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# DEGRADATION AND IMPURITY PROFILE REPORT: SODIUM CHLORIDE 5M SOLUTION

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## 1. PURPOSE AND SCOPE:

1.1. The impurity profiling of Sodium Chloride 5M solution is intended to identify and possibly quantify impurities found in the product manufactured and purified at BioSpectra, in the Bangor, Pa facility.

1.1.1. In the case where an impurity was detected, a limit was set to the maximum allowable without measurable compromise to predetermined critical quality attributes or toxicity. In the case where a limit could not be set, a procedure will be written and followed to identify if the possible impurity is present or not. (i.e. an identity test, which is qualitative and not quantitative.)

1.1.2. The stages of the Sodium Chloride 5M solution process that were tested were the Raw Materials (Sodium Chloride and Water for Injection), and the Finished Good.
One sample from each stage was used for analysis and a table was generated to include all sample results.

1.1.3. The profiling results and data allows BioSpectra to monitor the purity and characteristics of the material through the stages of manufacturing.

1.1.4. The tests that were used to determine the presence of impurities and degradation products were as follows:

1.1.4.1. Appearance and Color

1.1.4.1.1. Water for Injection, NaCl Raw Material, and Finished Good.

1.1.4.2. Assay/Molarity Concentration

1.1.4.2.1. NaCl Raw Material and Finished Good.

1.1.4.3. Elemental Impurities USP <232> and <233>

1.1.4.3.1. Water for Injection, NaCl Raw Material, and Finished Good.

1.1.4.4. Endotoxin

1.1.4.4.1. Water for Injection, NaCl Raw Material, and Finished Good

1.1.4.5. Identification Tests: Sodium & Chloride

1.1.4.5.1. NaCl Raw Material and Finished Good.

1.1.4.6. Microbial Content

1.1.4.6.1. Water for Injection, NaCl Raw Material, Finished Good.

1.1.4.7. Total Organic Carbon

1.1.4.7.1. Finished Good.

1.1.4.8. Finished Good only Trace Metals (Al, As, Cu, Fe, Pb)

1.1.4.8.1. Water for Injection, NaCl Raw Material, and Finished Good

1.2. Water for Injection testing was documented in a table for the week the tote(s) were filled for use, as Water for Injection is an approved Raw material for this process.

1.2.1. Totes for water for injection were previously filled for use in this process and were sampled for microbial and endotoxin content.

1.3. All results were recorded in the appropriate laboratory documentation. This report includes all relevant data, as well as references to the initial documented results. This report discusses any impurities found in the product and includes a specification for any limits on the impurities found, where applicable.

## 2. RESPONSIBILITIES:

2.1. The Executive Director of Quality Control or designee was responsible for control, implementation, training and maintenance of this procedure as well as for summarizing the results in this Degradation and Impurity Report.
2.2. The QC Analysts were responsible for performing the testing stated in the protocol.
2.3. The QC Compliance Team was responsible for creating and approving the Degradation and Impurity Profile Report.

## 3. REFERENCES:

3.1. Analytical Method Verification Protocol: Elemental Impurities via ICP-MS
3.2. Balance SOP
3.3. *Current EP*
3.4. *Current JP*
3.5. *Current USP*
3.6. ICH Q3D Guideline for Elemental Impurities
3.7. Degradation and Impurity Profiling SOP
3.8. Degradation and Impurity Profile Protocol: Sodium Chloride
3.9. Laboratory Notebooks
3.10. NexION 350X ICP-MS SOP
3.11. Sodium Chloride 5M Testing Methods
3.12. Sodium Chloride Raw Material Testing Methods
3.13. USP/EP Water for Injection Testing Methods
3.14. Water for Injection Elemental Impurity Profile 2020
3.15. Sodium Chloride 5M Elemental Impurity Profile 2020

## 4. PROCEDURE:

4.1. **APPEARANCE AND COLOR :**

4.1.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Appearance and Color are detailed in the table below. All results met requirements.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| E06DI01-061320 | Water for Injection | Clear and Colorless | Clear and Colorless |
| E06DI01-061420 | | | Clear and Colorless |
| E06DI01-080920 | | | Clear and Colorless |
| E06DI01-081020 | | | Clear and Colorless |
| E06DI01-081920 | | | Clear and Colorless |
| RI19357019 | Raw Material | Monitor | White/Crystals |
| NC3100-001-0620-PV | Finished Goods | Clear Colorless Solution | Clear Colorless Solution |
| NC3100-002-0820-PV | | | Clear Colorless Solution |
| NC3200-003-0820-PV | | | Clear Colorless Solution |

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## 4.2. ASSAY/MOLARITY CONCENTRATION :

4.2.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Assay/Molarity concentration are detailed in the table below. All results met requirements.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| RI19357019 | Raw Material | 99.0 – 100.5% | 100.25% |
| NC3100-001-0620-PV | Finished Goods | 4.9-5.1M | 5.0M |
| NC3100-002-0820-PV | | | 5.0M |
| NC3200-003-0820-PV | | | 5.0M |

## 4.3. ELEMENTAL IMPURITIES, OPTION 1. :

4.3.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Elemental Impurities are detailed in the table below.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| E06DI01-061320 | Water for Injection | Meets USP <232> <233> Option 1 Requirements | Refer to DCN: 21-001716 |
| E06DI01-061420 | | | |
| E06DI01-080920 | | | |
| E06DI01-081020 | | | |
| E06DI01-081920 | | | |
| RI19357019 | Raw Material | Meets USP <232> <233> Option 1 Requirements | Refer to DCN: 21-001717 |
| NC3100-001-0620-PV | Finished Goods | Meets USP <232> <233> Option 1 Requirements | |
| NC3100-002-0820-PV | | | |
| NC3200-003-0820-PV | | | |

## 4.4. ENDOTOXINS :

4.4.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Endotoxin analysis are detailed in the table below.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| E06DI01-061320 | Water for Injection | ≤0.25 EU/mL | 0.085EU/mL |
| E06DI01-061420 | | | 0.127EU/mL |
| E06DI01-080920 | | | 1.37 EU/mL |
| E06DI01-081020 | | | 0.530 EU/mL |
| E06DI01-081920 | | | 3.05 EU/mL |
| RI19357019 | Raw Material | <5 EU/g | <1 EU/g |
| NC3100-001-0620-PV | Finished Goods | ≤2.5 EU/mL | <0.3 EU/mL |
| NC3100-002-0820-PV | | | <0.3 EU/mL |
| NC3200-003-0820-PV | | | <0.3 EU/mL |

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4.5. **IDENTIFICATION TEST: Sodium :**

4.5.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Identification Sodium are detailed in the table below. All results met requirements.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| RI19357019 | Raw Material | Meets Requirements | Meets Requirements |
| NC3100-001-0620-PV | Finished Goods | Meet Requirements | Meets Requirements |
| NC3100-002-0820-PV | | | Meets Requirements |
| NC3200-003-0820-PV | | | Meets Requirements |

4.6. **IDENTIFICATION TEST: Chloride :**

4.6.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Identification Chloride are detailed in the table below. All results met requirements.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| RI19357019 | Raw Material | Meets Requirements | Meets Requirements |
| NC3100-001-0620-PV | Finished Goods | Meet Requirements | Meets Requirements |
| NC3100-002-0820-PV | | | Meets Requirements |
| NC3200-003-0820-PV | | | Meets Requirements |

4.7. **MICROBIAL CONTENT :**

4.7.1. TAMC/TYMC was performed by Mary Paul Laboratories. The results are detailed in the table below. All results met requirements.

| Lot Number | Stage of Material | Specification | Results and Identifications, where applicable |
|---|---|---|---|
| E06DI01-061320 | Water for Injection | Monitor for TAMC/TYMC | <10 CFU/g; <10 CFU/g |
| E06DI01-061420 | | | 4400 CFU/g; <10 CFU/g<br>Identification- *Ralstonia pickettii* |
| E06DI01-080920 | | | 70 CFU/mL; < 10 CFU/g<br>Identification- *Sphingomonas sp; Ralstonia pickettii* |
| E06DI01-081020 | | | 40 CFU/mL; < 10 CFU/g<br>Identification- *Sphingomonas sp; Ralstonia pickettii* |
| E06DI01-081920 | | | >2000 CFU/100 mL<br>Identification- *Staphylococcus sp; Ralstonia pickettii* |
| RI19357019 | Raw Material | Monitor for TAMC/TYMC | <10 CFU/g; <10 CFU/g |
| NC3100-001-0620-PV | Finished Goods | TAMC: ≤50 CFU/g<br>TYMC: ≤150 CFU/g | <10 CFU/g; <10 CFU/g |
| NC3100-002-0820-PV | | | <10 CFU/g; <10 CFU/g |
| NC3200-003-0820-PV | | | <10 CFU/g; <10 CFU/g |

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## 4.8. TOTAL ORGANIC CARBON :

4.8.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Total Organic Carbon are detailed in the table below. All results met the requirements.

| Lot Number | Stage of Material | Specification | Result |
|---|---|---|---|
| NC3100-001-0620-PV | Finished Goods | <0.03% Organic Carbon | <0.03% Organic Carbon |
| NC3100-002-0820-PV | | | <0.03% Organic Carbon |
| NC3200-003-0820-PV | | | <0.03% Organic Carbon |

## 4.9. TRACE METALS ANALYSIS :

4.9.1.1. Refer to Degradation and Impurity Profile Protocol: Sodium Chloride 5M Solution for testing methods. The results of Trace Metal Analysis are detailed in the table below.

| Lot Number | Stage of Material | Specification | | | | Result | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Al | As | Fe | Pb | Al | As | Fe | Pb |
| E06DI01-061320 | Raw Material | Monitor | | | | Refer to DCN: 21-001716 | | | |
| E06DI01-061420 | | | | | | | | | |
| E06DI01-080920 | | | | | | | | | |
| E06DI01-081020 | | | | | | | | | |
| E06DI01-081920 | | | | | | | | | |

| Lot Number | Stage of Material | Metal | Specification | result |
|---|---|---|---|---|
| RI19357019 | Raw Material | Arsenic | Monitor | <1ppm |
| | | Iron | | <2ppm |
| | | Lead | | <2ppm |
| | | Copper | NMT 2ppm | <2ppm |
| NC3100-001-0620-PV | Finished Goods | Arsenic | NMT 2 ppm | <2ppm |
| | | Iron | | <2ppm |
| | | Lead | | <2ppm |
| | | Copper | | <2ppm |
| NC3100-002-0620-PV | Finished Goods | Iron | NMT 2 ppm | <2ppm |
| | | Lead | | <2ppm |
| | | Copper | | <2ppm |
| | | Arsenic | | <2ppm |
| NC3100-003-0620-PV | Finished Goods | Lead | NMT 2 ppm | <2ppm |
| | | Copper | | <2ppm |
| | | Arsenic | | <2ppm |
| | | Iron | | <2ppm |

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4.10. **ROUTINE WATER FOR INJECTION ANALYSES :**

4.10.1. Refer to the USP/EP Water for Injection Testing Methods for testing methods. Routine Water for Injection testing was documented in the table for the week the tote(s) were filled for use, as Water for Injection was used for this process.

| Analysis | Specification | E06DI01-061020 | E06DI01-061720 | E06DI01-081220 | E06DI01-081920 |
|---|---|---|---|---|---|
| Pre-Sampling Conductivity | 1.1 µS/cm @ 20°C | 0.69µS/cm @ 23.1°C | 0.58µS/cm @ 25.0°C | 0.48µS/cm @ 25.4°C | 0.52 µS/cm @ 25.0°C |
| Post-Sampling Conductivity | 1.3 µS/cm @ 25.0°C | 0.69µS/cm @ 23.1°C | 0.58µS/cm @ 25.0°C | 0.48µS/cm @ 25.4°C | 0.48 µS/cm @ 24.8°C |
| Nitrate | ≤ 0.2 ppm | < 0.2 ppm | < 0.2 ppm | < 0.2 ppm | < 0.2 ppm |
| TOC | ≤ 500 ppb | 1.62 ppb | 2.68 ppb | 0.65 ppb | 0.87 ppb |
| Endotoxin | ≤ 0.25 EU/mL | <0.0100 EU/mL | <0.0100 EU/mL | <0.0100 EU/mL | <0.0100 EU/mL |
| Total Viable Bacteria | < 10 CFU/100mL | < 1 CFU/100mL | < 1 CFU/100mL | < 1 CFU/100mL | < 1 CFU/100mL |

## 5. CONCLUSION:

5.1. In conclusion, all samples from all stages of the process met specifications as dictated in the Degradation and Impurity Profile Protocol: 5M Sodium Chloride, with the exception of the three previously filled water tote samples: E06DI01-080920, E06DI01-081020 and E06DI01-081920. These specific water tote samples produced slightly elevated endotoxin results, according to the USP/EP Water for Injection specifications of ≤0.25EU/mL, however the water tote samples met the Finished good specification of ≤2.5EU/mL.

Full water testing for the E06 sample port is included in this report for the week the totes were filled for use and met USP/EP Water for Injection specifications. Endotoxin was removed through the filtration process and all finished goods met specification.

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