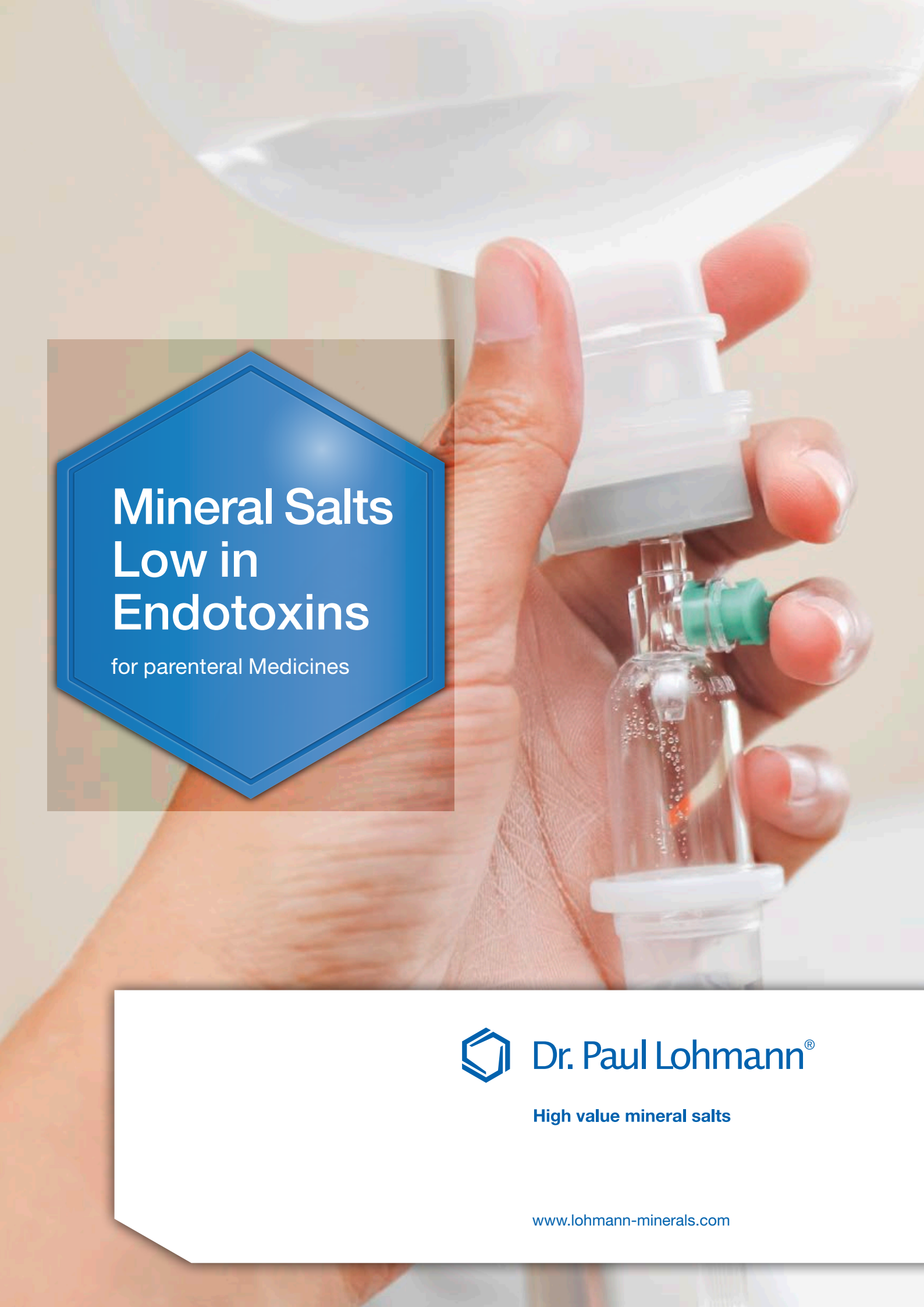

# Mineral Salts Low in Endotoxins

for parenteral Medicines

Dr. Paul Lohmann®

**High value mineral salts**

www.lohmann-minerals.com

# Low in Endotoxin Products

Endotoxins are lipopolysaccharides (LPS) which are outer membrane components of gram-negative bacteria. By decomposing, these bacteria release lipopolysaccharides, which are toxic.[1]

Parenteral medicines such as solutions for dialysis, hemo-filtration and osmotherapy constitute a marked quality standard. Systemic parenteral application of infusions or injections with endotoxin quantities as low as 0.1 ng per kilogram of bodyweight can cause various physiological reactions, including fever, inflammation and sickness behavior in humans and animals[2]. Due to the high sensitive application form, the manufacture of parenteral medicines requires particular caution: it is subject to strict and specific regulatory requirements and is regulated by Chapter 2.6.14 of the European Pharmacopoeia (Ph.Eur.)[3]. In order to support manufacturers of parenteral products to comply with legal and quality requirements, Dr. Paul Lohmann® offers Mineral Salts with a very low content of endotoxins.

Within the biotech industry, Low in Endotoxin qualities are of special interest for cell cultures. Endotoxins can cause undesirable effects on cell proliferation or cell function. Due to the high purity of our products, highly sensitive cell lines can develop in an optimal and laboratory controlled environment.

## Low in Endotoxin Qualities of Dr. Paul Lohmann® Products

In 2017, a purpose-built plant was brought into service. This plant is GMP-certified and solely dedicated for the production of low endotoxin qualities. Thus our production process of high purity mineral salts including the use of low endotoxin process water is especially conceptualized for the purpose of the production of parenteral medicines.

- LAL test* according to Ph.Eur. is performed on every single batch.
- Our customers can optimally integrate our low in endotoxin qualities in their process chain for the manufacture of parenteral dosage forms (please see blue text on the next page).

- Low in Endotoxin Minerals – exceeding purity
- For the production of parenteral medicines and biopharmaceuticals
- For optimal environment of cell lines
- GMP certified

# Applications

Low in Endotoxin mineral compounds can be used for the production of the following products:

- Solutions for parenterals:
  - Injections
  - Infusions
  - Nutrition
- Solutions for inhalants
- Solutions for
  - Dialysis
  - Peritoneal dialysis
  - Haemofiltration
  - Osmotherapy
- Ophthalmic preparations
- Biopharmaceuticals

Pharmaceutical manufacturers of preparations for infusion or injection are obliged to observe special regulations specified by the relevant pharmacopoeia and good manufacturing practices. We emphasize that our products are low in endotoxin content but not entirely free of endotoxins and not sterile. Therefore, these products must be treated with special procedures prior to their use in finished pharmaceutical products.

The pharmaceutical manufacturer must ensure that our products undergo special procedures and tests prior to being processed for infusion or injection preparations in order to induce their suitability for their intended purpose.

References

[1] Fennrich, S. et al.: More than 70 years of pyrogen detection: Current state and future perspectives; Alternatives to laboratory animals: ATLA, 06/2016, pp 239-53
[2] Salema, V., Pattnaik, P.: Removing endotoxin from biopharmaceutical solutions; Pharmaceutical Technology Europe, 10/2009, pp 36-38
[3] European Medicines Agency (EMEA): Guideline on the Replacement of Rabbit Pyrogen testing by an Alternative Test for Plasma Derived Medicinal Products; 04/2009

# Products in Low in Endotoxin Quality

| Product | Product no. | Quality*** | Metal content (per 100 g) | Endotoxins (LAL*) |
|---|---|---|---|---|
| **Acetates** | | | | |
| Calcium Acetate | 515001001 | Ph.Eur. \| USP-NF | approx. 24 % Ca | max. 6 EU**/g |
| Magnesium Acetate 4-hydrate | 511019001 | Ph.Eur. | approx. 11 % Mg | max. 6 EU**/g |
| Potassium Acetate, anhydrous | 515002001 | Ph.Eur. | approx. 40 % K | max. 6 EU**/g |
| Sodium Acetate 3-hydrate | 511016001 | Ph.Eur. \| USP-NF | approx. 17 % Na | max. 6 EU**/g |
| Zinc Acetate 2-hydrate | 515006004 | Ph.Eur. | approx. 30 % Zn | max. 25 EU**/g |
| **Aspartates** | | | | |
| Magnesium DL-Aspartate 4-hydrate | 501064001 | DAB | approx. 6 % Mg | max. 6 EU**/g |
| Potassium DL-Aspartate 0.5 hydrate | 501069001 | DAB | approx. 21.5 % K | max. 6 EU**/g |
| **Citrates** | | | | |
| Monosodium Citrate, anhydrous | 502015001 | DAC | approx. 10.5 % Na | max. 6 EU**/g |
| Trisodium Citrate, anhydrous | 502010012 | USP | approx. 27 % Na | max. 100 EU**/g |
| Trisodium Citrate 2-hydrate | 502009001 | Ph.Eur. \| USP-NF | approx. 23.5 % Na | max. 6 EU**/g |
| **EDTA** | | | | |
| Calcium Disodium EDTA | 511085002 | Ph.Eur. \| USP-NF | approx. 10 % Ca<br>approx. 11 % Ca | max. 6 EU**/g |
| Disodium EDTA 2-hydrate | 505062001 | Ph.Eur. \| USP-NF \| JP | approx. 12 % Na | max. 5 EU**/g |
| **Glycerophosphates** | | | | |
| Sodium Glycerophosphate | 512045001 | Ph.Eur. | approx. 15 % Na | max. 6 EU**/g |
| **Gluconates** | | | | |
| Calcium Gluconate 1-hydrate | 503071003 | Ph.Eur. | approx. 9 % Ca | max. 167 EU**/g |
| Magnesium Gluconate | 503074004 | Ph.Eur. | approx. 5.5 % Mg | max. 167 EU**/g |
| **Lactates** | | | | |
| Sodium Lactate Solution; approx. 50 %; from L-Lactic Acid | 512012112 | Ph.Eur. | approx. 10 % Na | max. 6 EU**/g |
| Sodium Lactate Solution; approx. 60 %; from L-Lactic Acid | 512012113 | Ph.Eur. \| USP-NF | approx. 12.5 % Na | max. 6 EU**/g |
| **Phosphates** | | | | |
| Monopotassium Phosphate | 505044002 | Ph.Eur. | approx. 28.5 % K<br>approx. 22.8 % P | max. 50 EU**/g |
| Dipotassium Hydrogen Phosphate | 505043004 | Ph.Eur. | approx. 45 % K;<br>approx. 18 % P | max. 3 EU**/g |
| Monosodium Phosphate, anhydrous | 503062002 | USP-NF | approx. 19 % Na<br>approx. 25.5 % P | max. 30 EU**/g |
| Monosodium Phosphate 2-hydrate | 503032002 | Ph.Eur. \| USP-NF | approx. 15 % Na | max. 6 EU**/g |
| Disodium Hydrogen Phosphate 2-hydrate | 503063003 | Ph.Eur. | approx. 26 % Na<br>approx. 17 % P | max. 20 EU**/g |
| Disodium Hydrogen Phosphate 7-hydrate NEW | 503048002 | USP-NF | approx. 17 % Na<br>approx. 12 % P | max. 5 EU**/g |
| Disodium Hydrogen Phosphate 12-hydrate | 503031002 | Ph.Eur. | approx. 13 % Na<br>approx. 8.5 % P | max. 6 EU**/g |
| **Succinates** | | | | |
| Sodium Succinate, anhydrous | 502080002 | NF | approx. 28 % Na | max. 6 EU**/g |
| Sodium Succinate 6-hydrate | 502045003 | NF | approx. 17 % Na | max. 6 EU**/g |
| **Sulfates** | | | | |
| Magnesium Sulfate 7-hydrate | 522014002 | Ph.Eur. | approx. 10 % Mg | max. 6 EU**/g |
| | 522014007 | Ph.Eur. | approx. 10 % Mg | max. 6 EU**/g |
| Sodium Sulfate, anhydrous | 522017013 | Ph.Eur. | approx. 32 % Na | max. 6 EU**/g |

Additional products can be developed or lower endotoxin limits (LAL) can be met upon customer request.

* Test for bacterial endotoxines (LAL test) is accomplished acc. to Ph.Eur.2.6.14 using product specific validated methods.

** EU = Endotoxin Unit (equal to IU, International Unit)

*** You can find the versions of the pharmacopoeias in the specifications.

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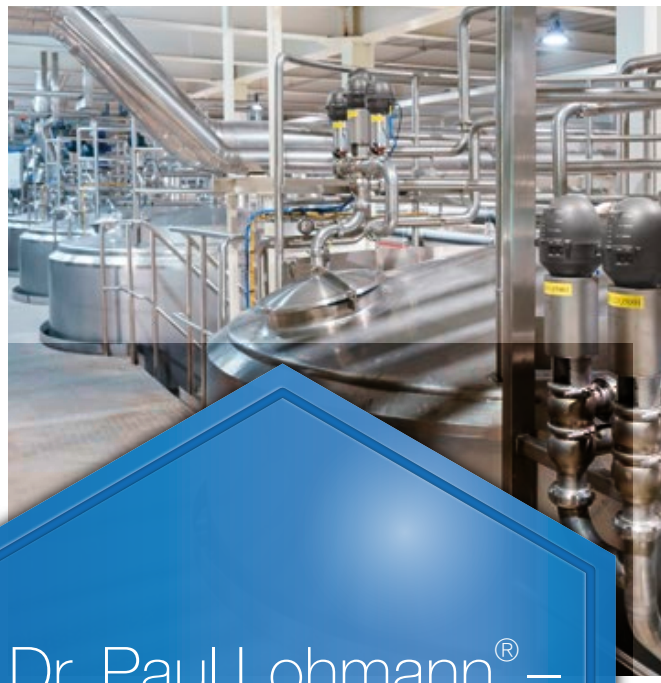


# Dr. Paul Lohmann® – Your Partner for high value Mineral Salts

With over 135 years of producing Mineral Salts that meet the highest quality standards we have been established as the leading global supplier to the pharmaceutical, biopharmaceutical, nutritional supplement, food and personal care industries.

## Our Expertise

- GMP and DIN EN ISO 9001 certified production sites
- FSSC 22000/ISO 22000 certified
- Processes according to HACCP
- Compliance and commitment with the FSMA (food safety modernization act)
- Tailor-made and innovative solutions according to customer requirements
- Highly qualified experts in R&D lab and application technology with long-term experience and a wide variety of possibilities to develop new products and applications
- Joint product and application development together with our customers
- Our manufactured products are exclusively Made in Germany
- A wide range of more than 400 different Mineral Salts
- Products in compliance with the most relevant pharmacopoeias (Ph.Eur., USP, BP), food codices (FCC, E-numbers, etc.) and customer specific requirements
- Regulatory documentation (CEP, ASMF, etc.)
- REACH compliance on request
- Wide range of production equipment
- Social and environmental standards (DIN EN ISO 50001, EcoVadis, Sedex)
- High purities can be realized according to specific requirements

## Modification

- Physical properties
- Chemical properties
- Packaging
- Labeling

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