Your claim can be filed electronic

Claim #42 Date Filed: 12/20/2024

ID: 26351304 PIN: g4QpqMpa

Fill in this information to identify the case:

Debtor Gritstone bio, Inc.

United States Bankruptcy Court for the District of Delaware

Case number 24-12305 (KBO)

Modified Official Form 410
Proof of Claim

04/22

Read the instructions before filling out this form. This form is for making a claim for payment in a bankruptcy case. Other than a claim under 11 U.S.C. § 503(b)(9), this form should not be used to make a claim for an administrative expense arising after the commencement of the case.

Filers must leave out or redact information that is entitled to privacy on this form or on any attached documents. Attach redacted copies or any documents that support the claim, such as promissory notes, purchase orders, invoices, itemized statements of running accounts, contracts, judgments, mortgages, and security agreements. **Do not send original documents;** they may be destroyed after scanning. If the documents are not available, explain in an attachment.

A person who files a fraudulent claim could be fined up to $500,000, imprisoned for up to 5 years, or both. 18 U.S.C. §§ 152, 157, and 3571.

Fill in all the information about the claim as of the date the case was filed.

Part 1: Identify the Claim

NameID: 15651824

1. Who is the current creditor?

JOINN Biologics US, Inc.
Name of the current creditor (the person or entity to be paid for this claim)

Other names the creditor used with the debtor _____

2. Has this claim been acquired from someone else?

☒ No

☐ Yes. From whom? _____

3. Where should notices and payments to the creditor be sent?

Federal Rule of Bankruptcy Procedure (FRBP) 2002(g)

Where should notices to the creditor be sent?

JOINN Biologics US, Inc.
2600 Hilltop Drive L3017
Richmond, CA 94806

_____
Address

Contact phone 240-441-1633

Contact email tao.he@joinnbio.com

Where should payments to the creditor be sent? (if different)

_____
Name

_____
Number Street

_____
City State ZIP Code

_____
Country

Contact phone _____

Contact email _____

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Uniform claim identifier for electronic payments in chapter 13 (if you use one):

_____

4. Does this claim amend one already filed?

☒ No

☐ Yes. Claim number on court claims registry (if known) _____ Filed on _____ MM / DD / YYYY

5. Do you know if anyone else has filed a proof of claim for this claim?

☒ No

☐ Yes. Who made the earlier filing? _____

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Part 2: Give Information About the Claim as of the Date the Case Was Filed

6. **Do you have any number you use to identify the debtor?**

☒ No

☐ Yes. Last 4 digits of the debtor's account or any number you use to identify the debtor: ____ ____ ____ ____

7. **How much is the claim?**

$ 61,500.00 . **Does this amount include interest or other charges?**

☒ No

☐ Yes. Attach statement itemizing interest, fees, expenses, or other charges required by Bankruptcy Rule 3001(c)(2)(A).

8. **What is the basis of the claim?**

Examples: Goods sold, money loaned, lease, services performed, personal injury or wrongful death, or credit card.

Attach redacted copies of any documents supporting the claim required by Bankruptcy Rule 3001(c).

Limit disclosing information that is entitled to privacy, such as health care information.

Service performed based on contract (attached) page 6, table footnote.

9. **Is all or part of the claim secured?**

☒ No

☐ Yes. The claim is secured by a lien on property.

Nature of property:

☐ Real estate: If the claim is secured by the debtor's principal residence, file a *Mortgage Proof of Claim Attachment* (Official Form 410-A) with this *Proof of Claim*.

☐ Motor vehicle

☐ Other. Describe: _____

Basis for perfection: _____

Attach redacted copies of documents, if any, that show evidence of perfection of a security interest (for example, a mortgage, lien, certificate of title, financing statement, or other document that shows the lien has been filed or recorded.)

Value of property: $_____

Amount of the claim that is secured: $_____

Amount of the claim that is unsecured: $_____ (The sum of the secured and unsecured amount should match the amount in line 7.)

Amount necessary to cure any default as of the date of the petition: $_____

Annual Interest Rate (when case was filed)_____%

☐ Fixed

☐ Variable

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10. **Is this claim based on a lease?**

☒ No

☐ Yes. **Amount necessary to cure any default as of the date of the petition.** $_____

11. **Is this claim subject to a right of setoff?**

☒ No

☐ Yes. Identify the property: _____

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12. **Is all or part of the claim entitled to priority under 11 U.S.C. § 507(a)?**

A claim may be partly priority and partly nonpriority. For example, in some categories, the law limits the amount entitled to priority.

☒ No

☐ Yes. *Check all that apply:* **Amount entitled to priority**

- ☐ Domestic support obligations (including alimony and child support) under 11 U.S.C. § 507(a)(1)(A) or (a)(1)(B). $_____
- ☐ Up to $3,350* of deposits toward purchase, lease, or rental of property or services for personal, family, or household use. 11 U.S.C. § 507(a)(7). $_____
- ☐ Wages, salaries, or commissions (up to $15,150*) earned within 180 days before the bankruptcy petition is filed or the debtor's business ends, whichever is earlier. 11 U.S.C. § 507(a)(4). $_____
- ☐ Taxes or penalties owed to governmental units. 11 U.S.C. § 507(a)(8). $_____
- ☐ Contributions to an employee benefit plan. 11 U.S.C. § 507(a)(5). $_____
- ☐ Other. Specify subsection of 11 U.S.C. § 507(a)(__) that applies. $_____

* Amounts are subject to adjustment on 4/01/25 and every 3 years after that for cases begun on or after the date of adjustment.

13. **Is all or part of the claim entitled to administrative priority pursuant to 11 U.S.C. § 503(b)(9)?**

☒ No

☐ Yes. Indicate the amount of your claim arising from the value of any goods received by the debtor within 20 days before the date of commencement of the above case, in which the goods have been sold to the Debtor in the ordinary course of such Debtor's business. Attach documentation supporting such claim.

$_____

Part 3: Sign Below

The person completing this proof of claim must sign and date it. FRBP 9011(b).

If you file this claim electronically, FRBP 5005(a)(2) authorizes courts to establish local rules specifying what a signature is.

A person who files a fraudulent claim could be fined up to $500,000, imprisoned for up to 5 years, or both. 18 U.S.C. §§ 152, 157, and 3571.

Check the appropriate box:

☒ I am the creditor.

☐ I am the creditor's attorney or authorized agent.

☐ I am the trustee, or the debtor, or their authorized agent. Bankruptcy Rule 3004.

☐ I am a guarantor, surety, endorser, or other codebtor. Bankruptcy Rule 3005.

I understand that an authorized signature on this *Proof of Claim* serves as an acknowledgement that when calculating the amount of the claim, the creditor gave the debtor credit for any payments received toward the debt.

I have examined the information in this *Proof of Claim* and have reasonable belief that the information is true and correct.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on date 12 18 2024
MM / DD / YYYY

T C H
Signature

Print the name of the person who is completing and signing this claim:

Name: Tao (First name) He (Last name) — Middle name

Title: General Manager

Company: JOINN Biologics US Inc.
Identify the corporate servicer as the company if the authorized agent is a servicer.

Address: 2600 Hilltop Dr. Building L
Number Street

Richmond CA 94806 USA
City State ZIP Code Country

Contact phone: 240-441-1633 Email: tao.he@joinnbio.com

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Gritstone bio, Inc.
c/o KCC dba Verita
222 N Pacific Coast Highway, Ste. 300
El Segundo, CA 90245

000795

Legal Notice Enclosed.
Direct to Attention of Addressee, President or Legal Department.

241230524121112223800161 9

PRF #: 138866 | Case No.: 24-12305 | Svc.: 2 | PackID: 795 | NameID: 15651824

JOINN Biologics US, Inc.
2600 Hilltop Drive L3017
Richmond, CA 94806

Your claim can be filed electronically on Verita's website at https://www.veritaglobal.net/gritstone

Your unique login information is:

ID: 26351304 PIN: g4QpqMpa

If you have questions regarding this notice, please call (877) 709-4754 (U.S./Canada) or +1 (424) 236-7233 (International), or email via www.veritaglobal.net/gritstone/inquiry.

Scope of Work #1

This Scope of Work #1 ("**SOW**") is effective May 17, 2021 (the "**SOW Effective Date**"), and is made by and between **Gritstone bio, Inc.** ("**Gritstone**") a Delaware corporation, located at 5959 Horton St., Ste 300, Emeryville, CA 94608, and **JOINN Biologics US, Inc.** ("**Provider**"), a Delaware corporation, located at 1267 Willis Street, Suite 200, Redding, CA 96001. Gritstone and Provider are each individually referred to herein as a "**Party**" and collectively as the "**Parties**".

1. **Governing Agreement.** This SOW constitutes a "**Scope of Work**" under that certain Master Services Agreement by and between the Parties, dated March 25, 2021, as may have been amended by the Parties from time to time, (the "**Agreement**"). This SOW and the Services contemplated herein include, and are subject to, the terms and conditions of the Agreement, which are incorporated by reference. Capitalized terms used in this SOW and not otherwise defined herein shall have the same meaning as set forth in the Agreement.

2. **Term.** The term of this SOW shall commence on the Effective Date and shall continue thereafter until April 30, 2022, unless sooner terminated hereunder.

3. **Scope of Services.** The Services to be provided by Provider pursuant to this SOW shall be pursuant to Provider's **GMP Buffer Preparation**, dated **May 4, 2021**, attached hereto as **Attachment 1** ("**Proposal**").

4. **Fees and Payment Terms.** Unless pre-authorized in writing by Gritstone, the total compensation for Services performed pursuant to this SOW shall not exceed **$365,000** (the "**Fees**"). Gritstone has already submitted payment for Stage 1 on April 28, 2021 in the amount of $122,000 under Invoice GS2940-0101. The remaining balance to be paid for Stage 1 is $38,000. Gritstone shall remit payment for undisputed line items in invoices within thirty (30) days of Gritstone's receipt of the invoice. Invoices shall contain detail reasonably required for Gritstone to understand the activities and amount of time being billed and shall be sent to ap@Gritstone.com. Gritstone shall pay Provider the Fees according to the pricing terms set forth in the Proposal.

5. **Reimbursable Expenses.** So long as Gritstone's prior written approval has been obtained, Provider shall be entitled to be reimbursed for any reasonable, out-of-pocket travel, lodging and incidental travel expenses incurred in performing the Services hereunder ("**Expenses**"); unless otherwise authorized in writing by Gritstone, plane travel shall be at economy fare. Gritstone shall have no obligation to reimburse Provider for any undocumented Expenses.

6. **Order of Precedence.** To the extent any terms or provisions of this SOW conflict with the terms and provisions of the Agreement, the terms and provisions of the Agreement shall control, except to the extent that this SOW expressly and specifically states an intent to supersede the Agreement on a specific matter. To the extent any terms or

provisions of the SOW conflict with the contents of the Proposal, the terms and provisions of this SOW shall control.

7. **Termination.** Gritstone in its sole discretion shall have the right to terminate this SOW without cause by giving Provider thirty (30) days' written notice thereof. Upon termination, Gritstone shall be liable to Provider only for the Fees earned and Expenses incurred for the Services actually performed prior to the notice of termination. In the event Gritstone has paid Provider any Fees in advance, Provider will promptly refund to Gritstone any and all pre-paid and unused Fees within thirty (30) days of the effective date of the termination.

8. **Execution.** This SOW may be executed in one or more counterparts (including by facsimile or .pdf), each of which shall constitute an original and all of which, when taken together, shall constitute one agreement.

IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound hereby, have caused this SOW to be executed and delivered by their proper and duly authorized officers effective as of the SOW Effective Date.

ACCEPTED AND AGREED TO:

GRITSTONE BIO, INC.

DocuSigned by:
By: James Cho
A18275C656864DF...
Name: James Cho
Its: Vice President, Finance
Date: May 24, 2021

JOINN BIOLOGICS US, INC.

By: _____
Name: _____
Its: _____
Date: _____

GRITSTONE BIO, INC.

DocuSigned by:
By: Vijay Yabannavar
DE609E6D097B425...
Name: Vijay Yabannavar
Its: Chief Mfg. & Tech. Ops. Officer
Date: May 24, 2021

provisions of the SOW conflict with the contents of the Proposal, the terms and provisions of this SOW shall control.

7. **Termination.** Gritstone in its sole discretion shall have the right to terminate this SOW without cause by giving Provider thirty (30) days' written notice thereof. Upon termination, Gritstone shall be liable to Provider only for the Fees earned and Expenses incurred for the Services actually performed prior to the notice of termination. In the event Gritstone has paid Provider any Fees in advance, Provider will promptly refund to Gritstone any and all pre-paid and unused Fees within thirty (30) days of the effective date of the termination.

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IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound hereby, have caused this SOW to be executed and delivered by their proper and duly authorized officers effective as of the SOW Effective Date.

ACCEPTED AND AGREED TO:

GRITSTONE BIO, INC.

DocuSigned by:

By: James Cho

Name: James Cho

Its: Vice President, Finance

Date: May 24, 2021

JOINN BIOLOGICS US, INC.

By:

Name: CHERYL TUCK

Its: Sr. Director, BD+MKT

Date: 25MAY2021

GRITSTONE BIO, INC.

DocuSigned by

By: Vijay Yabannavar

Name: Vijay Yabannavar

Its: Chief Mfg. & Tech. Ops. Officer

Date: May 24, 2021

ATTACHMENT 1

GMP Buffer Preparation

Dated: May 4, 2021

JOINN BIOLOGICS

Scope of Work for Contract Manufacturing Services:

GMP Buffer Preparation

Prepared for:

gritstone oncology

Client/Project Code:

2940-01

For Joinn Finance Department Use

Contact Information

GRITSTONE	JOINN Biologics US, Inc.
Adam Morgenthaler Process Development Engineer 4698 Willow Road Pleasanton, CA 94588 (408) 891 6012 amorgenthaler@gritstone.com	Cheryl Tuck Director, BD/Marketing 2600 Hilltop Drive Richmond, CA 94806 (405) 531-1300 cheryl.tuck@joinnbio.com

Executive Summary

JOINN Biologics US, Inc. was founded in 2018, located in beautiful San Francisco Bay at the JOINN Innovation park. We are a full-service premier Contract Development & Manufacturing Organization which provides you with quality, value and speed to market from DNA to Drug Product. We offer a comprehensive range of services across all the phases of the drug life cycle, which includes Cell Line development RCB & MCB manufacturing, Process and Analytical development, Formulation Development, Drug Substance Manufacturing and Drug Product fill/finish services, along with packaged services for material production, all under one quality system supported by global regulatory services. Additionally, IND enabling PKPD TOX services could be packaged together with JOINN Laboratories. Our scientists and engineers bring over two decades of development experience across a broad spectrum of both platform and novel technologies.

We advance optimal large-molecule clinical candidates & commercial products through our premier contract development and manufacturing services with continued innovation to achieve high quality, low cost, and fast speed.

Gritstone Oncologyis a biotechnology company with its goal to eradicate cancer by developing personalized immunotherapies to fight multiple cancer types.

Gritstone has asked JOINN Biologics US, Inc. ("JOINN") to provide a Scope of Work and price proposal for several GMP buffer preparation. This project-specific proposal is provided solely for Gritstone based on information provided and key assumptions.

Issue Date: **MAY 4, 2021** **Expiration Date: MAY 31, 2021**

Scope of Work

1. Project Setup

To make the facility ready for initiation of GMP buffer preparation.

- Prepare necessary documentation including batch records, bill of material, test records and etc.
- Review raw material, consumable vendor list and initiate raw material, consumable acquisition.
- Assign project management responsibility and coordinate internal/external activities

2. Small Scale Production and Hold Study

2.1. Prepare, test, hold study of small scale buffers based on requirements in the buffer list (attached)

Buffer Item	Volume/Container per timepoint:
GRIT1 Equilibration Buffer	1L ± 10% in 1L Bag
GRIT1 Wash Buffer	1L ± 10% in 1L Bag
GRIT1 Elution Buffer	1L ± 10% in 1L Bag
GRIT1 Strip Buffer	1L ± 10% in 1L Bag
GRIT1 Citrate buffer	1L ± 10% in 1L Bag
4M NaCl	1L ± 10% in 1L Bag
ADPS buffer	1L ± 10% in 1L Bag
1M NaOH	1L ± 10% in 1L Bag

2.2. Stability testing schedule:

- Develop hold study protocol & get approval from Gritstone before project initiation
- Ambient temperature:

0* 3* 6* 9 12* (months)
|_____|_____|_____|_____|

QC testing on timepoint 0 (initial release), 3, 6, 9 and 12 months
Time 0: 2 bags will be tested at JOINN Bio QC, and 2 bags will be shipped to Gritstone QC for testing
Time 3, 6, 9, 12 months: 3 bags will be tested at JOINN Bio QC

Time Point (months)	Joinn Testing (1L Bag)	Client Testing (1L Bag)
0	2	2
3	3	NA
6	3	1
9	3	NA
12	3	1

- Hold Study testing menu
    - pH, conductivity, endotoxin
    - Osmolarity
    - Functional test (Gritstone will do this test)
    - Bioburden for all buffers at timepoints: 0, 6, 12 months
    - No leachable/extractables testing needed
- Joinn will send remainder of the bag of the stability sample to Gritstone for functional testing.
- Joinn will produce final report and get approval from Gritstone.

3. GMP Buffer Preparation

3.1. Assumptions

- Raw material Compendial test desired for all buffers
  - USP identity test
  - Identity test by FTIR if necessary, agreed by both parties

- Final container requirement:
  - Need needle-free luer connection attached
  - Equilbration buffer need to be in 20 L bag with >3 luer connectors, Gritstone will review drawings prior to ordering the bags
  - 1 L buffer will be in 1 L bags, 2 L buffers will be in 2L bags, or in vented bottles (Flex Biosystems)
- Final product shipping container requirement:
  - Bucket with lock lid on top
- Filtration requirement:
  - 0.1 um filtration
- Storage temperature:
  - Ambient temperature
- Final test sepcifications (testing menu based on requirement in the attached buffer list)
  - pH, conductivity, endotoxin
  - Osmolarity (where applicable)
  - Sterility testing (Joinn will outsource)
  - Appearance
  - No leachable/extractables testing needed
- Quality requirement:
  - Quality agreement is needed;
  - Vendor qualification required;
  - On-site audit is an option
- Buffer list is attached at the end of this proposal
  - Each item in the buffer list is required for volume/container for 1 run;

3.2. Prepare GMP buffers based on requirements in the buffer list (attached)

Buffer Item	Required volume/Container for 1 Run:
GRIT1 Equilibration Buffer	11 L ± 5% in 20L Bag
	2 L ± 10% in 2-5L Bag
GRIT1 Wash Buffer	1 L ± 10% in 1L Bag
GRIT1 Elution Buffer	1 L ± 10% in 1L Bag
GRIT1 Strip Buffer	2X 1 L ± 10% in 1L Bag
GRIT1 Citrate buffer	2 L ± 5% in 2L Bag
4M NaCl	5 L ± 10% in 5L Bag (For 10 runs)
ADPS buffer	5 L ± 10% in 5L Bag
1M NaOH	2 L ± 10% in 2-5L Bag

3.3. Test, and release GMP buffers based on requirements in the buffer list (attached), and testing summary will be provided to Gritstone. Reference page 16

3.4. Shipping: JOINN Bio will arrange shipping vendor and Gritstone will approve vendor. JOINN will coordinate with Gritstone for delivery of manufactured buffers. Payment of shipping to be made by Gritstone.

Price Matrix

The price estimate below is based on client information and current assumptions. Pricing may be modified after detailed technical review, receipt of additional information, and mutual development and agreement of a detailed Scope of Work.

Note: Invoicing milestones and a signature page will be provided when a final scope is agreed upon between Gritstone and JOINN

Stage 1: Activity	Total volume	Total (USD)	Payment Term
1.1 Project Setup and Management	-	$20,000	
1.2. Small scale buffer production, hold study, and QC testing	(Adding two client time points and additional QC testing)	$100,000	
1.3. Raw Material to support stability studies	128 bags (16 buffers X (8 time points + 3 Client time points))	$40,000	
SUB TOTAL		**$160,000**	**Due at signing of contract**
Stage 2: Activity	**Total volume**	**Total (USD)**	**Payment Term**
2.1 Raw Material Testing for all Buffer material testing		20,000	
2.2. Generating GMP buffers for 6 months usage. (Q3 & Q4, 2021)*	1,068 L	$160,000	

2.4. QC Testing Cost		$25,000	
SUB TOTAL		**$205,000**	50% payment due at initiation of stage 2, 50% due at the completion of the project. Deliver of buffer & COA.
TOTAL COST		**$365,000**	
Sterility Testing for GMP Production	*Approximately 35 sterility bags to be tested*	*Est. to be $2200 per sample*	*Pass through cost, Joinn will charge 10% extra of 3rd party cost.*

*: JOINN charges 30% of stage 2 ($205,000) if the project is cancelled after JOINN has successfully completed stage 1. i.e. Buffers passed the hold testing stage. **Shipping to be paid by Gritstone.

Business Philosophy

JOINN Biologics US, Inc focuses on a strong client experience and was founded on the premise that an understanding of our customers' technical and business needs are required to efficiently serve the market. We offer a comprehensive quality-centric manufacturing service portfolio under reasonable terms and can provide continuity for the project duration. We believe technical excellence and appropriate compliance delivery is a given, and that we must differentiate ourselves and add significant value to our customers. Our business model allows us to meet customer needs by providing the following:

2 Multi-product cGMP manufacturing facility not retro-fitted space or converted from single/limited product use

3 Opportunity to grow: Facility design includes expansion space for larger scale production on a multi-product or client-specific basis; We have initiated the expansion plan for 2,000 L bioreactor suite in our facility, expected completion date: Q2, 2022

4 Comprehensive service offering that can provide a turnkey solution, but which allows clients maximum flexibility to take only the services they require. We are happy to undertake smaller stand-alone projects, and strive to allow our clients to focus time and resources on their core competencies.

5 Professional team with significant client-side experience supplemented by sound biopharmaceutical services market knowledge. We have a great appreciation for the larger drug development process picture, and use these experiences to build strong and long term collaborative relationships and to ensure that we are meeting customer needs.

6 Maximum strategic flexibility: We avoid use of royalty-bearing intellectual property unless specifically requested, and ensure that all methods, processes and systems are transferable. We hope to develop long-term relationships but will provide our full support if it becomes necessary to transfer a process to an alternative manufacturing site.

7 Understanding products we deliver are more than therapeutic proteins and associated documentation; processes we develop belong to our customers and must be economically viable, robust, compliant, scalable and transferable.

8 Range of strategic collaborators providing "seamless" access to necessary services not offered by JOINN Biologics US, Inc., including preclinical GLP-tox studies, and submission/registration support.

9 Executive-level oversight of every customer relationship.

Personnel

Dr. Bao-Lu Chen, COO

Dr. Bao-Lu Chen has 25 plus years of industry experience in both US and China in CMC operation, quality management and regulatory filing. Bao-Lu gained biologics and cell therapy product development experience by working in US for 20 years at Amgen, Chiron and Sangamo. He then went to China and worked there for about 5 years. As COO for two companies, he completed development and manufacture of several mAb and biologics from cell line construction to IND filing. As Chief Quality Officer and Sr. VP in Shanghai Henlius, he contributed to successful development of several mAb products from phase I to commercialization. One product received China NDA approval and another product received both China NDA and EMA MAA approval. He helped two Chinese companies to obtain QP declaration for their product GMP manufacturing. He's regulatory experience include successfully filing several INDs, CTAs and MAAs to China NMPA, FDA, EMA and other regulatory agencies.

Dr. Weng-Rong Jiang, Senior Director, Cell Line Development

Dr. Wen-Rong Jiang has over 20 years of biopharma industry experience (Pfizer, Roche) in biological drug R&D; expert in antibody drug & cell line development. Established Cell Line Development Function and workflow at JOINN Bio, and has successfully completed multiple stable cell line development client projects.

Dr. Shumin Yang, Senior Director, Process Development

Dr. Shumin Yang has over 20 years' experience with recombinant protein production, including: eight years of experience working on the development, scale up, and transfer of MFG processes from 500L to 12,000L scales for multiple therapeutic recombinant proteins at CDMO Boehringer Ingelheim (Fremont, CA) and Catalent (Bloomington, IN).

Dr. Loc Vo, Senior Director, Quality Control

Dr. Loc Vo is a biopharmaceutical professional with over 20 years of experience in Quality. Loc was the Director of BioMarin's Quality Control Analytical Technologies department. Loc managed four quality subgroups: 1) assay optimizations/validations/transfers, 2) special studies (manufacturing investigations and process comparability studies), 3) critical reagents and reference materials, and 4) in-country testing and CMO technology transfers. He was a major contributor in the authoring and review of the CMC sections for the successful global commercialization of seven drug products. Loc has participated in multiple on-site FDA and EMEA inspections and discussions with other global agencies.

Jon Stritch, Senior Director, Manufacturing

Mr. Jon Stritch has over 25 years of experience in biotech development and production from cell banking to fill/finish, including roles at Chiron, Calypte Biomedical, and XOMA. Additionally, he has experience in tech food scale-up and production at Ripple Foods. His expertise includes protein manufacturing, facility design, CMC project management, aseptic processing, process scale-up, and tech transfer.

John Vuong, Director, Quality

Mr. John Vuong has developed a very strong background in the area of setting up the GMP Manufacturing infrastructure and Quality System at Biotechnologies, Pharmaceuticals, Medical Devices, and CLIA labs during the past 20 years. John brought products from conception through to commercialization and improved manufacturing efficiency. In addition, John has over 20 years experiences in regulated environments successfully leading groups in Manufacturing, Product Transfer, Manufacturing Technical Support, Process Development, QC, Validation, QA and RA. He has provided comprehensive training to onsite staff regarding operational procedures, cGMP and compliance to FDA guidelines and has completed product transfers for Chiron Corporation, Novartis Corporation, Smithkline Beecham Corp, Quest Diagnostics Corp, Thermo Fishers, and Ortho Diagnostics. With Biochemistry degree John brings a unique technical background to the complex environment of GMP Operations.

GRIT1 Equilibration Buffer

Composition:

Volume	1L	13L	Actual
Sucrose 5 % (342.3 g/mol):	50.00 g	650g	
Phosphate 50mM (119.98 g/mol)	5.999 g	77.987g	
Sodium chloride 20mM (58.44 g/mol)	1.169 g	15.197g	
Tween 20, 0.5% (100%)	5.0 mL	65 mL	
Magnesium chloride 2mM (from 200 mM stock solution)	10.0 mL	130 mL	
2.5N NaOH	7.7mL	100mL	

Required Characteristics

pH: 6.5 +/- 0.1

Conductivity: 6.5 +/-3 mS/cm

Osmolality: 319 +/- 15 mOsm

Estimated Density:

1.02014 g/mL

Required volume/Container for 1 Run:

Equal numbers of

- 11 L ± 5% in 20L Bag
- 2 L ± 10% in 2-5L Bag

***Both sizes preferably from 1 batch if possible**

Currently used Components:

Sucrose	VWR	VWRB335
Sodium phosphate monobasic, anhydrous	Sigma-Aldrich	S2554
Sodium chloride	VWR	VWRB241-1KG
Tween 20	MilliporeSigma	8.17072.1000
Magnesium chloride	J.T.Baker	244801
2.5N NaOH	VWR Chemicals BDH	BDH7224-1

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding 2.5N NaOH
4. QS to desired volume/mass
5. Measure conductivity to verify within range
6. Verify pH is still within range

Buffer list & QC test matrix in the next pages

GRIT1 Wash Buffer

Composition per 1 L:

- Sucrose 5 % (342.3 g/mol): **50 g**
- Phosphate 50mM (119.98 g/mol): **5.999 g**
- Sodium chloride 241.3 mM (58.44 g/mol): **14.1 g**
- Tween 20, 0.5% (100%): **5.0 mL**
- Magnesium chloride 2mM (200 mM stock solution) **10.0 mL**
- 2.5N NaOH **~10mL**

Required Characteristics
pH: 6.5 +/- 0.1
Conductivity: 23 +/-2 mS/cm
Osmolality: 713 +/- 15 mOsm

Estimated Density:
1.02337 g/mL

Required volume/Container for 1 Run:

- 1 L ± 10% in 1L Bag

Currently used Components:

Sucrose	VWR	VWRB335
Sodium phosphate monobasic, anhydrous	Sigma-Aldrich	S2554
Sodium chloride	VWR	VWRB241-1KG
Tween 20	MilliporeSigma	8.17072.1000
Magnesium chloride	J.T.Baker	244801
2.5N NaOH	VWR Chemicals BDH	BDH7224-1

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding 2.5N NaOH
4. QS to desired volume/mass
5. Measure conductivity to verify within range

GRIT1 Elution Buffer

Composition per 1 L:

- Sucrose 5 % (342.3 g/mol): **50 g**
- Phosphate 50mM (119.98 g/mol): **5.999 g**
- Sodium chloride 337.1 mM (58.44 g/mol): **19.7 g**
- Tween 20, 0.5% (100%): **5.0 mL**
- Magnesium chloride 2mM (200 mM stock solution) **10.0 mL**
- 2.5N NaOH **~11mL**

Required Characteristics
pH: 6.5 +/- 0.1
Conductivity: 30+/-3 mS/cm
Osmolality: 804 +/- 15 mOsm

Estimated Density:
1.02659 g/mL

Required volume/Container for 1 Run:

- 1 L ± 10% in 1L Bag

Currently used Components:

Sucrose	VWR	VWRB335
Sodium phosphate monobasic, anhydrous	Sigma-Aldrich	S2554
Sodium chloride	VWR	VWRB241-1KG
Tween 20	MilliporeSigma	8.17072.1000
Magnesium chloride	J.T.Baker	244801
2.5N NaOH	VWR Chemicals BDH	BDH7224-1

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding 2.5N NaOH
4. QS to desired volume/mass
5. Measure conductivity to verify within range

GRIT1 Strip Buffer

Composition per 1 L:

- Sucrose 5 % (342.3 g/mol): **50 g**
- Phosphate 50mM (119.98 g/mol): **5.999 g**
- Sodium chloride 1M (58.44 g/mol): **58.44 g**
- Tween 20, 1.0% (100%): **10.0 mL**
- Magnesium chloride 2mM (200 mM stock solution) **10.0mL**
- 2.5N NaOH **~14mL**

Required Characteristics
pH: 6.5 +/- 0.1
Conductivity: 77 +/-5 mS/cm
Osmolality: N/A

Estimated Density:
1.05596 g/mL

Required volume/Container for 1 Run:

- 2X 1 L ± 10% in 1L Bag

Currently used Components:

Sucrose	VWR	VWRB335
Sodium phosphate monobasic, anhydrous	Sigma-Aldrich	S2554
Sodium chloride	VWR	VWRB241
Tween 20	MilliporeSigma	8.17072.1000
Magnesium chloride	J.T.Baker	244801
2.5N NaOH	VWR Chemicals BDH	BDH7224-1

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding 2.5N NaOH
4. QS to desired volume/mass
5. Measure conductivity & pH to verify within range

GRIT1 Citrate buffer

Composition per 1 L:

- Sodium citrate dihydrate (294.1 g/mol) **29.41 g**
- **3N HCL 3mL**

Required Characteristics
pH: 6.5 +/- 0.1
Conductivity: 10-20 mS/cm
Osmolality: 292 +/-15

Required volume/Container for 1 Run:

- 2 L ± **5%** in 2L Bag

Estimated Density:
1.0067 g/mL

Currently used Components:

Sodium citrate dihydrate	Fisher Chemical	S470-212
3N HCl	Ricca Chemical Company	R3720100-4A

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding HCl
4. QS to desired volume/mass
5. Measure conductivity &pH to verify within range

<table>
<tr>
<td>4M NaCl
Composition per 440mL:
• Sodium Chloride (58.44 g/mol) 102.8544 g

Required Characteristics
Conductivity: 219 +/- 10 mS/cm

Required volume/Container for 10 Runs: (Gritstone will purchase in 5L Volumes and aliquot as needed)
• 5 L ± 10% in 5L Bag</td>
<td>Currently used Components:

<table>
<tr><td>Sodium chloride</td><td>VWR</td><td>VWRB241-1KG</td></tr>
</table>
</td>
</tr>
</table>

ADPS buffer*

Composition

- 75mM NaCl
- 5mM Tris
- 1 mM MgCl2
- 5% (w/v) Sucrose

Required Characteristics
pH: 7.9 +/- 0.2
Conductivity: 84 +/-3 mS/cm
Osmolality: 303 ± 15 mOsm/kg

Required volume/Container for 1 Run:

- 5 L ± 10% in 5L Bag

Estimated Density:
1.0390 g/mL

Currently used Components:

Sodium chloride	VWR	VWRB241
Sucrose	VWR	VWRB335
Tris	J.T. Bake	4102-05
Magnesium chloride	J.T.Baker	244801
2.5N NaOH	VWR Chemicals BDH	BDH7224-1

Current Procedure:

1. Start with 80% desired volume of water
2. Add each component while stirring allowing time between each for dissolution
3. Adjust pH by adding 2.5N NaOH
4. QS to desired volume/mass
5. Measure conductivity & pH to verify within range

*: Final formulation buffer.

1M NaOH

Required Characteristics
Conductivity: 90 +/-5 mS/cm

Required volume/Container for 1 Run:

- 2 L ± 10% in 2-5L Bag

QC Testing Matrix

Buffer Item	Required volume/Container for 1 Run:	pH	Conductivity mS/cm	Osmolarity mOsm
GRIT1 Equilibration Buffer	11 L ± 5% in 20L Bag	6.5 +/- 0.1	6.5 +/- 3	319 +/- 15
	2 L ± 10% in 2-5L Bag	6.5 +/- 0.1	6.5 +/- 3	319 +/- 15
GRIT1 Wash Buffer	1 L ± 10% in 1L Bag	6.5 +/- 0.1	23 +/- 2	**TBD by GS**
GRIT1 Elution Buffer	1 L ± 10% in 1L Bag	6.5 +/- 0.1	31 +/- 3	**TBD by GS**
GRIT1 Strip Buffer	2X 1 L ± 10% in 1L Bag	6.5 +/- 0.1	77 +/- 5	NA
GRIT1 Citrate buffer	2 L ± 5% in 2L Bag	6.5 +/- 0.1	15+ – 20	292 +/- 15
4M NaCl	10 L ± 10% in 5L Bag	NA	229 +/- 10	NA
ADPS buffer	5 L ± 10% in 5L Bag	7.9+/- 0.2	84 +/- 3	303 +/- 15
1M NaOH	2 L ± 10% in 2-5L Bag	NA	90 +/- 5	NA

Volume & number of bags required for buffer production (Q3, Q4, 2021):

Buffer Item	Required volume/Container for 1 Run:	Volume per 6 months		Bags per 6 Months w/ QC Stability
GRIT1 Equilibration Buffer	11 L ± 5% in 20L Bag / 2 L ± 10% in 2-5L Bag	496		86
GRIT1 Wash Buffer	1 L ± 10% in 1L Bag	50		50
GRIT1 Elution Buffer	1 L ± 10% in 1L Bag	50		50
GRIT1 Strip Buffer	2X 1 L ± 10% in 1L Bag	86		86
GRIT1 Citrate buffer	2 L ± 5% in 2L Bag	86		50
4M NaCl	5 L ± 10% in 5L Bag	20		5
ADPS buffer	5 L ± 10% in 5L Bag	194		50
1M NaOH	2 L ± 10% in 2-5L Bag	86		50
	Total	**1068**		**427**

As discussed in stability testing, extra bags made will be used for QC testing:
Buffer provided semi-annually: 15 bags will be used for QC release and stability testing.

Outlook

RE: Gritstone buffer stability

From Christine Ho <cho@gritstone.com>
Date Fri 12/8/2023 10:11 AM
To Apoorva Patil <Apoorva.Patil@joinnbio.com>; Nilesh Shah <nshah@gritstone.com>
Cc John Vuong <John.vuong@joinnbio.com>; Tao He <tao.he@joinnbio.com>

1 attachment (6 MB)
JOINN Biologics Report.pdf;

Hi Apoorva,

My apologies for the delay. Our quality just approved the JOINN Biologics Report. See attached. Please let me know if you have any questions.

Happy Holidays!

Sincerely,
Christine

From: Apoorva Patil <Apoorva.Patil@joinnbio.com>
Sent: Monday, December 4, 2023 10:39 AM
To: Christine Ho <cho@gritstone.com>; Nilesh Shah <nshah@gritstone.com>

Cc: John Vuong <John.vuong@joinnbio.com>; Tao He <tao.he@joinnbio.com>
Subject: Re: Gritstone buffer stability

Hi Nilesh and Christine,

Please let me know if you will be able to send the finalized versions of the attached documents by 12/08. Otherwise, I'll use the attached versions to wrap up the stability report.

Best regards.

Apoorva Patil

Sr. Scientist
Tel: 510-295-0222 ext. 2257

apoorva.patil@joinnbio.com

JOINN Biologics US Inc.

2600 Hilltop Dr.,

Richmond, CA 94806

http://www.joinnbio.com

From: Apoorva Patil <Apoorva.Patil@joinnbio.com>
Sent: Monday, November 27, 2023 9:13 AM
To: Christine Ho <cho@gritstone.com>; Nilesh Shah <nshah@gritstone.com>

Cc: John Vuong <John.vuong@joinnbio.com>; Tao He <tao.he@joinnbio.com>
Subject: Re: Gritstone buffer stability

Hi Christine and Nilesh,

Please provide me with the following documents so we can wrap up the stability report.

1. A signed version of the Gritstone QC data sent to Joinn
2. The finalized version of the functionality testing report

Thank you!

Apoorva Patil

Sr. Scientist
Tel: 510-295-0222 ext. 2257

apoorva.patil@joinnbio.com

JOINN Biologics US Inc.

2600 Hilltop Dr.,

Richmond, CA 94806

http://www.joinnbio.com

From: Apoorva Patil <Apoorva.Patil@joinnbio.com>
Sent: Tuesday, November 14, 2023 11:24 AM
To: Christine Ho <cho@gritstone.com>
Cc: John Vuong <John.vuong@joinnbio.com>; Nilesh Shah <nshah@gritstone.com>
Subject: Fw: Gritstone buffer stability

Hi Christine,

We received the attached QC data for the Gritstone buffer stability study in email below. Could you please send a signed version of the data at your earliest convenience?

Thanks!

Apoorva Patil

Sr. Scientist
Tel: 510-295-0222 ext. 2257

apoorva.patil@joinnbio.com

JOINN Biologics US Inc.

2600 Hilltop Dr.,

Richmond, CA 94806

http://www.joinnbio.com

From: Jon Strich <jon.strich@joinnbio.com>
Sent: Monday, May 15, 2023 3:08 PM
To: Apoorva Patil <Apoorva.Patil@joinnbio.com>
Cc: Wenrong Jiang <wenrong.jiang@joinnbio.com>
Subject: Fw: Gritstone buffer stability

Hi Apoorva
Please see below and attached
thanks

Jon

From: Christine Ho <cho@gritstone.com>
Sent: Monday, May 15, 2023 10:55 AM
To: Jon Strich <jon.strich@joinnbio.com>; Nilesh Shah <nshah@gritstone.com>; Lyudmila Kaliberova <lkaliberova@gritstone.com>
Cc: Nilang Gor <ngor@gritstone.com>; Weiman Xu <weiman.xu@joinnbio.com>; Wenrong Jiang <wenrong.jiang@joinnbio.com>
Subject: RE: Gritstone buffer stability

Hi Jon,

Sorry for the delay. Attached is the QC data from the study at different timepoints. Please let me know if you need anything else.

Sincerely,

Christine

From: Christine Ho
Sent: Tuesday, May 9, 2023 12:52 PM
To: Jon Strich <jon.strich@joinnbio.com>; Nilesh Shah <nshah@gritstone.com>
Cc: Nilang Gor <ngor@gritstone.com>; Weiman Xu <weiman.xu@joinnbio.com>; Wenrong Jiang

<wenrong.jiang@joinnbio.com>
Subject: RE: Gritstone buffer stability

Hi Jon,

I can send you the data by Friday.

Sincerely,

Christine

From: Jon Strich <jon.strich@joinnbio.com>
Sent: Monday, May 8, 2023 2:04 PM
To: Nilesh Shah <nshah@gritstone.com>
Cc: Christine Ho <cho@gritstone.com>; Nilang Gor <ngor@gritstone.com>; Weiman Xu <weiman.xu@joinnbio.com>; Wenrong Jiang <wenrong.jiang@joinnbio.com>
Subject: Gritstone buffer stability

Hi Nilesh,

I hope all is well with you.

Attached is a preliminary data summary table of the 1 year stability program for the Gritstone buffers.

Our data is in the final review process with our QA and we would like to close out the study.

Please take a look and let us know if you have any questions.

In order to close out the report, we would like to have the Functional Testing results from Gritstone to complete our report.

Can you send us that data?

Many thanks,

Jon

CONFIDENTIALITY NOTICE:

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1 PURPOSE

Small scale development runs were performed at Gritstone bio to evaluate the performance of the buffers prepared by a contract development and manufacturing organization (CDMO), JOINN Biologics, over time using the Gen2 process (functional stability test of the buffers).

2 SCOPE

This report covers the process, materials, equipment, and quality control testing for small scale GRT-C901 Gen2 production from the upstream cell culture process to the downstream process through the anion exchange chromatography (AEX) step. The final tangential flow filtration (TFF) step is not included as the buffers evaluated here for storage stability should not impact the TFF step.

3 BACKGROUND

Currently, the Gritstone manufacturing team prepares buffers in-house for Gen2 process (**SOP-0297**). Gritstone is looking for an alternative to reduce time, resources, and potential inconsistencies between lots.

Gritstone has a contract with JOINN Biologics to provide buffers for the Gen2 process produced following cGMP and released under pre-determined acceptance criteria for cGMP manufacturing use at Gritstone. JOINN Biologics will manufacture buffers using the same or higher-grade buffer components compared to those used at Gritstone, the same concentrations of buffer components, the same buffer filter, and confirmation of the same physical characteristics via quality control (QC) testing.

This study was performed under **Protocol-0367** to demonstrate the functionality of the JOINN Biologics provided buffers for the Gen2 process. To establish shelf-life for these buffers prepared at JOINN Biologics, a buffer hold study using 1kg (or 1L) bags of buffers was conducted per JOINN **Protocol 2940-QC-PRO-001.01**. As part of the study design, Gritstone utilized the buffers to perform small scale functionality testing at varying time points in addition to the physical characteristic testing performed by JOINN Biologics and in-house at Gritstone by QC. Functionality testing was performed at 0-, 6-, and 12-month timepoints. The upstream and downstream portions of the Gen2 process used for this functionality test are discussed below.

This study tested the functionality of all buffers except ADPS. ADPS is not a new buffer for the Gen2 process and has been currently sourced from the contract manufacturer Teknova. JOINN Biologics used the same raw materials to produce ADPS. Regardless of vendor change, this like-for-like of raw materials provides sufficient assurance of equivalence. No functional testing of the ADPS buffer was needed. The GRIT1 Strip solution is also used for the TFF operation to remove host cell protein (HCP). However, it was not tested for the TFF operation because the Strip solution ingredients are the same as those of the GRIT1 Equilibration, Wash, and Elution solutions (differing only in the amount of NaCl and Tween 20). If the buffer stability affected the process performance, it would be most evident at the chromatography step where all three solutions with the same ingredient, but varying compositions are used.

4 MATERIALS AND EQUIPMENT

- 1L Flex Biosystems Bag
- 125mL Erlenmeyer Shake Flask
- FreeStyle™ 293 Expression Medium
- HEK293F-tTS Clone 17 cells
- Drug Product (DP) produced during the engineering run 2021-ENG-020, DOM:17Sep2021
- Sartorius Sartobind® Q Nano 1mL
- Corning PES 250mL Bottle Top Filter with 0.2 µm Pore Size
- VWR Spinbar, Octagon 1 x 5/16" (25.4 x 8 mm)
- Magnetic Stirrer
- 250mL Beaker
- ÄKTA Avant 25
- JOINN Biologics Prepared Buffers
  - 1kg or 1L of GRIT1 Equilibration Solution
  - 1kg or 1L of GRIT1 Wash Solution
  - 1kg or 1L of GRIT1 Elution Solution
  - 1kg or 1L of GRIT1 Strip Solution
  - 1kg or 1L of Citrate (used to prepare GRIT1 Precipitation Solution)
  - 1kg or 1L of 4 M NaCl (GRIT1 Salt Solution)
  - 1kg or 1L of 1 M NaOH

5 METHODS

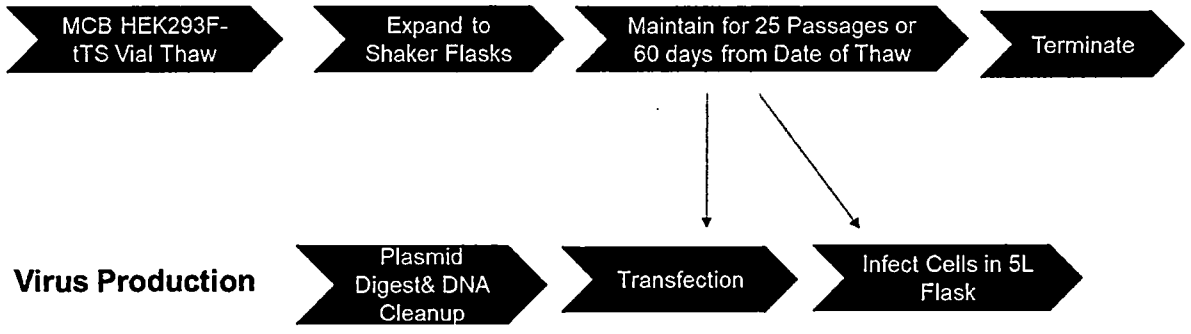
A small-scale Gen2 process is performed for Harvest and Chromatography steps using the Gen2 process buffers. Instead of the full-scale 2.4 L Gen2 process cell culture material, a scale-down production process at ~1:100th scale is performed for this functionality study (reducing the culture volume from 2400 mL to 24 mL). The small-scale process is performed using JOINN-provided buffers at specified time points (0 months, 6 months, 12 months) from their date of manufacture. The buffers up to 12 months were stored at 15°C to 25°C at JOINN Biologics GMP site and released at each timepoint to Gritstone to perform functionality test.

5.1 Upstream Process

Cells from a single vial of a cell bank are thawed and passaged through a series of shake flasks as a seed train culture. All cell culture activities are performed in FreeStyle™ 293 Expression Medium and the shake flasks are incubated in an incubator set at 37°C, 5% CO_2, and 120 rpm. Cells from the seed train are used for transfection and virus production. The virus production process begins with plasmid digest using Pac1 enzyme. The linearized DNA is cleaned up using a NucleoSpin®Gel and PCR Clean-up kit. Transfection is performed using PEIpro reagents and 30 µg DNA.

The primary virus stock after transfection is used to infect a 2.4 L cell culture in a 5L shake flask targeting multiplicity of infection (MOI) ≥3. The infected culture is harvested and purified for viral product. An overview of the cell culture and virus production is provided in **Figure 1**.

Figure 1 Upstream Process Flow Diagram



Cell culture is performed using HEK293F-tTS Clone 17 cells. Cells are passaged 1 day prior to infection targeting a cell density of 1.5 ± 0.2 x 10^6 viable cells/mL for the infection. The culture in 125mL Shake flask with the 30 mL of working volume is infected with 10 µL of Drug Product (DP) produced during the engineering run 2021-ENG-020, DOM:17Sep2021, Infectivity titer - 2.55 x 10^{10} IU/mL. After ~48 hours post infection, cells are harvested, and 24 mL (scale-down model) of infected culture is submitted for purification.

5.2 Downstream Process

Platform Purification Process for GRT-C901 is scaled-down for this study through the AEX chromatography step.

5.2.1 Cell Lysis & Precipitation

ChAd68 infected 293F-tTS Clone 17 cells are lysed to initiate the purification process (48 hours post-infection). The cell culture is mixed uniformly using a magnetic stir plate. Cells are lysed and cell debris and other impurities are precipitated using sequential addition of:

- 4.4 mL of GRIT1 Salt solution
- 1.4 mL GRIT1 Lysis solution (prepared in-house); 5-7 minutes of mixing
- 20 mL GRIT1 Precipitation solution

5.2.2 Harvest Clarification

Precipitated culture is clarified by 0.2 µm filtration using a Corning PES 250mL bottle top filter with 0.2 µm pore size. During filtration, the clarified lysate is collected in a vessel containing 110 mL of GRIT1 Equilibration solution.

5.2.3 Anion Exchange Membrane Chromatography

A single use 1mL Sartobind Q Nano membrane chromatography capsule (4 mm bed height) is first prepared by sequentially flushing with 1 M NaOH, GRIT1 Strip solution, and GRIT1 Equilibration solution. Processing steps are:

1. Entire chromatography load (lysate diluted into 110 mL of Equilibrium solution) is passed through the capsule
2. GRIT1 Equilibration solution is used to chase the load
3. The column is washed using GRIT1 Wash solution
4. Elution is performed using GRIT1 Elution solution

Tables 1-5 summarize the process steps, parameters, and buffers used in the functionality test at 0-month, 6- month, and 12- month timepoints. In this modified small-scale experimental design, after the AEX elution step, samples are collected, and the product is stored at -80°C. The subsequent steps of the full-scale Gen2 process including tangential flow filtration, sterile filtration, and concentration adjustment are not included in **Protocol-0367** and are not performed.

Table 1 lists the process parameters for the platform clinical process and the scale-down model process applicable for the functionality test run.

Table 1 Comparison of Full Scale and Scale-Down Purification Process

Process Step	Parameter/Material	Gen2 Full-Scale Production Process	Gen2 1:100th Small-Scale Process	Notes/Comments
Harvest	Cell Culture Volume	2400 mL	24 mL	None
	Cell Culture Vessel	5L Erlenmeyer Shake Flask	125mL Erlenmeyer Shake Flask	None
	Mixing	Mixing via stir bar at 400 rpm	Mixing via stir bar at 200 rpm	Stir speed for small scale process should be sufficient to create small vortex without entrainment of air
	Quantity of GRIT1 Salt for Pre-conditioning the culture	440 mL	4.4 mL	None
	Quantity of GRIT1 Lysis added	140 mL	1.4 mL	Note: Lysis buffer not provided by JOINN Biologics
	Quantity of GRIT1 Precipitation/Citrate to add	2000 mL	20 mL	None
	Filtration	Meissner Everlux 0.2µm PES filter capsule	0.2µm PES 250mL Bottle Top Filter	No appropriately sized scale-down versions of the production filter are available. However, the 250mL Bottle top filters were used for development work and have the same pore size and membrane material. This difference will not change the process performance

Process Step	Parameter/Material	Gen2 Full-Scale Production Process	Gen2 1:100th Small-Scale Process	Notes/Comments
	Dilution	Clarified Lysate diluted into 11 L of GRIT1 Equilibration Buffer	110 mL of GRIT1 Equilibration buffer added to Clarified Lysate	Order of addition is not critical to process performance
Chrom	Column	Sartobind Q 75mL 4mm Bed Height	Sartobind Q Nano 1mL 4mm Bed Height	Though the 1mL column is larger than a 1:100th scale column, the Gen2 process does not operate near the binding capacity of the column as such there isn't any expected impact to process performance
	Chrom. Prep	5 column volumes of 1 M NaOH at 5 CV/min	Same	None
		60 min -5 hr hold	Same	None
		5 column volumes of 1 M NaOH at 5 CV/min	Same	None
		10 column volumes of GRIT1 Strip at 5 CV/min	Same	None
		10 column volumes (750 mL) of GRIT1 Equil at 5 CV/min	Same (10 mL)	None
	Loading	Load ~16 L onto 75 mL column at 5 CV/min	Load ~160 mL onto 1mL column at 5 CV/min	None
	Chase	Chase with 5 CV of GRIT1 Equil at 5 CV/min	Same	None
	Wash	Wash with 5 CV GRIT1 Wash at 5 CV/min	Same	None
	Elution	Elute with 6 CV GRIT1 Elution at 5 CV/min	Same	None

For more detailed full scale process parameters refer to **Report-0358**

6 RESULTS AND DISCUSSION

The small-scale Gen2 process was successfully performed for JOINN Biologics buffers at 0-, 6- and 12-month timepoints. These timepoints were selected for the stability study to monitor buffer stability. The functionality tests were performed under **Protocol-0367**, which instructs to perform a modified Gen2 small-scale study.

Upon receiving the JOINN Biologics buffers, PD took pH, osmolality, and conductivity readings. Gritstone QC also performed their own testing of the buffers for each time point 0-month, 6-months, and 12-months to evaluate their properties. The test methods QC performed were pH, osmolality, conductivity, and endotoxin. QC results are not included in this report.

For all functionality tests, the cell culture performed as expected without any observable differences compared to the platform process. A summary of these cell cultures is provided in **Table 2.**

Table 2 Summary of Upstream Process

Run	Gen2-SS-FT-PD1	Gen2-SS-FT-PD2	Gen2-SS-FT-PD3	Gen2-SS-FT-PD4	Gen2-SS-FT-PD5
Date, timepoints	09-11Nov2021 0-month stability	25-27Jan2022 0-month stability	01-03Feb2022 0-month stability	03-05Aug2022 6-month stability	30Jan-01Feb2023 12-month stability
Passage	P.8	P.6	P.8	P.12	P.7
Viable cell density (VCD) at infection, cells/mL	1.45×10^6	1.60×10^6	1.56×10^6	1.42×10^6	1.41×10^6
Multiplicity of infection (MOI), IU/cell	5.9	5.3	5.4	5.99	6.03
Viability at harvest, %	94.5	94	96	96.1	94
Total cell density (TCD) at harvest, cells/mL	2.01×10^6	2.43×10^6	2.29×10^6	2.42×10^6	2.38×10^6
Aggregation	9	11	16	10	15
Infectivity titer for PRE-HRV, IU/mL	7.62×10^8	4.44×10^8	1.07×10^9	2.24×10^9	1.32×10^9

Harvest, clarification, and loading on the AEX chromatography capsule were performed as described above in the method section.

The Unicorn software of ÄKTA Avant 25 generated a chromatogram after the completion of each chromatography method. The buffer functionality was then analyzed by reviewing the chromatogram's

A260, pH, and conductivity traces. The AEX chromatogram demonstrated an increase of A260 trace at the beginning of the sample application, and then it stabilized once the AEX column was saturated with the load. The A260 trace for wash steps showed both unbound and weekly bound impurities eluting. The A260 peak in the elution step demonstrated successful elution of the ChAd. At timepoint 0-month, the functionality test was performed three times due to technical difficulties when running the tests, which were not related to the buffer preparation as described below.

For the first test at month 0, lot Gen2-SS-FT-PD1 run was performed on 11Nov2021, and a deviation from the protocol was observed. Due to the unavailability of the viral hood, the AEX-ELT sample was temporarily stored in a 15mL conical at –80°C. **Protocol-0367** states, "collect samples of the Anion Exchange Eluate for analysis." Aliquots were not made at this time. The AEX-ELT sample was later thawed, and aliquots were made on 27Jan2022 before being submitted to analytical testing. The viral concentration of the AEX-ELT sample from this run was 2.83 x 1011 VP/mL, which is lower compared to the historical data for the Gen2 process at this step. This could be due to freeze-thaw-related issues.

A second run, lot Gen2-SS-FT-PD2, was performed on 27Jan2022 to investigate the cause of lower level of virus particle count observed for the lot Gen2-SS-FT-PD1 in the AEX eluate. Prior to loading onto the ÄKTA Avant 25 chromatography system, the clarification Corning PES 250mL Bottle Top Filter with 0.2 µm pore size got clogged. An additional filter was then used to clarify the material. **Protocol-0367** states, "in a biological safety cabinet, decant the precipitated cell culture into the top of a 250mL 0.2µm PES vacuum filter bottle and try to minimize the amount of precipitate transferred." A deviation occurred as the instruction only allows to use one 250mL 0.2µm PES vacuum filter bottle for clarification.

Additionally, during the chromatography run, a method error occurred, resulting in the elution instruction not being executed. A manual instruction was provided to elute the virus off the column, and a second file was created to capture this elution peak chromatogram (data not shown, but the peak was as expected and comparable to the first run). However, the manually instructed elution peak chromatogram could not be retrieved from the AKTA due to a system error. **Protocol-0367** states to "review chromatogram for abnormalities and verify all steps occurred as expected. Attach chromatogram to test data write." Since the chromatogram of the elution peak could not be retrieved, it was decided to perform the buffer functionality testing again.

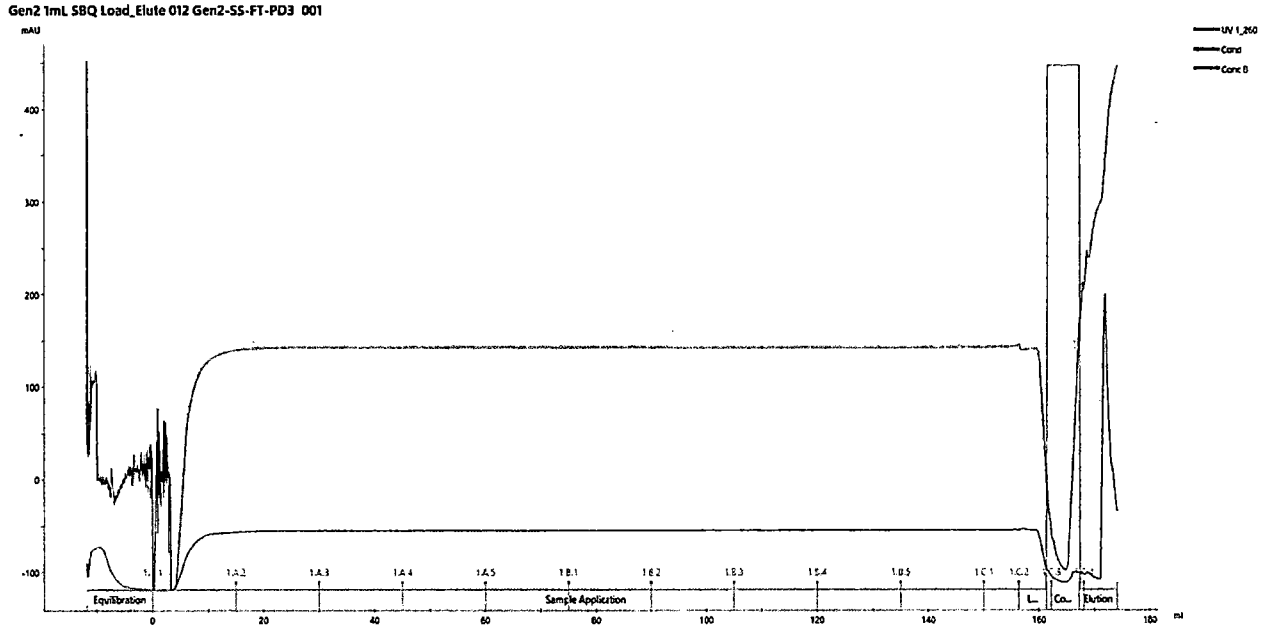
A third functionality test for timepoint 0-month was performed as lot Gen2-SS-FT-PD3 on 03Feb2022, and the run performed as expected. The chromatogram of Gen2-SS-FT-PD3 was compared with the chromatograms of 6 months and 12 months' time points to analyze the JOINN Biologics Gen2 buffer stability based on the functional test.

The equilibration buffer allows the virus to attach to the column, the wash buffer removes the impurities, and the elution buffer allows the virus to detach from the column. All three runs performed for timepoint 0-month showed similar trends for equilibration, sample loading, wash, and elution except for lot Gen2-SS-FT-PD2. The elution peak for this run was not available for confirmation. Based on the profile trends, it can be concluded that the buffers were functioning as expected and the time

taken, almost three months, to perform the test for timepoint 0-month, has no impact on the performance of buffers.

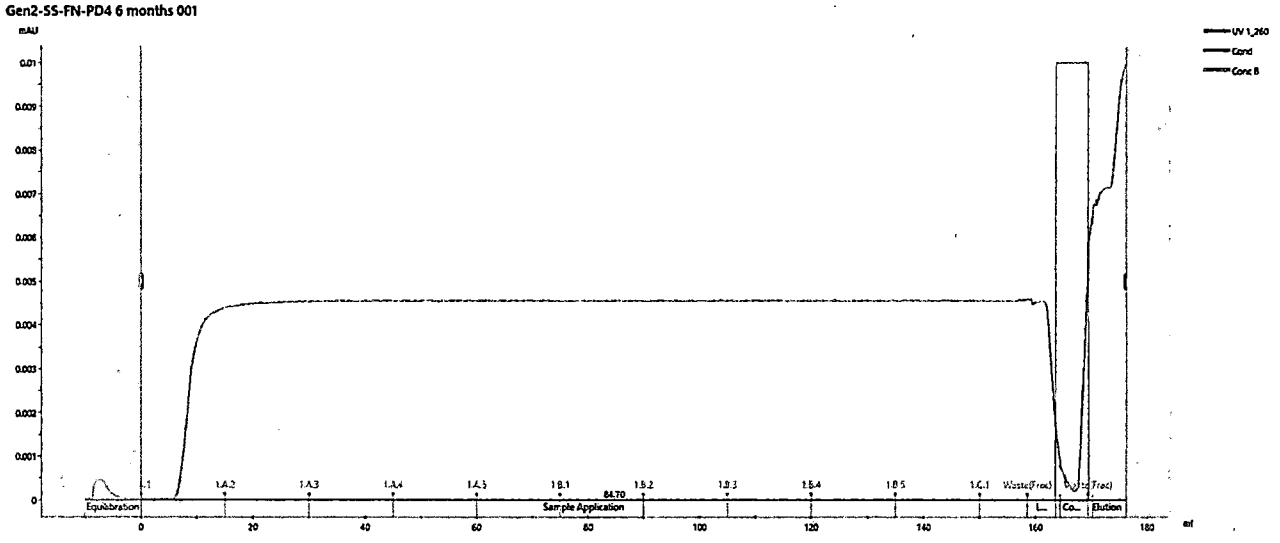
Below are the chromatograms from the three 0-month timepoints, 6-month timepoint, and 12-month timepoint.

Figure 2 SBQ Chromatogram for Gen2-SS-FT-PD3



In **Figure 2**, chromatogram for lot Gen2-SS-FT-PD3 indicates successfully Gen2 process performance using JOINN Biologics buffers at 0-month timepoint. The chromatogram of Gen2-SS-FT-PD3 demonstrates that JOINN Biologics buffers functioned as expected in purifying the clarified harvest containing the ChAd. The conductivity trace increases during the wash steps with a small A260 peak. It shows successful removal of the weakly bound host cell impurities. The successful elution of the ChAd is demonstrated by the sharp A260 peak with the increasing conductivity trace during the elution step. Gen2-SS-FT-PD3 can be compared with the chromatograms of 6- and 12-months timepoint for analyzing any impact on the JOINN Biologics buffer storage stability on the functionality of these buffers.

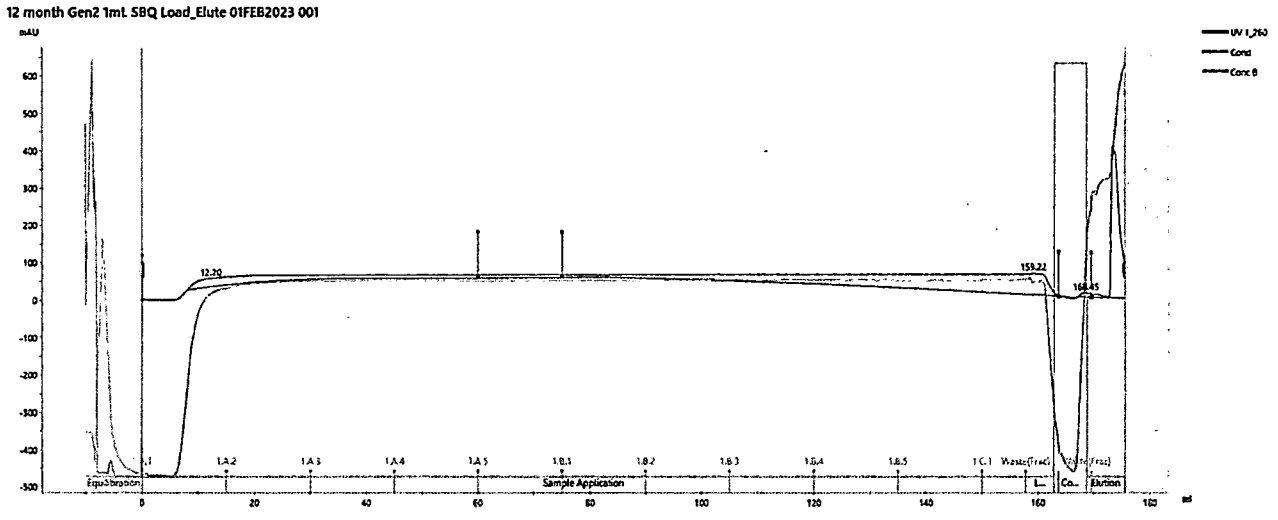
Figure 3 SBQ Chromatogram for Gen2-SS-FT-PD4



Note: A260 and A280 sensors malfunctioned during the run and hence there is no data for them.

In **Figure 3**, for lot Gen2-SS-FT-PD4, the JOINN Biologics Gen2 buffers functioned as expected for timepoint 6-months. Although in this test run, the A260 was not captured due to the UV sensor error in ÄKTA Unicorn, the chromatogram allowed comparison of the conductivity and pH traces. The conductivity and pH follow similar trends to lot Gen2-SS-FT-PD3 indicating that the buffers were functioning as expected. The chromatogram along with Nanodrop data verified the successful elution of the ChAd (although A260 profile is not available, eluate pool had expected quantity of ChAd as measured using Nanodrop). The HPLC-SEC and HPLC-AEX results (**Table 4**) further support the stability of the buffers at 6-month timepoint.

Figure 4 SBQ Chromatogram for Gen2-SS-FT-PD5



In **Figure 4,** for lot Gen2-SS-FT-PD5, the JOINN Biologics Gen2 buffers functioned as expected for timepoint 12-months. The UV was not initially set to zero and hence the profile during loading and pre-loading equilibration is not captured properly. However, the A260 chromatogram trend thereafter matches the lot Gen2-SS-FT-PD3 trend.

The conductivity and pH trends are consistent for all three lots indicating that the JOINN Biologics buffers functioned as expected to purify the ChAd for all timepoints.

The A260/280 ratio for purified ChAd virus in the ADPS is ~1.21, and the ratio A320/260 ~0.25 based on previously observed values. Samples were collected at AEX elution step for the functionality test in this study and there is likelihood that the product will not be as pure as that seen in the formulation buffer for the historical runs. The A260/280 ratio is slightly lower than the expected ~1.21 as expected for these three functionality tests, but they were comparable to each other. The A260/280 and A320/260 ratios for AEX-ELT virus are summarized below in **Table 3.**

The A260/280 and A320/260 ratios as well as A260 elution peak area were consistent for all three time points. It indicates no impact on the functionality of the Gen2 buffers when stored up to 12 months.

Table 3 AEX Chromatography SBQ Eluate Peak Area & Ratio Calculations

Gen2-SS-FT-PD3		Wavelength (nm)	Area (mL x mAU)	Ratio	Ratio value
	03Feb2022	260	483.9	260/280	1.17
		280	412.6	320/260	0.23
		320	109.9		

Gen2-SS-FT-PD4		Wavelength (nm)	Area (mL x mAU)	Ratio	Ratio value
	05Aug2022	260	N/A	260/280	N/A
		280	N/A	320/260	N/A
		320	N/A		
Gen2-SS-FT-PD5		**Wavelength (nm)**	**Area (mL x mAU)**	**Ratio**	**Ratio value**
	01Feb23	260	667.5	260/280	1.18
		280	567.7	320/260	0.22
		320	149.9		

The AEX elution samples were submitted for HPLC-SEC, HPLC-AEX and viral infectivity assays. The HPLC-SEC and HPLC-AEX assays measure the purity of the ChAd samples. As mentioned above, the AEX eluate undergoes further purification and buffer exchange into formulation buffer, the HPLC-SEC and HPLC-AEX data compares purity of the samples at varying timepoints to show any impact of buffer storage stability on the process performance. Analytical results are summarized and compared in **Table 4**. Since the amount of AEX eluate collected for this process is constant, the viral infectivity and viral particle concentration in the AEX eluate indicates process performance. Data for IU/mL and VP/mL in **Table 4** are comparable for the three timepoints tested and once again indicates that the buffers performed as expected even after storage of 12 months.

Table 4 Error! Reference source not found.**Analytical Results**

Test	Gen2-FT-SS-PD3	Gen2-FT-SS-PD4	Gen2-FT-SS-PD5
Sample	AEX-ELT	AEX-ELT	AEX-ELT
HPLC-SEC, % Purity (Monomer)	80.87	100.0	99.90
HPLC-AEX, % Purity (Main Peak)	97.90	93.52	91.94
Viral Infectivity (x 10^9 IU/mL)	4.95	7.95	6.36
Viral Particle Concentration (x 10^{11} VP/mL)	4.74	5.72	7.39

7 CONCLUSION

The functionality tests that were performed in the PD lab using a ~1:100th harvest and a modified, scale down purification process based on the platform GRT-C901 Gen2 process had comparable results for timepoints 0 months, 6 months, and 12 months. This study demonstrated no impact on the process performance from storing JOINN Biologics Gen2 buffers up to 12 months.

8 REFERENCES

Protocol-0367: Gen2 Small-Scale Buffer Function Testing

Report-0358: GRT-C901 Gen2 Process Description

SOP-0297: Gen2 Buffer Preparation

9 REVISION AND APPROVAL HISTORY

All approval details are maintained and controlled in MasterControl electronic system. Please refer to the MasterControl electronic system for the full approval and revision record.

Revision	Date Effective	Summary of Changes
00	See Document Header	Original revision

Signature Manifest

Document Number: Report-0468 **Revision:** 00

Title: Summary Report for JOINN Biologics Buffers Functionality Tests

Effective Date: 08 Dec 2023

All dates and times are in US/Pacific.

Summary Report for JOINN Biologics Functionality Tests

1 - Supervisor Approval

Name/Signature	Title	Date	Meaning/Reason
Adam Morgenthaler (AMORGENTHALER)	Sr. Product Development Engineer	14 Oct 2021, 06:02:28 AM	Approved

2 - Collaborate/Review

Name/Signature	Title	Date	Meaning/Reason
Nilesh Shah (NSHAH)	Sr. Director, Process Development	06 Dec 2023, 04:55:10 PM	Complete

5a - Originator Approval

Name/Signature	Title	Date	Meaning/Reason
Christine Ho (CHO)	Research Associate, PD	07 Dec 2023, 08:30:41 AM	Approved

5b - Supervisor Approval

Name/Signature	Title	Date	Meaning/Reason
Nilesh Shah (NSHAH)	Sr. Director, Process Development	07 Dec 2023, 08:25:50 AM	Approved

6 - QA Approval

Name/Signature	Title	Date	Meaning/Reason
Luis Cabassa-Latoni (LCABASSA)	Vice President, Quality	08 Dec 2023, 07:54:51 AM	Approved

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CERTIFICATE OF TESTING

REV. 00

Sample Submission #: 04118 Submission Date: 15FEB2022

Lot Number(s): 21-SO-0214, 21-SO-0215, 21-SO-0216, 21-SO-0217, 21-SO-0218, 21-SO-0220, 21-SO-0221, 21-SO-0224

Description of Testing: JOINN GEN2 buffer testing

Sample Name	Test Method #	Results (units)
Equilibration Buffer Lot # 21-SO-0221	pH	6.566
	Osmolality	309 mOsm/kg H2O
	Conductivity	6.3652 mS/cm
	Endotoxin	0.614 EU/mL
Wash Buffer Lot # 21-SO-0215	pH	6.562
	Osmolality	735 mOsm/kg H2O
	Conductivity	24.7822 mS/cm
	Endotoxin	0.269 EU/mL
Elution Buffer Lot # 21-SO-0214	pH	6.614
	Osmolality	916 mOsm/kg H2O
	Conductivity	32.2028 mS/cm
	Endotoxin	0.270 EU/mL
Strip Buffer Lot # 21-SO-0216	pH	6.593
	Conductivity	76.3818 mS/cm
	Endotoxin	1.32 EU/mL
Citrate Buffer Lot # 21-SO-0217	pH	6.602
	Osmolality	289 mOsm/kg H2O
	Conductivity	17.4901 mS/cm
	Endotoxin	< 0.150 EU/mL
4M NaCl Lot # 21-SO-0224	Conductivity	216.9264 mS/cm

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Sample Name	Test Method #	Results (units)
1M NaOH Lot # 21-SO-0218	Conductivity	174.4579 mS/cm
ADPS Lot # 21-SO-0220	pH	7.349
	Osmolality	304 mOsm/kg H2O
	Conductivity	7.4815 mS/cm
	Endotoxin	0.273 EU/mL
	Bioburden	< 1 CFU/30mL (Total Count)

Performed by — Date: 23 Mar 2022

Reviewed by — Date: 23MAR22

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CERTIFICATE OF TESTING

REV. 00

Sample Submission #: 04464 Submission Date: 19Aug2022

Lot Number(s): Gen2-SS-FT-PD4 (6 months)

Description of Testing: Gen2-SS-FT-PD4 (6 months)

Sample Name	Test Method #	Results (units)
2940 Equilibration Buffer	pH	6.565
	Osmolality	312 mOsm/kg H2O
	Conductivity	6.4627 mS/cm
	Endotoxin	<0.500 EU/mL
2940 Wash Buffer	pH	6.584
	Osmolality	741 mOsm/kg H2O
	Conductivity	25.4114 mS/cm
	Endotoxin	<0.170 EU/mL
2940 Elution Buffer	pH	6.597
	Osmolality	918 mOsm/kg H2O
	Conductivity	32.6617 mS/cm
	Endotoxin	0.117 EU/mL
2940 Strip Buffer	pH	6.620
	Conductivity	77.2992 mS/cm
	Endotoxin	<0.625 EU/mL
2940 Citrate Buffer	pH	6.566
	Osmolality	291 mOsm/kg H2O
	Conductivity	17.9424 mS/cm
	Endotoxin	<0.150 EU/mL
2940 4M NaCl	Conductivity	219.5414 mS/cm

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Sample Name	Test Method #	Results (units)
2940 1M NaOH	Conductivity	177.5021 mS/cm
2940 ADPS	pH	8.039
	Osmolality	303 m/kg H2O
	Conductivity	7.5580 mS/cm
	Endotoxin	0.210 EU/mL
	Bioburden	<1 CFU/30mL (Total Count)

Performed by — Date: 030CT22

JK
Reviewed by — Date: 03OCT22

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CERTIFICATE OF TESTING

REV. 00

Sample Submission #: 04926 Submission Date: 08FEB2023

Lot Number(s): Gen2-SS-FT-PD5 (12 months)

Description of Testing: Gen2-SS-FT-PD5 (12 months)

Sample Name	Test Method #	Results (units)
2940 Equilibration Buffer (Lot # 21-SO-0221)	pH	6.524
	Osmolality	315 mOsm/kg H2O
	Conductivity	6.3994 mS/cm
	Endotoxin	< 0.5 EU/mL
2940 Wash Buffer (Lot # 21-SO-0215)	pH	6.554
	Osmolality	742 mOsm/kg H2O
	Conductivity	25.3457 mS/cm
	Endotoxin	0.2 EU/mL
2940 Elution Buffer (Lot # 21-SO-0214)	pH	6.578
	Osmolality	921 mOsm/kg H2O
	Conductivity	32.6561 mS/cm
	Endotoxin	0.2 EU/mL
2940 Strip Buffer (Lot # 21-SO-0216)	pH	6.625
	Conductivity	78.4696 mS/cm
	Osmolality[1]	230 mOsm/kg H2O
	Endotoxin	< 0.6 EU/mL
2940 Citrate Buffer (Lot # 21-SO-0217)	pH	6.590
	Osmolality	293 mOsm/kg H2O
	Conductivity	17.717 mS/cm
	Endotoxin	< 0.2 EU/mL

[1] 1:10 dilution of 2940 Strip Buffer was used for Osmolality. The dilution was done with 50µl of stock Strip Buffer and 50µl of LAL water.

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Sample Name	Test Method #	Results (units)
2940 4M NaCl (Lot # 21-SO-0224)	Conductivity	224.1681 mS/cm
2940 1M NaOH (Lot # 21-SO-0218)	Conductivity	182.6852 mS/cm
2940 ADPS (Lot # 21-SO-0220)	pH	7.882
	Osmolality	306 m/kg H2O
	Conductivity	7.6013 mS/cm
	Endotoxin	0.1 EU/mL
	Bioburden	< 1 CFU/30mL (Total Count)

Performed by — Date: 24 Mar 23

Reviewed by — Date: 24MAR23