



Elemental Impurities

Starches

Product group: Starch
 Brand name: Solani Amylum,
 Prejel PA5 PH
 Product description: Pregelatinized potato
 starch, Native potato
 starch
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Dear Customer,

In framework of the ICH Q3D (R2) guideline, DFE Pharma tested batches of Starches, originating from the production sites located in Europe (Tilburg, The Netherlands, Lüchow, Germany) representing the brand names mentioned above.

Neither the elements listed below, nor other elements classified as class 2B, are intentionally added during the production process.

DFE Pharma performed analysis on relevant elemental impurities categorized as class 1, class 2A and some class 2B, class 3 and other relevant elements by the ICH Q3D (R2) guideline (according to table 5.1: Elements to be considered in the Risk Assessment – Oral Dosage Form).

Analysis was performed using the analysis technique ICP-MS (Inductively Coupled Plasma-Mass Spectrometry) conforming to USP-NF <233> and Ph. Eur 2.4.20.

Table 1: Table of elemental impurities following ICH Q3D

| Metal | Class | Limit in ppm oral | Required for oral route | Tested at DFE Pharma |
|------------|-------|-------------------|-------------------------|----------------------|
| Cadmium | 1 | 0.5 | Yes | Yes |
| Lead | 1 | 0.5 | Yes | Yes |
| Arsenic | 1 | 1.5 | Yes | Yes |
| Mercury | 1 | 3.0 | Yes | Yes |
| Cobalt | 2A | 5 | Yes | Yes |
| Vanadium | 2A | 10 | Yes | Yes |
| Nickel | 2A | 20 | Yes | Yes |
| Selenium | 2B | 15 | No | Yes |
| Lithium | 3 | 55 | No | Yes |
| Antimony | 3 | 120 | No | Yes |
| Barium | 3 | 140 | No | Yes |
| Molybdenum | 3 | 300 | No | Yes |
| Copper | 3 | 300 | No | Yes |
| Tin | 3 | 600 | No | Yes |
| Chromium | 3 | 1100 | No | Yes |
| Aluminium | None | - | No | Yes |
| Strontium | None | - | No | Yes |

*1: Limits are based on option 1 of the ICH Q3D (R2) guidelines, based on administration of not more than 10g of drug product per day (stated in table A.2.2).



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In Table 2 and 3 the data of Prejel PA5 PH and Solani Amylum is presented.
 Neither the elements listed in Table 1, nor other elements classified as class 2B, are intentionally added during the production process.

Table 2: Results of elemental impurities in Prejel PA5 PH

| Product and Batch | | | Prejel PA5 PH 1081WRN (ppm) | Prejel PA5 PH 10BoJZT (ppm) | Prejel PA5 PH 10BP7HD (ppm) |
|-------------------|----------------|--------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Metal | Limit (ppm) | Report limit (ppm) | | | |
| Cadmium | 0.5 | 0.005 | <0.005 | <0.005 | <0.005 |
| Lead | 0.5 | 0.01 | <0.01 | <0.01 | <0.01 |
| Arsenic | 1.5 | 0.005 | <0.010* | <0.005 | <0.005 |
| Mercury | 3 | 0.006 | <0.006 | <0.006 | <0.006 |
| Cobalt | 5 | 0.005 | <0.005 | <0.005 | <0.005 |
| Vanadium | 10 | 0.002 | 0.005 | 0.004 | 0.003 |
| Nickel | 20 | 0.030 | 0.042 | <0.03 | <0.03 |
| Selenium | 15 | 0.004 | <0.004 | <0.004 | <0.004 |
| Lithium | 55 | 0.004 | 0.012 | 0.012 | 0.010 |
| Antimony | 120 | 0.005 | <0.005 | <0.005 | <0.005 |
| Barium | 140 | 0.005 | 0.300 | 0.410 | 0.150 |
| Molybdenum | 300 | 0.020 | <0.02 | <0.02 | <0.02 |
| Copper | 300 | 0.010 | 0.130 | 0.140 | 0.680 |
| Tin | 600 | 0.25 | <0.01* | <0.01* | <0.25 |
| Chromium | 1100 | 0.030 | 0.074 | 0.033 | <0.03 |
| Aluminium | None | 0.200 | 0.78 | 0.54 | 0.35 |
| Strontium | None | 0.005 | 1.0 | 1.3 | 0.97 |

*At time of measurement the reporting limit was different



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Table 3: Results of elemental impurities in Solani Amylum

| Product and Batch | | | Solani Amylum 1061DTL (ppm) | Solani Amylum 10BoMXH (ppm) | Solani Amylum 10CMKN9 (ppm) |
|-------------------|----------------|--------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Metal | Limit (ppm) | Report limit (ppm) | | | |
| Cadmium | 0.5 | 0.005 | <0.005 | <0.005 | <0.005 |
| Lead | 0.5 | 0.01 | <0.02* | <0.01 | <0.01 |
| Arsenic | 1.5 | 0.005 | <0.010* | <0.005 | <0.005 |
| Mercury | 3 | 0.006 | <0.006 | <0.006 | <0.006 |
| Cobalt | 5 | 0.005 | <0.005 | <0.005 | <0.005 |
| Vanadium | 10 | 0.002 | 0.003 | 0.002 | 0.004 |
| Nickel | 20 | 0.030 | <0.03 | <0.03 | <0.03 |
| Selenium | 15 | 0.004 | <0.004 | <0.004 | <0.004 |
| Lithium | 55 | 0.004 | <0.004 | <0.004 | 0.007 |
| Antimony | 120 | 0.005 | <0.005 | <0.005 | <0.005 |
| Barium | 140 | 0.005 | 0.013 | 0.006 | 0.007 |
| Molybdenum | 300 | 0.020 | <0.02 | <0.02 | <0.02 |
| Copper | 300 | 0.010 | <0.010 | <0.010 | <0.010 |
| Tin | 600 | 0.25 | <0.01* | <0.01* | <0.25 |
| Chromium | 1100 | 0.030 | <0.03 | <0.03 | <0.03 |
| Aluminium | None | 0.200 | <1* | 0.63 | 1.3 |
| Strontium | None | 0.005 | <0.025* | 0.0070 | 0.014 |

*At time of measurement the reporting limit was different



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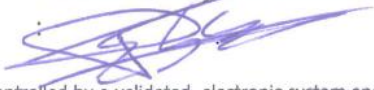
Starches

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Brand name: Solani Amylum,
Prejel PA5 PH
Product description: Pregelatinized potato
starch, Native potato
starch
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A risk assessment was performed. This document and raw data is available for review during audits. Conclusion of the risk assessment is that all values obtained are below 30% of the limits and thus do not need additional control, the change control procedure is the key to maintain this situation. The levels of ICH Q3D relevant elemental impurities are monitored on regular basis.

This statement substitutes all previous versions issued for the brand names mentioned above. We trust this information, which is made up to the best of our knowledge, will be helpful to you.

With kindest regards,

Name : Peter Ebben
Job title : Global Quality Control Manager
Signature : 

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