BIOSPECTRA

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

Effective Date:	26-Oct-2021		: Date of Next Review
Initiated By:	Uhlig, Mark W	N/A	: Supersedes
Reason for Print:	MasterControl		

Approval:	Approvers			
	Date	Time	Group	Name
	25-Oct-2021	01:25:56 PM	MANAGEMENT	Uhlig, Mark W
	25-Oct-2021	01:32:31 PM	QUALITY	Hrizuk, Stephen
	26-Oct-2021	08:16:50 AM	EDITOR	McCormick, Sean R

STABILITY INDICATING REPORT:

GALACTOSE

Printed On:	08-Nov-2021 12:07:50 PM	Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.		
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.		

TABLE OF CONTENTS

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

1. PURPOSE:

1.1. The purpose of this Report is to report which analytical analyses are stability indicating through assessment of results on chemically and physically stressed galactose.

    1.1.1. Chemical and Physical Stressors:

        1.1.1.1. Temperature

        1.1.1.2. Humidity

        1.1.1.3. Light

        1.1.1.4. pH

            1.1.1.4.1. Acid

            1.1.1.4.2. Base

        1.1.1.5. Oxidative

    1.1.2. Analytical analyses:

        1.1.2.1. Appearance of Solution (NF)

        1.1.2.2. Appearance and Color

        1.1.2.3. Acidity/Alkalinity (NF)

        1.1.2.4. Assay % w/w (NF)

        1.1.2.5. Chromatographic Purity/ Related Substances (NF)

        1.1.2.6. Identification A, B, C (NF)

        1.1.2.7. Specific/Optical Rotation

        1.1.2.8. Water (KF)

    1.1.3. The following tests were not performed after material manipulations:

        1.1.3.1. Microbial Enumeration Tests / Tests for Specified Microorganisms

        1.1.3.2. Residual Solvents (Excluding Water, via Karl Fischer)

        1.1.3.3. Heavy Metals /Elemental Impurities / Limit of Pb or Fe

        1.1.3.4. Residue on Ignition /Sulfated Ash

2. SCOPE:

2.1. This Report applies to the stability testing requirements of BioSpectra manufactured Galactose, the findings in this report are to be used to determine the tests that will be tested at each stability time interval and represented on the stability data card.

3. RESPONSIBILITIES:

3.1. The Executive Director of Quality Control is responsible for the control, implementation, training and maintenance of this procedure.

3.2. The QC Analysts were responsible for performing the testing stated in this Report and recording all results in current laboratory documentation.

3.3. The Executive Director of Quality or qualified personnel is responsible for completing the Stability Indicating Report.

3.4. Standard laboratory safety regulations apply. Before working with any chemical, read and understand the safety data sheet (SDS).

4. REFERENCES:

4.1. Balance SOP, DCN: 16-000368

4.2. Blue M Convection Oven Operation and Calibration SOP, DCN: 16-000502

4.3. Current USP/ NF

4.4. Fisher Scientific Isotemp Water Bath Operation Calibration SOP, DCN: 16-001355

4.5. Laboratory Notebooks, DCN: 16-000482

4.6. Muffle Furnace SOP and Calibration, DCN:16-000364

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

4.7. [NexION 350X ICP-MS SOP, DCN: 16-001923](#)
4.8. [Stability Indication Report, DCN: 16-001384](#)
4.9. [VWR Gravity Convection Oven Operation and Calibration (Model Number 414005-106), DCN: 16-001319](#)
4.10. *ICH Q1A*

5. EQUIPMENT:

5.1. Analytical Balance
  5.1.1. MSE 224S S/N 24801744
  5.1.2. Practum 612 1-S S/N 0031950175
  5.1.3. Secura 124-1S S/N 29212172
5.2. Oven
  5.2.1. S/N 1100001176D009
5.3. Calibrated Thermometer
  5.3.1. S/N 210354608
5.4. Calibrated Timer 5.4.1.
    S/N 2100126915.4.2.
    S/N 200299683
5.5. Eppendorf Micropipette
  5.5.1. S/N J18397D
  5.5.2. S/N K53394I
  5.5.3. S/N 034393G
5.6. Lux Meter
  5.6.1. S/N 0037D
5.7. MCP Polarimeter 300
  5.7.1. S/N 80974130
5.8. Metrohm 907 Auto Titrator
  5.8.1. S/N 12155
5.9. Perkin Elmer Spectrum Two UATR
  5.9.1. S/N 97561
5.10. Perkin Elmer Flexar HPLC
  5.10.1. Solvent Manager   260S13111110F
  5.10.2. Autosampler   293H3080804A
  5.10.3. Pump   291S13111109F
  5.10.4. RI Detector   292J3110505B
  5.10.5. Oven   0VHF130915868

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

Stability Indicating Report: Galactose   DCN: 21-002392   v. 1.0

6. PROCEDURE:

6.1. Stress Procedures – Galactose Lot GALP-0121-00002:

   6.1.1. Control:
       6.1.1.1. Unstressed Material

   6.1.2. Thermal Stress:
       6.1.2.1. Transferred 100.0100g of galactose to a suitable tray and evenly spread to increase exposure area.
       6.1.2.2. Heated sample at 130°C for 18 hours to degrade.
       6.1.2.3. Froze sample for 14 hours after heat exposure.
       6.1.2.4. Brought sample back to room temperature before analysis.

   6.1.3. Acid Stress:
       6.1.3.1. Applied 2.5mL of hydrochloric acid (Lot 201292 Exp. 6/30/25) to 100.0019g of sample; mixed the acidic mixture thoroughly in a suitable container.
       6.1.3.2. Dried the sample using a well-ventilated tray and use a mortar and pestle to homogenize after drying.

   6.1.4. Basic Stress:
       6.1.4.1. Applied 2.5mL of 50% sodium hydroxide (Lot 196090 Exp 11/21) to 100.0082g of sample; mixed the basic mixture thoroughly in a suitable container.
       6.1.4.2. Dried the sample using a well-ventilated tray and use a mortar and pestle to homogenize after drying

   6.1.5. Oxidative Stress:
       6.1.5.1. Applied 2.5mL of 30% hydrogen peroxide (175412 Exp. 9/21) to 100.0153g of sample. Mixed the mixture thoroughly and allow to react in an open container or vessel.
       6.1.5.2. After reaction ceased, transferred material to a well-ventilated tray and use a mortar and pestle to homogenize after drying.

   6.1.6. Humidity/Hydrolytic Stress:
       6.1.6.1. Transferred material to a suitable tray and evenly spread to increase exposure area.
       6.1.6.2. Exposed sample to 40°C temperature and 75% relative humidity for 48 hours before removing for test.

   6.1.7. Photolytic Stress:
       6.1.7.1. Exposed sample to approx. 1.2 million lux hours of light.

               Lux hours = (Average Lux Intensity * Hours of Exposure)

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

DCN: BSI-RPT-0775, Revision: 1.0, Effective Date: 06 Jun 2016 12:00 AM, Date of Next Review: 06 Jun 2017 12:00 AM

Stability Indicating Report: Galactose   DCN: 21-002392 v. 1.0

7. ANALYTICAL PROCEDURES AND RESULTS:

7.1. APPEARANCE AND COLOR   White to off white crystalline powder:

7.1.1. Testing Reference: BD4P36

7.1.2. Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Light Brown Crystalline Powder	
GALP-0121-00002 Acidic Stress	White to Almost White, Crystalline Powder	
GALP-0121-00002 Basic Stress	Light Brown Crystalline Powder	
GALP-0121-00002 Oxidative Stress	White to Almost White, Crystalline Powder	Yes
GALP-0121-00002 Humidity Stress	White to Almost White, Crystalline Powder	
GALP-0121-00002 Photolytic Stress	White to Almost White, Crystalline Powder	

7.2. ACIDITY/ALKALINITY   Passes Test:

7.2.1. Testing Reference: BD4P37

7.2.2. Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Passes Test	
GALP-0121-00002 Acidic Stress	Does Not Pass Test	
GALP-0121-00002 Basic Stress	Does Not Pass Test	
GALP-0121-00002 Oxidative Stress	Does Not Pass Test	Yes
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Passes Test	

7.3. ASSAY   98.0-102.0%:

7.3.1. Testing Reference: HPLC06 pp37-39, 57

7.3.2. Stressed Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Does Not Pass Test	
GALP-0121-00002 Acidic Stress	Does Not Pass Test	
GALP-0121-00002 Basic Stress	Does Not Pass Test	
GALP-0121-00002 Oxidative Stress	Does Not Pass Test	Yes
GALP-0121-00002 Humidity Stress	Does Not Pass Test	
GALP-0121-00002 Photolytic Stress	Does Not Pass Test	

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

7.4. <u>APPEARANCE OF SOLUTION</u>   <u>Refer to Summary Sheet:</u>

       7.4.1.   Testing Reference: BD4P36

       7.4.2.   Results**:**

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Does Not Pass Test	
GALP-0121-00002 Acidic Stress	Does Not Pass Test	
GALP-0121-00002 Basic Stress	Does Not Pass Test	
GALP-0121-00002 Oxidative Stress	Passes Test	Yes
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Passes Test	

7.5. <u>IDENTIFICATION TEST A</u>   <u>Conforms to Standard:</u>

       7.5.1.   Testing Reference: BD4P37

       7.5.2.   Results**:**

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Passes Test	
GALP-0121-00002 Acidic Stress	Passes Test	
GALP-0121-00002 Basic Stress	Passes Test	
GALP-0121-00002 Oxidative Stress	Passes Test	No
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Passes Test	

7.6. <u>IDENTIFICATION TEST B</u>   <u>Corresponds to Standard:</u>

       7.6.1.   Testing Reference: HPLC06P67

       7.6.2.   Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Passes Test	
GALP-0121-00002 Acidic Stress	Passes Test	
GALP-0121-00002 Basic Stress	Passes Test	
GALP-0121-00002 Oxidative Stress	Passes Test	No
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Passes Test	

       7.7.7.7.

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

7.8.   IDENTIFICATION TEST C   Passes Test:

7.8.1.   Testing Reference: BD4P37

7.8.2.   Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Passes Test	
GALP-0121-00002 Acidic Stress	Passes Test	
GALP-0121-00002 Basic Stress	Passes Test	
GALP-0121-00002 Oxidative Stress	Passes Test	No
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Passes Test	

7.9.   RELATED SUBSTANCES   Refer to Summary Sheet:

7.9.1.   Testing Reference: HPLC06 pp37-39, 57

7.9.2.   Stressed Results:

Lot ID	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	Passes Test	
GALP-0121-00002 Acidic Stress	Does Not Pass Test	
GALP-0121-00002 Basic Stress	Does Not Pass Test	
GALP-0121-00002 Oxidative Stress	Does Not Pass Test	Yes
GALP-0121-00002 Humidity Stress	Passes Test	
GALP-0121-00002 Photolytic Stress	Does Not Pass Test	

7.10. SPECIFIC ROTATION/OPTICAL ROTATION   +78.0° to +81.5@ 20°C:

7.10.1. Testing Reference: BD4P39

7.10.2. Results:

Lot ID	Measured Value	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	+80.18	Passes Test	
GALP-0121-00002 Acidic Stress	+80.54	Passes Test	
GALP-0121-00002 Basic Stress	+74.50	Fails Test	
GALP-0121-00002 Oxidative Stress	+80.27	Passes Test	Yes
GALP-0121-00002 Humidity Stress	+80.41	Passes Test	
GALP-0121-00002 Photolytic Stress	+80.37	Passes Test	

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

7.11. **WATER (By Karl Fischer Titration)**   **1.0% Max:**

    7.11.1. Testing Reference: BD4P43 - 44

    7.11.2. Results:

Lot ID	Measured Value	Result	Stability Indicating (Yes/No)
GALP-0121-00002 Thermal Stress	0.26%	Passes Test	
GALP-0121-00002 Acidic Stress	0.48%	Passes Test	
GALP-0121-00002 Basic Stress	2.13%	Fails Test	Yes
GALP-0121-00002 Oxidative Stress	0.28%	Passes Test	
GALP-0121-00002 Humidity Stress	0.42%	Passes Test	
GALP-0121-00002 Photolytic Stress	0.59%	Passes Test	

8. **ANALYTICAL CONCLUSIONS:**

    8.1. **APPEARANCE AND COLOR**   **White to off white crystalline powder:**

        8.1.1. Stability Indicating: Yes

        8.1.2. Recommended for inclusion in stability test program: Yes

        8.1.3. Notes: Appearance and color is considered a stability indicating analyses and will be included in the stability test program.

    8.2. **ACIDITY/ALKALINITY**   **Passes Test:**

        8.2.1. Stability Indicating: Yes

        8.2.2. Recommended for inclusion in stability test program: Yes

        8.2.3. Notes: Acidity/Alkalinity is considered a stability indicating analyses and will be included in the stability test program.

    8.3. **ASSAY**   **98.0-102.0%:**

        8.3.1. Stability Indicating: Yes

        8.3.2. Recommended for inclusion in stability test program: Yes

        8.3.3. Notes: Forced degradation of the samples may have created artificial failures during HPLC analysis. The cation H+ chemical mechanism of separation may be affected by deliberate injections with excess base, acids, or oxidizing agents. The system suitability on day of analysis demonstrated USP compliant system suitability resolution, sensitivity, and repeatability and all of the assay results were out of specification. The results will be considered OOS and the USP assay method of analysis will be included in the stability testing program.

    8.4. **APPEARANCE OF SOLUTION**   **Refer to Summary Sheet:**

        8.4.1. Stability Indicating: Yes

        8.4.2. Recommended for inclusion in stability test program: Yes

        8.4.3. Notes: Appearance of solution is considered a stability indicating analyses and will be included in the stability test program.

    8.5. **IDENTIFICATION TEST A**   **Conforms to Standard:**

        8.5.1. Stability Indicating: No

        8.5.2. Recommended for inclusion in stability test program: Yes

        8.5.3. Notes: Identification A is not considered a stability indicating analyses, however, will be included in the stability test program to satisfy one of two required identification analyses throughout the stability life cycle.

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

8.6.   **IDENTIFICATION TEST B**   **Corresponds to Standard:**

   8.6.1.   Stability Indicating: No
   8.6.2.   Recommended for inclusion in stability test program: Yes
   8.6.3.   Notes: Identification B is not considered a stability indicating analyses, however, will be included in the stability test program based on being a mutually inclusive analyses during assay analysis by means of HPLC.

8.7.   **IDENTIFICATION TEST C**   **Passes Test:**

   8.7.1.   Stability Indicating: No
   8.7.2.   Recommended for inclusion in stability test program: No
   8.7.3.   Notes: Identification C is not considered a stability indicating analyses and since identity A and B will be tested, this is not required for stability testing.

8.8.   **RELATED SUBSTANCES**   **Refer to Summary Sheet:**

   8.8.1.   Stability Indicating: Yes
   8.8.2.   Recommended for inclusion in stability test program: Yes
   8.8.3.   Notes: Forced degradation was clear to demonstrate the generation of organic impurities that were clearly resolved from the parent peak. The method of measurement can quantify and detect these unknown degradant products and other related substances.

8.9.   **SPECIFIC ROTATION/OPTICAL ROTATION**   **+78.0° to +81.5@ 20°C:**

   8.9.1.   Stability Indicating: Yes
   8.9.2.   Recommended for inclusion in stability test program: Yes
   8.9.3.   Notes: Specific Rotation/Optical rotation is considered a stability indicating analyses and will be included in the stability test program.

8.10.   **WATER (By Karl Fischer Titration)**   **1.0% Max:**

   8.10.1. Stability Indicating: Yes
   8.10.2. Recommended for inclusion in stability test program: Yes
   8.10.3. Notes: Water determination by means of Karl Fischer is considered a stability indicating analyses and will be included in the stability test program.

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022

9. STABILITY INDICATING SUMMARY:

Recommended Stability Indicating Tests and Specifications		
Analytical Test		Specification
Appearance and Color		White to off white crystalline powder
Acidity/Alkalinity		Passes Test
Assay		98.0-102.0%
Appearance of Solution		Passes Test
Identification A (USP)		Conforms to Standard
Identification B (USP)		Corresponds to Standard
Related Substances	Lactose and 1,6-galactosyl-galactose	≤0.6%
	Galacturonic Acid	≤0.6%
	Dextrose	≤0.6%
	Tagatose	≤0.6%
	Dulcitol	≤0.6%
	Arabinose	≤0.6%
	Unspecified (Single)	≤1.0%
	Total Organic Impurities	≤1.0%
Specific / Optical Rotation		+78.0° to +81.5@ 20°C
Water (By Karl Fischer Titration)		≤1.0%

Printed On:	08-Nov-2021 12:07:50 PM		Lobb, Jared	: Printed By
Print Expiration:	This document expires on the Date of Next Review listed in the header of this document or upon next revision.			
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.			

Controlled Copy Number: 4, Controlled Copy Location: Placement on Website
Printed By: ALISSA.LEDERGERBER, on 09 Feb 2022