification of the HVAC (Heating, Ventilation & Air-Conditioning) system
- Regular validation of cleanroom (monitoring)

Quality Control by Hedinger

The Quality Control department of Hedinger runs a full monograph testing according to current Ph. Eur. and USP (JP and ChP on request) under EU-GMP Part I conditions. Every batch is released by a Qualified Person according to EU-GMP. A Certificate of Analysis signed by a Qualified Person with all compendial data will be provided with each delivery.

- Full analysis according to Ph. Eur. and USP (JP and ChP on request)
- GMP laboratory in compliance with EU-GMP Part I, Chapter 6
  - GMP documentation of analytical results
  - Equipment qualification and maintenance
  - Out-of-specification result investigations
  - Qualification of standards and reference materials
  - Batch documentation and shelf life control of reagents
  - Regular qualification and requalification of personnel
  - Stringent pharmacopoeia revision management
  - Method validation according to ICH Q2
  - Trending and PQR

Certificates of Analysis signed by a Qualified Person

- Manufacturing authorization according to EU drug regulations
- Batch release by a Qualified Person according to EU-GMP
- Certificate of Analysis signed by a Qualified Person for each individual delivery
- Format of Certificate of Analysis according to “IPEC Certificate of Analysis Guide”
- Since all pharmaceutical analyses and Certificate of Analysis fully comply with relevant regulations, customers may reduce full incoming testing to save costs (EU-GMP I, chapter 5.35-36.)




Quality Control Laboratory, Stuttgart


Teutschenthal

Repackaging in cleanrooms by Hedinger

The product is packaged by Hedinger under clean room conditions into customized packaging sizes following EXCiPACT / IPEC-PQG GMP requirements for excipients:

- Cleanrooms according to EU-GMP Part I, Annex 1 (classification and operating conditions) and ISO 14644 (Back-Up cleanroom at Hedinger site in Teutschenthal for repackaging of Propylene Glycol in case of shut-down of the Stuttgart site)
- Grade D (100,000) / ISO 8
- Standard quantities (5 L - 1000 kg HDPE containers or 1 and 2.5 L brown glass bottle)
- Qualification of the HVAC (Heating, Ventilation & Air-Conditioning) system according to EU-GMP Part I, Annex 15, and ISO 14644
- Regular validation of cleanroom conditions (monitoring)
  - Airborne particles
  - Microbiology
- State-of-the-art preventive maintenance of HVAC systems
- Hygiene program for staff and premises
  - Regular hygiene training
  - Appropriate gowning and sanitation practices
- Qualified packaging material
  - Audited suppliers
  - Defined specifications
  - Incoming inspection with verification of key quality parameters and batch release
- Exclusively use of brand-new primary packaging materials

Repackaging of Propylene Glycol in Hedinger cleanroom Grade D

Distribution according to GTDP (Good Trade and Distribution Practice) by Hedinger and Dow

- Transport in qualified and dedicated bulk ISO containers
  - Defined preload
  - Validated cleaning procedure for foodstuff trucks
- Compliance with IPEC Good Distribution Practices Guide for Pharmaceutical Excipients and EXCiPACT GMP/GDP
  - Full traceability through documentation of the entire supply chain
  - Prevention of cross-contamination through appropriate GMP handling and use of dedicated equipment
  - Ideal storage conditions
- Transparent and short supply chain

Additional customer-specific services

- Quality assurance agreements including
  - Change control
  - Regulatory information
  - Extended liability
- GMP-Audit report by a Qualified Person about the manufacturing site available for customers after signing a Confidentiality Agreement
- Customer-specific on-site audit dates at Hedinger possible
- Customer-specific packaging sizes
- Customer-specific labelling (customer's data)
- Provision of analytical raw data (chromatograms etc.)

Parenteral Grade

- Propylene glycol is available as special grade for parenteral applications
  - Bioburden and Endotoxin specification
  - Bioburden and Endotoxin testing per batch
  - Highest level of controls during filling processes (especially qualified supervisors)
  - Key point controls during filling processes (sampling from filled containers)
  - GDP transport is available for parenteral grade products