

*To whom it may concern*

## **Statement of advice**

### **Conformity to Good Manufacturing Practice (GMP) for active pharmaceutical ingredients (APIs)**

We herewith confirm, that we comply with the Good Manufacturing Practice (GMP) requirements referred to in Article 47 of Directive 2001/83/EC for the products PharSQ® Active DCF and PharSQ® Active DM.

This compliance has been confirmed by a Certificate of GMP Compliance (Certificate No. DE\_RP\_01\_GMP\_2019\_0022) issued following an inspection in accordance with Article 111 (5) of Directive 2001/83/EC, transposed in the national legislation Section 64 Paragraph 1 Arzneimittelgesetz (German Drug Law) by the competent authority of Germany (Landesamt für Soziales, Jugend und Versorgung, Rheinland-Pfalz).

According to the EMA stakeholder letter regarding regulatory expectations for medicinal products for human use during the COVID-19 pandemic the validity of GMP certificates for manufacturing sites of active substances in the EEA is automatically extended until the end of 2022 without the need for further action from the holder of the certificate.

That means, that named Certificate of GMP Compliance with number DE\_RP\_01\_GMP\_2019\_0022 remains valid.

Furthermore we would like to confirm, that the latest surveillance GMP inspection by the competent authority of Germany, dated from 27.- 28.10.2021, was successfully passed confirming the GMP requirements referred to in Article 47 of Directive 2001/83/EC.

However due to the high workload at the authority of Germany, caused by the continuing pandemic situation, the inspection report as well as the issuing of a new Certificate of GMP compliance, dating from the GMP inspection from 27.-28.10.2021 have not yet been finished. We will pass this new Certificate on to you as soon as it is available.

Please note this non-transferable confirmation is restricted to aforementioned products and cannot be transferred to other products.

\*\*\* This statement is computer generated and therefore not signed \*\*\*

Any information contained herein is made to the best of our ability on the basis of current industrial practice and our own knowledge and experience. Any responsibility for damages resulting from the use of or reliance upon such information or products such information refers to is limited pursuant to our Conditions of Sale and Supply. The information contained herein shall not cause the purchaser or any other person or entity using or intending to use our products to refrain from testing our products and/or reviewing (and, if relevant, respecting) any conflicting patent and other proprietary rights; and we expressly request and invite the customer or such other user of our products to perform such tests, have such tests performed prior to any commercial use or other application of our products for the specific use and application intended and to review (and, if relevant, to respect) any conflicting patent and other proprietary rights relevant for the specific product and/or use.

<b>File Name:</b>	BDE_Statement_of_conformity_GMP_APIs.pdf	<b>Version:</b> 001
<b>created by:</b>	Dr. Thomas Willmes / QM Pharma	<b>Date:</b> December 15 <sup>th</sup> , 2021
<b>approved by:</b>	Udo Arenz / Head of Marketing Pharma	<b>Date:</b> December 16 <sup>th</sup> , 2021
<b>QS review by:</b>	Dr. Gabriele Zache / Head of QM&QA	<b>Date:</b> December 16 <sup>th</sup> , 2021
<b>valid until further notice from:</b>	December / 2021	<b>until:</b> December / 2022



Zertifikat-Nr./Certificate no:  
DE\_RP\_01\_GMP\_2019\_0022

**BESTÄTIGUNG DER ÜBEREINSTIMMUNG EINES  
HERSTELLERS MIT GMP**

**Teil 1**

**Ausgestellt nach einer Inspektion gemäß**

- **Art. 111 (5) der Richtlinie 2001/83/EG**

Die zuständige deutsche Überwachungsbehörde bestätigt:

Der Hersteller  
**Chemische Fabrik Budenheim KG**

Anschrift der Betriebsstätte  
**Chemische Fabrik Budenheim KG  
Rheinstraße 27  
55257 Budenheim  
Deutschland**

- Ist Wirkstoffhersteller und wurde inspiziert gemäß  
- Art. 111 (1) der Richtlinie 2001/83/EG  
umgesetzt in deutsches Recht durch:  
§ 64 Abs. 1 Arzneimittelgesetz

Aufgrund der aus der letzten Inspektion vom 06. November 2018 gewonnenen Erkenntnisse wird für die oben genannte Betriebsstätte des Herstellers die Übereinstimmung mit den Anforderungen der Guten Herstellungspraxis festgestellt, die sich aus

- den GMP-Grundsätzen für Wirkstoffe gemäß  
- Artikel 47 der Richtlinie 2001/83/EG

ergeben.

Dieses Zertifikat bestätigt den Status der Betriebsstätte zum Zeitpunkt der oben genannten Inspektion. Es sollte nicht zur Bestätigung der Übereinstimmung herangezogen werden, wenn seit der genannten

**CERTIFICATE OF GMP COMPLIANCE OF A  
MANUFACTURER**

**Part 1**

**Issued following an inspection in accordance with**

- **Art. 111 (5) of Directive 2001/83/EC**

The competent authority of GERMANY confirms the following:

The manufacturer  
**Chemische Fabrik Budenheim KG**

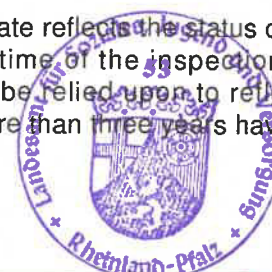
Site address  
**Chemische Fabrik Budenheim KG  
Rheinstraße 27  
55257 Budenheim  
Germany**

- Is an active substance manufacturer that has been inspected in accordance with  
- Art. 111 (1) of Directive 2001/83/EC  
transposed in the following national legislation:  
Sect 64 para 1 Arzneimittelgesetz (German Drug Law)

From the knowledge gained during the inspection of this manufacturer, the latest of which was conducted on 06 November 2018, it is considered that it complies with the Good Manufacturing Practice requirements referred to in

- the principles of GMP for active substances referred to in  
- Article 47 of Directive 2001/83/EC

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the





Inspektion mehr als drei Jahre vergangen sind. Nach Ablauf dieser Zeit sollte mit der zuständigen Behörde Kontakt aufgenommen werden. Das Zertifikat ist nur bei Vorlage sämtlicher Seiten inklusive der Teile 1 und 2 gültig. Die Echtheit dieses Zertifikates kann ggf. durch die ausstellende Behörde bestätigt werden.

date of that inspection, after which time the issuing authority should be consulted. This certificate is valid only when presented with all pages and both parts 1 and 2. The authenticity of this certificate may be verified with the issuing authority.



• Wirkstoffe

• Substances

**1 HERSTELLUNGSTÄTIGKEITEN****1 MANUFACTURING OPERATIONS****1.4 Andere Produktart oder Herstellungstätigkeit****1.4 Other products or manufacturing activity**
 1.4.3 Andere  
 Wirkstoffe

 1.4.3 Other  
 Active Pharmaceutical Ingredients

 Wirkstoffherstellung. Substanzen, die Gegenstand der  
 Inspektion waren:

 Manufacture of active substance. Names of substances  
 subject to inspection:

**Dicalciumphosphat wasserfrei (PharSQ Active  
 DCF)**
**Dicalcium-phosphate anhydrous (PharSQ Active  
 DCF)**
**Ausgangsstoffe: Ca(OH)<sub>2</sub> und H<sub>3</sub>PO<sub>4</sub>**
**API starting materials: Ca(OH)<sub>2</sub> and H<sub>3</sub>PO<sub>4</sub>**

 3.1 Herstellung von chemisch synthetisierten  
 Wirkstoffen

 3.1 Manufacture of Active Substance by Chemical  
 Synthesis

 3.1.3 Salzbildung / Aufreinigungsschritte  
 Kristallisation

 3.1.3 Salt formation / Purification steps  
 Crystallisation

3.6 Qualitätskontrolle

3.6 Quality control testing

3.6.1 Physikalische / chemische Prüfung

3.6.1 Physical / Chemical testing

**Dimagnesiumphosphat-3-hydrat (PharSQ Active  
 DM)**
**Dimagnesium-phosphate-3-hydrate (PharSQ  
 Active DM)**
**Ausgangsstoffe: Mg(OH)<sub>2</sub> und H<sub>3</sub>PO<sub>4</sub>**
**API starting materials: Mg(OH)<sub>2</sub> und H<sub>3</sub>PO<sub>4</sub>**

 3.1 Herstellung von chemisch synthetisierten  
 Wirkstoffen

 3.1 Manufacture of Active Substance by Chemical  
 Synthesis

 3.1.3 Salzbildung / Aufreinigungsschritte  
 Kristallisation

 3.1.3 Salt formation / Purification steps  
 Crystallisation

3.6 Qualitätskontrolle

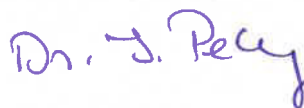
3.6 Quality control testing

3.6.1 Physikalische / chemische Prüfung

3.6.1 Physical / Chemical testing

 03. April 2019  
 Im Auftrag

 03 April 2019  
 On behalf



 Name und Unterschrift des Bearbeiters der zuständigen  
 Behörde

 Name and signature of the authorised person of the  
 Competent Authority

Dr. Ilka Petry

Dr. Ilka Petry



Landesamt für Soziales, Jugend und Versorgung  
Gesundheit und Pharmazie  
Referat 54 - Pharmazie  
Baedekerstraße 2-20  
56073 Koblenz  
Deutschland

Landesamt für Soziales, Jugend und Versorgung  
Gesundheit und Pharmazie  
Referat 54 - Pharmazie  
Baedekerstraße 2-20  
56073 Koblenz  
Deutschland

Tel.: +49(0)6131 967391  
Fax: +49(0)6131 96712391

Tel.: +49(0)6131 967391  
Fax: +49(0)6131 96712391

