BIOSPECTRA
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DEGRADATION AND IMPURITY PROFILE REPORT: D-GALACTOSE

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1. PURPOSE AND SCOPE:

1.1. The impurity profiling of D-Galactose was intended to identify and possibly quantify impurities found in the product manufactured and purified at BioSpectra.

1.1.1. In the case where an impurity was found, a limit was set to the maximum allowable present without measurable compromise to predetermined critical quality attributes or toxicity. In the case where a limit could not be set, a procedure was 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 profiling results and data allowed BioSpectra to further understand the purity and characteristics of D-Galactose.

1.1.3. The four stages of the D-Galactose process that were tested are the Raw Material, the Mother Liquor, Wet Crystal, and the Finished Good.

1.1.3.1. Finished Good results were represented by a single sample: Beginning Drum, Batch 1.

1.1.4. A table was generated to include all sample results in the Degradation and Impurity Profile Report.

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

1.1.5.1. Appearance and Color

1.1.5.1.1. Raw material and Finished Goods

1.1.5.2. Assay

1.1.5.2.1. This demonstrated the purity of the material as it proceeds through the manufacturing process.

1.1.5.2.1.1. All four stages

1.1.5.3. Acidity

1.1.5.3.1. Raw Material and Finished Goods

1.1.5.4. Elemental Impurities with addition of Iron, Manganese and Zinc

1.1.5.4.1. USP <232> and <233>, and GALP Product codes.

1.1.5.4.1.1. All four stages

1.1.5.5. Identification Test A

1.1.5.5.1. All four stages.

1.1.5.6. Impurities (Related Substances NF)

1.1.5.6.1. This analysis evaluated if there was any degradation to the material during the manufacturing process.

1.1.5.6.1.1. All four stages

1.1.5.7. Proteins

1.1.5.7.1. Raw Material and Finished Goods

1.1.5.8. Specific Rotation/Optical Rotation

1.1.5.8.1. Raw Material and Finished Goods

1.1.5.9. Residue on Ignition

1.1.5.9.1. Raw Material and Finished Goods

1.1.5.10. Residual Solvents: Ethanol, IPA, Methanol, MIBK

1.1.5.10.1. Finished Goods

1.1.5.11. Water (By Karl Fischer Titration)

1.1.5.11.1. Raw Material and Finished Goods

1.1.6. Analytical data was used to support conclusions and statements of process performance in the Degradation and Impurity Profile Report. This report includes all relevant data as well as references to the initial documented results. This report details any impurities found in the product and includes a limit specification on any impurities observed where applicable.

2. RESPONSIBILITIES:

2.1. The QC Analysts or other qualified personnel were responsible for performing the testing stated in the protocol.

2.2. QC Lab Supervisor, or designee, was responsible for completing the degradation and impurity testing report.

3. REFERENCES:

3.1. BSI-ATM-0026, D-Galactose Testing Methods

3.2. BSI-ATM-0069, Analytical Method: Determination of Elemental Impurities by ICP-MS in Galactose

3.3. BSI-SOP-0098, Balance SOP

3.4. BSI-SOP-0102, Degradation and Impurity Profiling SOP

3.5. BSI-SOP-0126, Laboratory Notebooks

3.6. BSI-SOP-0303, NexION 350X ICP-MS SOP

3.7. *Current EP*

3.8. *Current JP*

3.9. *Current USP*

4. PROCEDURE:

4.1. **APPEARANCE AND COLOR:**

4.1.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Appearance and Color analyses are detailed in the table below:

TABLE 1: APPEARANCE AND COLOR

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	White Powder
GALP-0121-00004-PV Drum 1	Finished Good	White to Almost White Crystalline or Finely Granulated Powder	White to Almost White Crystalline or Finely Granulated Powder

4.2. **ASSAY** :

4.2.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the assay analysis are detailed in the table below:

TABLE 2: ASSAY

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	99.69%
GALP-0121-00004 ML	Mother Liquor		28.76%
GALP-0121-00004-PV WC	Wet Crystal		90.31%
GALP-0121-00004-PV Drum 1	Finished Good	98.0-102.0%	98.6%

4.3. **ACIDITY** :

4.3.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the acidity analysis are detailed in the table below:

TABLE 3: ACIDITY

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	Passes Test
GALP-0121-00004-PV Drum 1	Finished Good	Passes Test	Passes Test

4.4. **ELEMENTAL IMPURITIES W/FE, MN, AND ZN** :

4.4.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Elemental Impurity analysis are detailed in the table below:

TABLE 4: ELEMENTAL IMPURITIES

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	Refer to BSI-RPT-0844 for Elemental Impurity Assessment D-Galactose 2021
GALP-0121-00004 ML	Mother Liquor		
GALP-0121-00004-PV WC	Wet Crystal		
GALP-0121-00004-PV Drum 1	Finished Good	Refer to BSI-FRM-0699	

4.5. **IDENTIFICATION TEST A** :

4.5.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Identification A analysis are detailed in the table below:

TABLE 5: IDENTIFICATION A

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	0.995238
GALP-0121-00004 ML	Mother Liquor		0.197526
GALP-0121-00004-PV WC	Wet Crystal		0.98445
GALP-0121-00004-PV Drum 1	Finished Good	Conforms to Reference	0.984888

4.6. IMPURITIES (RELATED SUBSTANCES NF) :

4.6.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Impurities analysis are detailed in the table below:

TABLE 6: IMPURITIES (RELATED SUBSTANCES)

Lot Number	Stage	Specification	Result			
			Lactose and 1,6-galactosyl-galactose	Galacturonic Acid	Dextrose	Tagatose
PG-19-092	Raw Material	Monitor	0.22%	None Detected	None Detected	None Detected
GALP-0121-00004 ML	Mother Liquor		0.23%	None Detected	None Detected	None Detected
GALP-0121-00004-PV WC	Wet Crystal		0.08%	None Detected	None Detected	None Detected
GALP-0121-00004-PV Drum 1	Finished Good	Refer to BSI-FRM-0699	0.1%	<0.6%	<0.6%	<0.6%

TABLE 7: IMPURITIES (RELATED SUBSTANCES) CONTINUED

Lot Number	Stage	Specification	Result			
			Dulcitol	Arabinose	Unspecified Impurity	Total Impurities
PG-19-092	Raw Material	Monitor	None Detected	0.07%	None Detected	0.28%
GALP-0121-00004 ML	Mother Liquor		None Detected	None Detected	None Detected	0.23%
GALP-0121-00004-PV WC	Wet Crystal		None Detected	0.04%	None Detected	0.12%
GALP-0121-00004-PV Drum 1	Finished Good	Refer to BSI-FRM-0699	<0.6%	<0.6%	<0.2%	0.1%

4.7. PROTEINS :

4.7.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Proteins analysis are detailed in the table below:

TABLE 8: PROTEINS

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	0.0628mg/mL
GALP-0121-00004-PV Drum 1	Finished Goods	≤0.1mg/mL	<0.1mg/mL

4.8. SPECIFIC ROTATION/OPTICAL ROTATION :

4.8.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Specification Rotation/Optical Rotation analysis are detailed in the table below:

TABLE 9: SPECIFIC ROTATION

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	+80.6°
GALP-0121-00004-PV Drum 1	Finished Goods	+78.0° to +81.5°	+80.5°

4.9. RESIDUE ON IGNITION :

4.9.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Residue on Ignition analysis are detailed in the table below:

TABLE 10: RESIDUE ON IGNITION

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	<0.0200%
GALP-0121-00004-PV Drum 1	Finished Goods	≤0.1%	<0.1%

4.10. RESIDUAL SOLVENTS :

4.10.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The result of the Residual Solvents analysis are detailed in the table below:

TABLE 11: RESIDUAL SOLVENTS

Lot Number	Stage	Specification				Result			
		Ethanol	IPA	Methanol	Methyl Isobutyl Ketone	Ethanol	IPA	Methanol	Methyl Isobutyl Ketone
GALP-0121-00004-PV Drum 1	Finished Goods	≤500 ppm	≤5000 ppm	≤100 ppm	≤500 ppm	<500 ppm	<5000 ppm	<100 ppm	<500 ppm

4.11. WATER (BY KARL FISCHER TITRATION) :

4.11.1. Refer to the Degradation and Impurity Profile Protocol: Galactose for testing methods and requirements. The results of the Water by Karl Fischer analysis are detailed in the table below:

TABLE 12: WATER BY KARL FISCHER

Lot Number	Stage	Specification	Result
PG-19-092	Raw Material	Monitor	0.10%
GALP-0121-00004-PV Drum 1	Finished Goods	≤1.0%	0.2%

5. CONCLUSION:

5.1. All samples met the required specifications for each analysis, as dictated by the Degradation and Impurity Profile Protocol: Galactose.

5.2. It is conclusive that there are no unintentionally introduced impurities present in the manufacturing process of D-Galactose Bio Excipient material at any stage, as currently validated.