



100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

DEGRADATION AND IMPURITY PROFILE REPORT: D-GALACTOSE

TABLE OF CONTENTS

1. PURPOSE AND SCOPE:	3
2. RESPONSIBILITIES:	4
3. REFERENCES:.....	4
4. PROCEDURE:	5
5. CONCLUSION:	8

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 was 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. Tables were generated to include all sample results in the 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 will demonstrate 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 will evaluate if there is 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 Director of Laboratory Testing or designee was responsible for control, implementation, training and maintenance of this procedure.
- 2.2. The Laboratory Analysts or other qualified personnel were responsible for performing the testing stated in the protocol.
- 2.3. The Laboratory Manger with help from Laboratory Analysts if needed, was responsible for completing the degradation and impurity testing report and recording all results in the associated laboratory notebook.

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 D-Galactose
- 3.3. BSI-ATM-0101, Residual Solvents for D-Galactose
- 3.4. BSI-PRL-0437, Degradation and Impurity Profile Protocol: Galactose
- 3.5. BSI-RPT-1286, Elemental Impurity Assessment: D-Galactose E06 2023 Process Validation
- 3.6. BSI-SOP-0098, Balance SOP.
- 3.7. BSI-SOP-0102, Degradation and Impurity Profiling SOP
- 3.8. BSI-SOP-0126, Laboratory Notebooks
- 3.9. BSI-SOP-0303, NexION 350X ICP-MS SOP
- 3.10. *Current EP*
- 3.11. *Current JP*
- 3.12. *Current USP*

4. PROCEDURE:

4.1. For all testing below, refer to the Degradation and Impurity Profile Protocol: D-Galactose for testing methods and requirements.

4.2. APPEARANCE AND COLOR :

4.2.1. The results of the appearance and color testing are detailed in the table below.

TABLE 1: APPEARANCE AND COLOR RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	White to Almost White Crystalline Powder
GALP-0123-00007-PV Beginning	Finished Good	White to Almost White Crystalline or Finely Granulated Powder	White to Almost White Crystalline Powder

4.3. ASSAY :

4.3.1. The results of the assay testing are detailed in the table below.

TABLE 2: ASSAY RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	98.9%
GALP-0123-00007-PV ML	Mother Liquor		28.0%
GALP-0123-00007-PV WC	Wet Crystal		79.0%
GALP-0123-00007-PV Beginning	Finished Good	98.0-102.0%	98.5%

4.4. ACIDITY :

The results of the acidity testing are detailed in the table below.

TABLE 3: ACIDITY RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	Passes Test
GALP-0123-00007-PV Beginning	Finished Good	Passes Test	Passes Test

4.5. ELEMENTAL IMPURITIES W/FE, MN, AND ZN :

4.5.1. The results of the Elemental Impurities with Iron, Manganese and Zinc testing are detailed in the table below.

TABLE 4: ELEMENTAL IMPURITIES RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	Refer to BSI-RPT-1286 for Elemental Impurity Assessment
GALP-0123-00007-PV ML	Mother Liquor		
GALP-0123-00007-PV WC	Wet Crystal		
GALP-0123-00007-PV Beginning	Finished Good	Meets BSI-FRM-0699 Requirements	

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4.6. **IDENTIFICATION TEST A** :

4.6.1. The results of the identification A testing are detailed in the table below.

TABLE 5: IDENTIFICATION TEST A RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	0.996494; Passes Test
GALP-0123-00007-PV ML	Mother Liquor		0.998243; Passes Test
GALP-0123-00007-PV WC	Wet Crystal		0.949203; Passes Test
GALP-0123-00007-PV Beginning	Finished Good	Conforms to Reference	0.966575; Conforms to Reference

4.7. **IMPURITIES (RELATED SUBSTANCES NF)** :

4.7.1. The results of the impurities (Related Substances) testing are detailed in the table below.

TABLE 6: IMPURITIES RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	See below for additional table of results.
GALP-0123-00007-PV ML	Mother Liquor		
GALP-0123-00007-PV WC	Wet Crystal		
GALP-0123-00007-PV Beginning	Finished Good	Meets BSI-FRM-0699 Requirements	

Lot Number	Result			
	Lactose and 1,6-galactosyl-galactose	Galacturonic Acid	Dextrose	Tagatose
RMAT-1122-0017	0.07%	<0.6%	<0.6%	<0.6%
GALP-0123-00007-PV ML	<0.6%	<0.6%	<0.6%	<0.6%
GALP-0123-00007-PV WC	<0.6%	<0.6%	<0.6%	<0.6%
GALP-0123-00007-PV Beginning	<0.6%	<0.6%	<0.6%	<0.6%
Lot Number	Additional Results			
	Any Unspecified Impurities	Dulcitol	Arabinose	Total
RMAT-1122-0017	<0.6%	<0.6%	0.36%	0.43%
GALP-0123-00007-PV ML	<0.6%	<0.6%	0.36%	0.36%
GALP-0123-00007-PV WC	<0.6%	<0.6%	0.16%	0.20%
GALP-0123-00007-PV Beginning	<0.2%	<0.6%	0.14%	0.14%

4.8. **PROTEINS** _____ :

4.8.1. The results of the Proteins testing are detailed in the table below.

TABLE 7: PROTEINS RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	0.1 mg/mL
GALP-0123-00007-PV Beginning	Finished Good	Passes Test	<0.1 mg/mL

4.9. **SPECIFIC ROTATION/OPTICAL ROTATION** _____ :

4.9.1. The results of the Specific Rotation testing are detailed in the table below.

TABLE 8: SPECIFIC ROTATION/OPTICAL ROTATION RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	+80.6° @ 20°C
GALP-0123-00007-PV Beginning	Finished Good	+78.0 to +81.5° @ 20°C	+80.8° @ 20°C

4.10. **RESIDUE ON IGNITION** _____ :

4.10.1. The results of the Residue on Ignition testing are detailed in the table below.

TABLE 9: RESIDUE ON IGNITION RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	<0.0187%
GALP-0123-00007-PV Beginning	Finished Good	≤0.1%	<0.0200%

4.11. **RESIDUAL SOLVENTS** _____ :

4.11.1. The results of the Residual Solvents testing are detailed in the table below.

TABLE 10: RESIDUAL SOLVENTS

Lot Number	Stage	Specification (ppm)				Result (ppm)			
		Ethanol	IPA	Methanol	MIBK	Ethanol	IPA	Methanol	MIBK
GALP-0123-00007-PV Beginning	Finished Good	≤500	≤5000	≤100	≤500	ND	<2520	ND	ND

4.12. **WATER (BY KARL FISCHER TITRATION)** _____ :

4.12.1. The results of the Water by Karl Fischer testing are detailed in the table below.

TABLE 11: WATER BY KARL FISCHER RESULTS

Lot Number	Stage	Specification	Result
RMAT-1122-0017	Raw Material	Monitor	0.09%
GALP-0123-00007-PV Beginning	Finished Good	≤0.1%	0.2%

5. CONCLUSION:

- 5.1. All samples met the specifications for required analyses as dictated in the Degradation and Impurity Profile Protocol: Galactose.
- 5.2. It can be concluded that there are no additional identifiable impurities present in the Galactose material manufactured in Bangor process room E06 at any stage of the process at this time.